2011-08-30

pubmed Results

NOPHO publications

Items 1 -75 of 75

1. Eur J Haematol. 2011 Aug 20. doi: 10.1111/j.1600-0609.2011.01695.x. [Epub ahead of print]

Pneumocystis jiroveci pneumonia prophylaxis during maintenance therapy influences methotrexate/6-mercaptopurine dosing but not event-free survival for childhood acute lymphoblastic leukaemia.

Levinsen M, Shabaneh D, Bohnstedt C, Harila-Saari A, Jonsson OG, Kanerva J, Lindblom A, Lund B, Andersen EW, Schmiegelow K; for the Nordic Society of Paediatric Haematology and Oncology (NOPHO).

Source

Department of Pediatrics, The University Hospital Rigshospitalet, Copenhagen, Denmark Department of Pediatrics, University Hospital, Oulu, Finland Department of Pediatrics, University Hospital, Reykjavik, Iceland Department of Pediatrics Oncology, Children's Hospital, University of Helsinki, Helsinki University Central Hospital, Helsinki, Finland Center for Molecular Medicine, Karolinska Hospital, Stockholm, Sweden Department of Pediatrics, University Hospital, Trondheim, Norway Department for laboratory Medicine, Children's and Women's Health, Norwegian University of Science and Technology, Trondheim, Norway Department of Biostatistics, University of Copenhagen, Denmark The Institute of Gynaecology, Obstetrics, and Pediatrics, The Faculty of Medicine, University of Copenhagen, Denmark.

Abstract

Trimethoprim-sulfamethoxazole (TMP/SMX) is used in children with acute lymphoblastic leukaemia to prevent Pneumocystis pneumonia (PCP). We explored to which extent TMP/SMX influenced methotrexate (MTX)/6-mercaptopurine (6MP) dosage,

myelosuppression, and event-free survival during maintenance therapy. Of 447 study patients treated by the NOPHO ALL92 protocol, 120 patients received TMP/SMX continuously 2-7 days/week (TMP/SMX(2-7)) and 287 patients never received TMP/SMX (TMP/SMX(never)). Ten patients (all TMP/SMX(never)) developed PCP, 8 of which occurred within 7 months from the start of maintenance therapy. The TMP/SMX(2-7) group received lower oral 6MP doses than TMP/SMX(never) patients (50.6 vs. 63.9 mg/m(2) /day; P<0.001), but had lower absolute neutrophil counts (ANC) (median 1.7 vs. 2.0x10(9) /L; P<0.001). In Cox multivariate analysis, higher ANC levels (P=0.04) and male gender (P=0.06) were related to reduced event-free survival. ANC had no effect on event-free survival among TMP/SMX(2-7) patients (P=0.40), but did for TMP/SMX(never) patients (P=0.02). The difference in the effect on event-free survival between TMP/SMX(2-7) and TMP/SMX(never) patients was not significant (P=0.46). Event-free survival did not differ between TMP/SMX(2-7) and TMP/SMX(never) patients (0.83 vs. 0.83; P=0.82). These results suggest that TMP/SMX is effective in preventing PCP and may have an antileukaemic effect. TMP/SMX should be given the entire duration of maintenance therapy.

PMID:

21854453

[PubMed - as supplied by publisher]

Related citations

2. Br J Haematol. 2011 Aug 18. doi: 10.1111/j.1365-2141.2011.08835.x. [Epub ahead of print]

Individualized toxicity-titrated 6-mercaptopurine increments during high-dose methotrexate consolidation treatment of lower risk childhood acute lymphoblastic leukaemia. A Nordic Society of Paediatric Haematology and Oncology (NOPHO) pilot study.

Frandsen TL, Abrahamsson J, Lausen B, Vettenranta K, Heyman M, Behrentz M, Castor A, Wehner PS, Frost BM, Andersen EW, Schmiegelow K.

Source

Department of Paediatrics, Rigshospitalet, Copenhagen, Denmark Department of Paediatrics, Queen Silvias Childrens Hospital, Gothenburg, Sweden Dept of Paediatrics, University of Tampere, Finland Department of Paediatrics, University Hospitals, Astrid Lindgrens Barnsjukhus, Stockholm, Sweden Department of Paediatrics, University Hospital Linköping, Linköping , Sweden Department of Paediatrics, Lund University Hospital, Lund, Sweden Department of Paediatrics, Syddanmarks University Hospital, Odense, Denmark Department of Paediatrics, University Hospital of Uppsala, Uppsala, Sweden Department of Biostatistics, University of Copenhagen The Institute of Gynecology, Obstetrics and Paediatrics, The Faculty of Medicine, University of Copenhagen, Copenhagen, Denmark.

Abstract

0·03). This study shows individualized toxicity-titrated 6MP dosing during consolidation is feasible without increased risk of toxicity. = mg/m(2) per day had significantly shorter duration of treatment interruptions of 6MP than the remaining patients (P weeks after HDM. 6MP could be increased in 31 patients (81%). Toxicity was acceptable and did not differ significantly between groups. Patients receiving 75 mg 6MP/m(2) per day if they did not develop myelotoxicity within 2 mg/m(2) , ×3) in 38 patients with Childhood (ALL). Patients were increased in steps of 25 This study explored the feasibility and toxicity of individualized toxicity-titrated 6-mercaptopurine (6MP) dose increments during post-remission treatment with High-dose methotrexate (HDM) (5000

PMID:

21848519

[PubMed - as supplied by publisher]

Related citations

3. Mediterr J Hematol Infect Dis. 2011;3(1):e2011020. Epub 2011 May 16.

Epidemiology of therapy-related myeloid neoplasms after treatment for pediatric

acute lymphoblastic leukemia in the nordic countries.

Schmiegelow K.

Source

Faculty of Medicine, Institute of Gynecology, Obstetrics and Pediatrics, and the Department of Pediatrics, the University Hospital Rigshospitalet, Copenhagen, Denmark.

Abstract

Of 1614 Nordic children with ALL that were treated according to the NOPHO ALL92 protocol, 20 developed an SMN (cumulative risk at 12 years: 1.6%). Sixteen of the twenty SMNs were acute myeloid leukemias or myelodysplasias, and 9 of these had either monosomy 7 (n=7) or 7q deletions (n=2). In Cox multivariate analysis longer duration of oral MTX/6MP maintenance therapy (p=0.02; being longest for standard risk patients) and presence of high-hyperdiploidy (p=0.07) were related to an increased risk of SMN. In 524 patients we determined the erythrocyte activity of thiopurine methyltransferase (TPMT), which methylates 6MP and its metabolites, and thus reduces cellular levels of cytotoxic 6-thioguanine nucleotides. The TPMT activity was significantly lower in those that did compared to those that did not develop an SMN (Median: 12.1 vs 18.1 IU/ml; p=0.02). Among 427 TPMT wild type patients, those who developed SMN received higher 6MP doses than the remaining (69.7 vs 60.4 mg/m(2), p=0.03), which may reflect increased levels of methylated metabolites that inhibit purine de novo synthesis and thus enhance incorporation of 6-thioguanine nucleotides into DNA. In conclusion, the duration and intensity of 6MP/MTX maintenance therapy of childhood ALL may influence the risk of SMN.

PMCID: PMC3113279

Free PMC Article
PMID:

21713078

[PubMed]
Related citations

4. Pediatr Blood Cancer. 2011 Apr;56(4):551-9. doi: 10.1002/pbc.22719. Epub 2010 Dec 8.

Risk factors for treatment related mortality in childhood acute lymphoblastic leukaemia.

Lund B, Åsberg A, Heyman M, Kanerva J, Harila-Saari A, Hasle H, Söderhäll S, Jónsson ÓG, Lydersen S, Schmiegelow K; Nordic Society of Paediatric Haematology and Oncology.

Collaborators: Åsberg A, Harila-Saari A, Hasle H, Söderhäll S.

Source

Department of Pediatrics, St Olavs Hospital, Trondheim University Hospital, Trondheim, Norway. bendik.lund@ntnu.no

Abstract

BACKGROUND:

In spite of major improvements in the cure rate of childhood acute lymphoblastic leukaemia (ALL), 2-4% of patients still die from treatment related complications.

PROCEDURE:

We investigated the pattern of treatment related deaths (TRDs) and possible risk factors in the NOPHO ALL-92 and ALL-2000 protocols. Fifty-five TRDs were identified among the 1,645 ALL-92 patients and 33 among the 1,090 ALL-2000 patients.

RESULTS:

There was no significant difference in the incidence of TRDs between the two protocols (3.4% vs. 3.2%). Five patients died before initiation of therapy (0.2%), and the overall subsequent risk of induction death and death in first complete remission (CR1) was 1.2% and 1.8%, respectively. Infections were the major cause of death comprising 72% of all cases including 9 deaths from Pseudomonas aeruginosa and 11 deaths from fungal infections. Other causes of death included bleeding or thrombosis (eight patients), tumour burden related toxicities (seven patients) and organ toxicity (seven patients). Female gender (hazard ratio (HR): 2.2, 95% confidence interval (95% CI): 1.4-3.4), high white blood cell count ($\geq 200 \times 10(9)$ /L) at diagnosis (HR: 3.5, 95% CI: 1.7-7.1), T-cell disease (HR: 1.9, 95% CI: 1.01-3.7), Down syndrome (HR: 7.3, 95% CI: 3.6-14.9) and haematopoietic stem cell transplantation in CR1 (HR: 8.0, 95% CI: 3.3-19.5) were identified as independent risk factors for TRD.

CONCLUSION:

Several TRDs were potentially preventable and future efforts should be directed towards patients at risk.

PMID:

21298739

[PubMed - indexed for MEDLINE]
Related citations

5. Leukemia. 2011 Apr;25(4):622-8. Epub 2011 Jan 18.

The frequency and prognostic impact of dic(9;20)(p13.2;q11.2) in childhood B-cell precursor acute lymphoblastic leukemia: results from the NOPHO ALL-2000 trial.

Zachariadis V, Gauffin F, Kuchinskaya E, Heyman M, Schoumans J, Blennow E, Gustafsson B, Barbany G, Golovleva I, Ehrencrona H, Cavelier L, Palmqvist L, Lönnerholm G, Nordenskjöld M, Johansson B, Forestier E, Nordgren A; Nordic Society of Pediatric Hematology, Oncology (NOPHO); Swedish Cytogenetic Leukemia Study Group (SCLSG).

Source

Department of Molecular Medicine and Surgery, Karolinska Institutet, Stockholm, Sweden.

Abstract

The dic(9;20)(p13.2;q11.2) is reported to be present in □ 2% of childhood B-cell precursor acute lymphoblastic leukemia (BCP ALL). However, it easily escapes detection by G-banding analysis and its true prevalence is hence unknown. We performed interphase fluorescence in situ hybridization analyses-in a three-step manner-using probes for: (i) CDKN2A at 9p21, (ii) 20p and 20q subtelomeres and (iii) cen9 and cen20. Out of 1033 BCP ALLs diagnosed from 2001 to 2006, 533 were analyzed; 16% (84/533) displayed 9p21 deletions, of which 30% (25/84) had dic(9;20). Thus, dic(9;20)-positivity was found in 4.7% (25/533), making it the third most common genetic subgroup after high hyperdiploidy and t(12;21)(p13;q22). The

dic(9;20) was associated with a female predominance and an age peak at 3 years; 18/25 (72%) were allocated to non-standard risk treatment at diagnosis. Including cases detected by G-banding alone, 29 dic(9;20)-positive cases were treated according to the NOPHO ALL 2000 protocol. Relapses occurred in 24% (7/29) resulting in a 5-year event-free survival of 0.69, which was significantly worse than for t(12;21) (0.87; P=0.002) and high hyperdiploidy (0.82; P=0.04). We conclude that dic(9;20) is twice as common as previously surmised, with many cases going undetected by G-banding analysis, and that dic(9;20) should be considered a non-standard risk abnormality.

PMID:

21242996

[PubMed - indexed for MEDLINE]

Related citations

6. Br J Haematol. 2011 Mar;152(5):623-30. doi: 10.1111/j.1365-2141.2010.08554.x. Epub 2011 Jan 17.

Treatment-related deaths in second complete remission in childhood acute myeloid leukaemia.

Molgaard-Hansen L, Möttönen M, Glosli H, Jónmundsson GK, Abrahamsson J, Hasle H; Nordic Society of Paediatric Haematology and Oncology (NOPHO).

Collaborators: Rosthøj S, Østergaard E, Clausen N, Hasle H, Schrøder H, Schmiegelow K, Yssing M, Rechnitzer C, Lausen B, Carlsen N, Hejl M, Hovi L, Siimes MA, Vettenranta K, Pihkala U, Perkkiö M, Riikonen P, Mäkipernaa A, Arrola M, Parto K, Salmi T, Lanning M, Möttönen M, Jónmundsson G, Kristinsson J, Lie S, Glomstein A, Zeller B, Glosli H, Hellebostad M, Helgestad J, Moström B, Kolmannskog S, Nygaard R, Lund B, Stockland T, Flaegstad T, Mellander L, Abrahamsson J, Behrendtz M, Heldrup J, Garwicz S, Hjorth L, Gustafsson G, Soderhall S, Heyman M, Forestier E, Johansson K, Sandstrøm P, Kreuger A, Lönnerholm G, Frost BM, Palle J.

Source

Department of Paediatrics, Aarhus University Hospital Skejby, Aarhus, Denmark.

lene.molgaard@dadlnet.dk

Abstract

The frequency and causes of treatment-related deaths (TRD) in second complete remission (CR2) in acute myeloid leukaemia (AML) were investigated in a historical, prospective cohort study of 429 children included in the Nordic Society of Paediatric Haematology and Oncology (NOPHO)-AML-88 and -93 trials. Relapse occurred in 158 children (39%). Seventeen (18%) of the 96 patients entering CR2 suffered TRD. The main causes were infection (59%) and complications from graft-versus-host disease (22%). Fourteen (82%) of 17 TRDs occurred in children undergoing haematopoietic stem cell transplantations (HSCT). Optimal supportive care after HSCT is essential, and studies on risk factors for TRD are needed.

PMID:

21241281

[PubMed - indexed for MEDLINE]

Related citations

7. Br J Haematol. 2011 Mar;152(5):615-22. doi: 10.1111/j.1365-2141.2010.08532.x. Epub 2011 Jan 17.

Interphase fluorescent in situ hybridization deletion analysis of the 9p21 region and prognosis in childhood acute lymphoblastic leukaemia (ALL): results from a prospective analysis of 519 Nordic patients treated according to the NOPHO-ALL 2000 protocol.

Kuchinskaya E, Heyman M, Nordgren A, Söderhäll S, Forestier E, Wehner P, Vettenranta K,

Jonsson O, Wesenberg F, Sahlén S, Nordenskjöld M, Blennow E.

Source

Centre of Molecular Medicine and Department of Molecular Medicine and Surgery, Karolinska University Hospital Solna, Karolinska Institutet, Stockholm, Sweden.
ekaterina.kuchinskaya@lio.se

Abstract

Interphase fluorescent in situ hybridization (FISH) was applied on diagnostic BM smears from 519 children with acute lymphoblastic leukaemia (ALL) in order to establish the frequency and prognostic importance of 9p21 deletion in children enrolled in the Nordic Society of Paediatric Haematology and Oncology (NOPHO) - 2000 treatment protocol. Among the patients, 452 were diagnosed with B-cell precursor (BCP)-ALL and 66 with T-ALL. A higher incidence of 9p21 deletions was found in T-ALL (38%) compared to BCP-ALL (15·7%). Homozygous deletions were found in 19·7% of T-ALL and 4·0% of BCP-ALL; hemizygous deletions were found in 18·2% and 11·7% respectively. In our series, 9p21 deletions were detected in all age groups with a steady rise in the frequency with age. There was no significant difference in outcome between cases with or without 9p21 deletion or between cases with hemi- or homozygous deletions of 9p21. In conclusion, in this large series of childhood ALL deletion of 9p21 was not associated with worse prognosis. However, interphase FISH deletion analysis of 9p21 could be used as a first step to detect unfavourable subtle cytogenetic aberrations such as the dic(9;20) rearrangement.

PMID:

21241277

[PubMed - indexed for MEDLINE]

Related citations

8. Pediatr Blood Cancer. 2010 Dec 22. [Epub ahead of print]

Quality of health in survivors of childhood acute myeloid leukemia treated with

chemotherapy only: A NOPHO-AML study.

Molgaard-Hansen L, Glosli H, Jahnukainen K, Jarfelt M, Jónmundsson GK, Malmros-Svennilson J, Nysom K, Hasle H; On behalf of the Nordic Society of Pediatric Hematology and Oncology (NOPHO).

Source

Department of Pediatrics, Aarhus University Hospital Skejby, Aarhus, Denmark.

Abstract

BACKGROUND:

More than 60% of children with acute myeloid leukemia (AML) become long-term survivors, and approximately 50% are cured with chemotherapy only. Limited data exist about their long-term morbidity and social outcomes. The aim of the study was to compare the self-reported use of health care services, health experience, social outcomes, and lifestyle behavior of AML survivors with that of their sibling controls.

METHODS:

This population-based study included 138 children treated for AML according to the Nordic Society of Pediatric Hematology and Oncology (NOPHO)-AML-84, -88, and -93 trials, and alive by June 30, 2007. Patients treated with hematopoietic stem cell transplantation (HSCT) or relapse were not included. Altogether, 102 (74%) survivors and 91% of their siblings completed a questionnaire.

RESULTS:

The median follow-up was 11 (range 4-25) years after diagnosis. AML survivors had no increased rate of hospitalization compared with sibling controls, but were more often receiving prescription drugs, especially for asthma (23% vs. 9%, P = 0.03). Self-reported health experience was excellent or very good in 77% and comparable with that of siblings. Educational achievement, employment, and marital status were comparable in the two groups. Among surviving AML patients, 23% were current smokers and 24% of their siblings were current smokers.

CONCLUSIONS:

The self-reported health of children treated on NOPHO-AML protocols without HSCT was good, and their use of health care services was limited. Reported health and social outcomes were comparable to those of their siblings. Many survivors were smoking which may increase the risk of late effects. Pediatr Blood Cancer © 2010 Wiley-Liss, Inc.

PMID:

21181875

[PubMed - as supplied by publisher]
Related citations

9. Pediatr Blood Cancer. 2010 Dec 8. [Epub ahead of print]

Risk factors for treatment related mortality in childhood acute lymphoblastic leukaemia.

Lund B, Asberg A, Heyman M, Kanerva J, Harila-Saari A, Hasle H, Söderhäll S, Jónsson OG, Lydersen S, Schmiegelow K; On behalf of the Nordic Society of Paediatric Haematology and Oncology (NOPHO).

Source

Department of Pediatrics, St. Olavs Hospital, Trondheim University Hospital, Trondheim, Norway.

Abstract

BACKGROUND:

In spite of major improvements in the cure rate of childhood acute lymphoblastic leukaemia (ALL), 2-4% of patients still die from treatment related complications.

PROCEDURE:

We investigated the pattern of treatment related deaths (TRDs) and possible risk factors in the NOPHO ALL-92 and ALL-2000 protocols. Fifty-five TRDs were identified among the 1,645 ALL-92 patients and 33 among the 1,090 ALL-2000 patients.

RESULTS:

There was no significant difference in the incidence of TRDs between the two protocols (3.4% vs. 3.2%). Five patients died before initiation of therapy (0.2%), and the overall subsequent risk of induction death and death in first complete remission (CR1) was 1.2% and 1.8%,

respectively. Infections were the major cause of death comprising 72% of all cases including 9 deaths from Pseudomonas aeruginosa and 11 deaths from fungal infections. Other causes of death included bleeding or thrombosis (eight patients), tumour burden related toxicities (seven patients) and organ toxicity (seven patients). Female gender (hazard ratio (HR): 2.2, 95% confidence interval (95% CI): 1.4-3.4), high white blood cell count (≥200 × 10(9)/L) at diagnosis (HR: 3.5, 95% CI: 1.7-7.1), T-cell disease (HR: 1.9, 95% CI: 1.01-3.7), Down syndrome (HR: 7.3, 95% CI: 3.6-14.9) and haematopoietic stem cell transplantation in CR1 (HR: 8.0, 95% CI: 3.3-19.5) were identified as independent risk factors for TRD.

CONCLUSION:

Several TRDs were potentially preventable and future efforts should be directed towards patients at risk. Pediatr Blood Cancer.

PMID:

21154447

[PubMed - as supplied by publisher]

Related citations

10. J Clin Oncol. 2011 Jan 20;29(3):310-5. Epub 2010 Dec 13.

Response-guided induction therapy in pediatric acute myeloid leukemia with excellent remission rate.

Abrahamsson J, Forestier E, Heldrup J, Jahnukainen K, Jónsson OG, Lausen B, Palle J, Zeller B, Hasle H.

Source

Institution of Clinical Sciences, Department of Pediatrics, Sahlgrenska University Hospital, 41685 Gothenburg, Sweden. jonas.abrahamsson@vgregion.se

Abstract

PURPOSE:

To evaluate the early treatment response in children with acute myeloid leukemia (AML) using a response-guided induction strategy that includes idarubicin in the first course.

PATIENTS AND METHODS:

All Nordic children with AML younger than 15 years (n = 151) were treated on the Nordic Society for Pediatric Hematology and Oncology (NOPHO) AML 2004 protocol. After the first course of idarubicin, cytarabine, etoposide, and 6-thioguanin, patients with good response were allowed hematologic recovery before the second course, whereas patients with a poor (≥ 15% blasts) or intermediate (5% to 14.9% blasts) were recommended to proceed immediately with therapy. Patients not in remission after the second course received fludarabine, cytarabine, and granulocyte colony-stimulating factor. Poor responders received allogeneic stem-cell transplantation (SCT) as consolidation.

RESULTS:

Seventy-four percent of patients had good response, 17% had intermediate response, and 7% had poor response after the first course. The overall remission frequency was 97.4%, with 92% in remission after the second course. The rate of induction death was 1.3%. Patients with an intermediate response had a lower event-free survival of 35% compared with good (61%) and poor responders (82%).

CONCLUSION:

The NOPHO-AML 2004 induction strategy gives an excellent remission rate with low toxic mortality in an unselected population. Outcome is worse in patients with intermediate response but may be improved by intensifying consolidation in this group using SCT.

PMID:

21149663

[PubMed - indexed for MEDLINE]

Related citations

11. Eur J Haematol. 2011 Jan;86(1):38-46. doi: 10.1111/j.1600-0609.2010.01522.x. Epub 2010 Nov 15.

High white blood cell count at diagnosis of childhood acute lymphoblastic leukaemia:

biological background and prognostic impact. Results from the NOPHO ALL-92 and ALL-2000 studies.

Vaitkevičienė G, Forestier E, Hellebostad M, Heyman M, Jonsson OG, Lähteenmäki PM, Rosthoej S, Söderhäll S, Schmiegelow K; Nordic Society of Paediatric Haematology and Oncology (NOPHO).

Source

Centre for Paediatric Oncology and Haematology, University Childrens Hospital, Vilnius, Lithuania.

Abstract

Prognostic impact of peripheral blood white blood cell count (WBC) at the diagnosis of childhood acute lymphoblastic leukaemia (ALL) was evaluated in a population-based consecutive series of 2666 children aged 1-15 treated for ALL between 1992 and 2008 in the five Nordic countries (Denmark, Finland, Iceland, Norway and Sweden). Ten-year event-free (pEFS(10 y)) survival and overall (pOS(10 y)) survival were 0.75 ± 0.01 and 0.85 ± 0.01, respectively. Although treatment intensity was determined by WBC, non-remission and relapsed patients still had significantly higher WBC than those in remission for B-cell precursor (BCP) (median WBC: 24.8 vs. 14.0 vs. 8.3 × 10(9) /L, P < 0.001), but not for T-lineage (T-ALL) (median WBC: 127.8 vs. 113.0 vs. 86.8 × 10(9) /L, P = 0.22). pEFS was inversely related to WBC for BCP (P < 0.001), but not for T-ALL. WBC was not associated with risk of event for BCP or T-ALL for patients with minimal residual disease at the end of induction (MRD(d29)) <10(-3). In contrast, for MRD(d29) ≥ 10(-3) and <5% leukaemic blasts in bone marrow at day 29, the pEFS(5 y) for WBC < 100.0 (N = 152) vs. ≥ 100.0 (N = 19) was 0.76 vs. 0.50 (P = 0.001). That was the case both for BCP (pEFS(5 y) 0.76 vs. 0.58) and for T-ALL (pEFS(5 y) 0.71 vs. 0.38). Whether the inferior EFS for the subset of patients with high WBC and slow initial response to treatment reflects rare or overlooked cytogenetic aberrations as well as the factors that determine WBC levels at diagnosis awaits exploration.

PMID:

21077959

[PubMed - indexed for MEDLINE]

Related citations

12. Br J Haematol. 2010 Dec;151(5):447-59. doi: 10.1111/j.1365-2141.2010.08389.x. Epub 2010 Oct 19.

Early and treatment-related deaths in childhood acute myeloid leukaemia in the Nordic countries: 1984-2003.

Molgaard-Hansen L, Möttönen M, Glosli H, Jónmundsson GK, Abrahamsson J, Hasle H; Nordic Society of Paediatric Haematology and Oncology (NOPHO).

Collaborators: Rosthøj S, Oestergaard E, Clausen N, Hasle H, Schroeder H, Schmiegelow M, Yssing M, Rechnitzer C, Lausen B, Carlsen N, Hejl M, Hovi L, Siimes MA, Vettenranta K, Pihkala U, Perkkiö M, Riikonen P, Mäkipernaa A, Arrola M, Parto K, Salmi T, Lanning M, Möttönen M, Jónmundsson G, Kristinsson J, Lie S, Glomstein A, Zeller B, Glosli H, Hellebostad M, Helgestad J, Moström B, Kolmannskog S, Nygaard R, Stockland T, Flaegstad T, Mellander L, Abrahamsson J, Behrendtz M, Heldrup J, Garwicz S, Hjorth L, Gustafsson G, Soderhall S, Heyman M, Forestier E, Johansson K, Sandström P, Kreuger A, Lönnerholm G, Frost BM, Palle J.

Source

Department of Paediatrics, Aarhus University Hospital Skejby, Aarhus, Denmark. lene.molgaard@dadlnet.dk

Abstract

Despite major improvements in the cure rate of childhood acute myeloid leukaemia (AML), 5-15% of patients still die from treatment-related complications. In a historical prospective cohort study, we analysed the frequency, clinical features and risk factors for early deaths (ED) and treatment-related deaths (TRD) in 525 children included in the Nordic Society of Paediatric Haematology and Oncology (NOPHO)-AML-84, -88 and -93 trials. Seventy patients (13%) died before starting treatment or from treatment-related complications. The death rate rose from 11% in NOPHO-AML-84 to 29% in -88, but then fell to 8% in -93. Sixteen patients (3%) died within the first 2 weeks, mainly from bleeding or leucostasis. Hyperleucocytosis, age <2 or ≥10 years were risk factors. After day 15, 10% of patients died from treatment-related complications with infection as the main cause of death. Risk factors were age <2 or ≥10 years and treatment according to the NOPHO-AML-88 protocol. The number of EDs and TRDs in AML is high. Therefore optimal antifungal prophylaxis is essential, and studies on the benefit of antibacterial prophylaxis and individual risk factors for ED and TRD are needed.

PMID:

20955398

[PubMed - indexed for MEDLINE]
Related citations

13. Leukemia. 2010 Apr;24(4):715-20. Epub 2010 Feb 4.

The degree of myelosuppression during maintenance therapy of adolescents with B-lineage intermediate risk acute lymphoblastic leukemia predicts risk of relapse.

Schmiegelow K, Heyman M, Gustafsson G, Lausen B, Wesenberg F, Kristinsson J, Vettenranta K, Schroeder H, Forestier E, Rosthoej S; Nordic Society of Paediatric Haematology and Oncology (NOPHO).

Source

Department of Pediatric Oncology, The University Hospital Rigshospitalet, Copenhagen, Denmark. kschmiegelow@rh.dk

Abstract

Drug doses, blood levels of drug metabolites and myelotoxicity during 6-mercaptopurine/methotrexate (MTX) maintenance therapy were registered for 59 adolescents (>or=10 years) and 176 non-adolescents (<10 years) with B-cell precursor acute lymphoblastic leukemia (ALL) and a white blood cell count (WBC) <50 x 10(9)/l at diagnosis. Event-free survival was lower for adolescents than non-adolescents (pEFS(12y):0.71 vs 0.83, P=0.04). For adolescents staying in remission, the mean WBC during maintenance therapy (mWBC) was related to age (r(S)=0.36, P=0.02), which became nonsignificant for those who relapsed (r(S)=0.05, P=0.9). The best-fit multivariate Cox regression model to predict risk of relapse included mWBC and thiopurine methyltransferase

activity, which methylates mercaptopurine and reduces the intracellular availability of cytotoxic 6-thioguanine nucleotides (coefficient: 0.11, P=0.02). The correlation of mWBC to the risk of relapse was more pronounced for adolescents (coefficient=0.65, P=0.003) than for non-adolescents (coefficient=0.42, P=0.04). Adolescents had higher mean neutrophil counts (P=0.002) than non-adolescents, but received nonsignificantly lower mercaptopurine and MTX doses during maintenance therapy. Red blood cell MTX levels were significantly related to the dose of MTX among adolescents who stayed in remission (r(S)=0.38, P=0.02), which was not the case for those who developed a relapse (r(S)=0.15, P=0.60). Thus, compliance to maintenance therapy may influence the risk of relapse for adolescents with ALL.

PMID:

20130603

[PubMed - indexed for MEDLINE]

Related citations

14. J Cancer Surviv. 2010 Jun;4(2):110-8. Epub 2010 Jan 16.

Social outcomes in young adult survivors of low incidence childhood cancers.

Jóhannsdóttir IM, Hjermstad MJ, Moum T, Wesenberg F, Hjorth L, Schrøder H, Lähteenmäki P, Jónmundsson G, Loge JH.

Source

National Resource Centre for Studies of Long-term Effects after Cancer, Department of Clinical Cancer Research, Oslo University Hospital, Montebello, Oslo, Norway. i.m.johannsdottir@medisin.uio.no

Abstract

INTRODUCTION:

The intensity and duration of childhood cancer treatment may disrupt psychosocial development and thereby cause difficulties in transition into adulthood. The study objective was to assess social outcomes in early adulthood after successful treatment for childhood

acute myeloid leukemia (AML), Wilms tumor (WT) and infratentorial astrocytoma (IA).

METHODS:

Nordic patients treated for AML, WT and IA from 1985 to 2001 identified from a database administered by NOPHO (Nordic Society of Paediatric Haematology and Oncology) were invited to participate in a postal survey. All cancer-free survivors treated at age >1 year who were >19 years at time of study were eligible. Seventy-four percent; 247/335 responded. An age-equivalent group (N = 1,814) from a Norwegian Census Study served as controls.

RESULTS:

Mean age of survivors was 23 years (range 19-34), 55% females. The proportion with academic education (>/=4 years) was similar in survivors and controls (28 vs. 32%). Fifty-nine percent of survivors were employed compared to 77% among controls ($p < .01$). More survivors were recipients of social benefits (6.7 vs. 3.1%, $p < .01$). There were no differences in marital status but parenthood was more common among controls (37 vs. 27%, $p = .01$). Controls lived longer in their parental homes ($p = .01$). Cancer type or treatment intensity had no statistically significant impact on results, except for parenthood. CONCLUSIONS AND IMPLICATIONS FOR CANCER SURVIVORS: The study revealed important differences in social outcomes between survivors and controls early in adult life. Specific difficulties pertain to studying social status in early adulthood because of the natural transition characteristics for this age group. Therefore, longer follow-up is warranted.

PMID:

20082150

[PubMed - indexed for MEDLINE]

Related citations

15. Leukemia. 2010 Feb;24(2):345-54. Epub 2009 Dec 10.

Long-term results of NOPHO ALL-92 and ALL-2000 studies of childhood acute lymphoblastic leukemia.

Schmiegelow K, Forestier E, Hellebostad M, Heyman M, Kristinsson J, Söderhäll S,

Taskinen M; Nordic Society of Paediatric Haematology and Oncology.

Source

Faculty of Medicine, The Institute of Gynaecology, Obstetrics, and Paediatrics, University of Copenhagen, Copenhagen, Denmark. kschmiegelow@rh.dk

Erratum in

- Leukemia. 2010 Mar;24(3):670.

Abstract

Analysis of 2668 children with acute lymphoblastic leukemia (ALL) treated in two successive Nordic clinical trials (Nordic Society of Paediatric Haematology and Oncology (NOPHO) ALL-92 and ALL-2000) showed that 75% of all patients are cured by first-line therapy, and 83% are long-term survivors. Improvements in systemic and intrathecal chemotherapy have reduced the use of central nervous system (CNS) irradiation to <10% of the patients and provided a 5-year risk of isolated CNS relapse of 2.6%. Improved risk stratification and chemotherapy have eliminated the previous independent prognostic significance of gender, CNS leukemia and translocation t(1;19)(q23;p13), whereas the post-induction level of minimal residual disease (MRD) has emerged as a new risk grouping feature. Infant leukemia, high leukocyte count, T-lineage immunophenotype, translocation t(4;11)(q21;q23) and hypodiploidy persist to be associated with lower cure rates. To reduce the overall toxicity of the treatment, including the risk of therapy-related second malignant neoplasms, the current NOPHO ALL-2008 protocol does not include CNS irradiation in first remission, the dose of 6-mercaptopurine is reduced for patients with low thiopurine methyltransferase activity, and the protocol restricts the use of hematopoietic stem cell transplantation in first remission to patients without morphological remission after induction therapy or with high levels of MRD after 3 months of therapy.

PMID:

20010622

[PubMed - indexed for MEDLINE]

Related citations

16. Eur J Haematol. 2010 Feb 1;84(2):117-27. Epub 2009 Nov 6.

Applicability of IG/TCR gene

rearrangements as targets for minimal residual disease assessment in a population-based cohort of Swedish childhood acute lymphoblastic leukaemia diagnosed 2002-2006.

Thörn I, Forestier E, Thuresson B, Wasslavik C, Malec M, Li A, Lindström-Eriksson E, Botling J, Barbany G, Jacobsson S, Olofsson T, Porwit A, Sundström C, Rosenquist R.

Source

Department of Genetics and Pathology, Rudbeck Laboratory, Uppsala University, Uppsala, Sweden.

Abstract

Minimal residual disease (MRD) detection during the early treatment phase has become an important stratification parameter in many childhood acute lymphoblastic leukaemia (ALL) treatment protocols. Here, we aimed to address the applicability of rearranged antigen-receptor genes as potential MRD markers using real-time quantitative polymerase chain reaction (RQ-PCR) in a Swedish population-based cohort. From 334 childhood ALL cases diagnosed during 2002-2006, we analysed 279 diagnostic samples (84%) by screening for rearranged immunoglobulin (IG) and T-cell receptor (TCR) genes. Allele-specific oligonucleotides were designed, and the sensitivity and quantitative level was determined for each target. Overall, clonal IG/TCR rearrangements were detected in 97% (236/244) of B-cell precursor ALL (BCP ALL) and 94% (33/35) of T-ALL. A sensitive RQ-PCR analysis (< or = 10(-4)) was obtained in 89% (216/244) of BCP ALL and in 74% (26/35) of T-ALL, whereas two sensitive targets were only available in 47% (115/244) of BCP ALL and 29% (10/35) of T-ALL cases. With the stratification threshold of > or = 10(-3), which is applied in the current Nordic treatment protocol (NOPHO-ALL 2008) for the identification of high-risk patients, 93% of BCP ALL and 86% of T-ALL reached this quantitative range by at least one target gene. Taken together, this national retrospective study demonstrates that an IG/TCR target for MRD monitoring can be identified in the majority of childhood ALL cases, whereas identification of a second sensitive target gene needs to be improved.

PMID:

19895569

[PubMed - indexed for MEDLINE]

Related citations

17. J Pediatr Hematol Oncol. 2009 Jun;31(6):406-15.

Quality control of flow cytometry data analysis for evaluation of minimal residual disease in bone marrow from acute leukemia patients during treatment.

Björklund E, Matinlauri I, Tierens A, Axelsson S, Forestier E, Jacobsson S, Ahlberg AJ, Kauric G, Mäntymaa P, Osnes L, Penttilä TL, Marquart H, Savolainen ER, Siitonen S, Torikka K, Mazur J, Porwit A.

Source

Department of Pathology and Cytology, Karolinska University Hospital, Solna, Karolinska Institute, Stockholm SE 171 76, Sweden. elisabet.bjorklund@karolinska.se

Abstract

Low levels of leukemia cells in the bone marrow, minimal residual disease (MRD), are considered to be a powerful indicator of treatment response in acute lymphatic leukemia (ALL). A Nordic quality assurance program, aimed on standardization of the flow cytometry MRD analysis, has been established before implementation of MRD at cutoff level 10 as one of stratifying parameters in next Nordic Society of Pediatric Hematology and Oncology (NOPHO) treatment program for ALL. In 4 quality control (QC) rounds 15 laboratories determined the MRD levels in 48 follow-up samples from 12 ALL patients treated according to NOPHO 2000. Analysis procedures were standardized. For each QC round a compact disc containing data in list-mode files was sent out and results were submitted to a central laboratory. At cutoff level 10, which will be applied for clinical decisions, laboratories obtained a high concordance (91.6%). If cutoff level 10 was applied, the concordance would be lower (85.3%). The continuing standardization resulted in better concordance in QC3 and QC4 compared with QC1 and QC2. The concordance was higher in precursor B as compared with T-cell ALL. We conclude that after standardization, flow cytometry MRD detection can be reliably applied in international, multicenter treatment protocols.

PMID:

19648789

[PubMed - indexed for MEDLINE]
Related citations

18. J Pediatr Hematol Oncol. 2009 Jun;31(6):385-92.

Oral methotrexate/6-mercaptopurine may be superior to a multidrug LSA2L2 Maintenance therapy for higher risk childhood acute lymphoblastic leukemia: results from the NOPHO ALL-92 study.

Schmiegelow K, Heyman M, Kristinsson J, Mogensen UB, Rosthøj S, Vettenranta K, Wesenberg F, Saarinen-Pihkala U; Nordic Society of Paediatric Haematology and Oncology (NOPHO).

Source

Institute of Gynecology, Obstetrics, and Pediatrics, Department of Pediatrics, University Hospitals, Rigshospitalet Copenhagen, Denmark. kschmiegelow@rh.dk

Comment in

- J Pediatr Hematol Oncol. 2009 Jun;31(6):383-4.

Abstract

The importance of maintenance therapy for higher risk childhood acute lymphoblastic leukemia (ALL) is uncertain. Between 1992 and 2001 the Nordic Society for Pediatric Haematology/Oncology compared in a nonrandomized study conventional oral methotrexate (MTX)/6-mercaptopurine (6MP) maintenance therapy with a multidrug cyclic LSA2L2 regimen. 135 children with B-lineage ALL and a white blood count > or =50 x 10/L and 98 children with T-lineage ALL were included. Of the 234 patients, the 135 patients who received MTX/6MP maintenance therapy had a lower relapse risk than the 98 patients who received LSA2L2 maintenance therapy, which was the case for both B-lineage (27%+/-5% vs. 45%+/-9%; P=0.02) and T-lineage ALL (8%+/-5% vs. 21%+/-5%; P=0.12). In multivariate Cox regression analysis stratified for immune phenotype, a higher white blood

count (P=0.01) and administration of LSA2L2 maintenance therapy (P=0.04) were both related to an increased risk of an event (overall P value of the Cox model: 0.003), whereas neither sex, age at diagnosis, administration of central nervous system irradiation, nor presence of a day 15 bone marrow with > or =25% versus <25% lymphoblasts were of statistical significance. These results indicate that oral MTX/6MP maintenance therapy administered after the first year of remission can improve the cure rates of children with T-lineage or with higher risk B-lineage ALL.

PMID:

19648786

[PubMed - indexed for MEDLINE]

Related citations

19. Genes Chromosomes Cancer. 2009 Sep;48(9):795-805.

Clinical and cytogenetic features of a population-based consecutive series of 285 pediatric T-cell acute lymphoblastic leukemias: rare T-cell receptor gene rearrangements are associated with poor outcome.

Karrman K, Forestier E, Heyman M, Andersen MK, Autio K, Blennow E, Borgström G, Ehrencrona H, Golovleva I, Heim S, Heinonen K, Hovland R, Johannsson JH, Kerndrup G, Nordgren A, Palmqvist L, Johansson B; Nordic Society of Pediatric Hematology, Oncology (NOPHO); Swedish Cytogenetic Leukemia Study Group (SCLSG); NOPHO Leukemia Cytogenetic Study Group (NLCSG).

Source

Department of Clinical Genetics, Lund University Hospital, Lund, Sweden. kristina.karrman@med.lu.se

Abstract

Clinical characteristics and cytogenetic aberrations were ascertained and reviewed in a population-based consecutive series of 285 pediatric T-cell acute lymphoblastic leukemias (T-ALLs) diagnosed between 1992 and 2006 in the Nordic countries. Informative karyotypic results were obtained in 249 (87%) cases, of which 119 (48%) were cytogenetically abnormal. Most (62%) of the aberrant T-ALLs were pseudodiploid. Structural changes were more common than numerical ones; 86% displayed at least one structural abnormality and 41% at least one numerical anomaly. The most frequent abnormalities were T-cell receptor (TCR) gene rearrangements (20%) [TCR;11p13 (10%), TCR;10q24 (3%), TCR;other (8%)], del(9p) (17%), +8 (14%), del(6q) (12%), and 11q23 rearrangements (6%). The TCR;other group comprised the rare rearrangements t(X;14)(p11;q11), t(X;7)(q22;q34), t(1;14)(p32;q11), ins(14;5)(q11;q?q?), inv(7)(p15q34), t(8;14)(q24;q11), t(7;11)(q34;p15), and t(12;14)(p13;q11). The clinical characteristics of this Nordic patient cohort agreed well with previous larger series, with a median age of 9.0 years, male predominance (male/female ratio 3.1), median white blood cell (WBC) count of 66.5 x 10(9)/l, and a high incidence of mediastinal mass and central nervous system involvement (59% and 9.5%, respectively). These features did not differ significantly among the various genetic subgroups. 5-year event-free survival (EFS) and overall survival for all patients were 0.61 (+/-0.03) and 0.67 (+/-0.03), respectively. In a multivariate analysis, two factors affected negatively the EFS, namely a WBC count of > or =200 x 10(9)/l ($P < 0.001$) and the presence of rare TCR rearrangements ($P = 0.001$). In conclusion, in this large series of childhood T-ALLs from the Nordic countries, the cytogenetic findings were not associated with risk of therapy failure with the exception of the TCR;other group. However, further prospective and collaborative investigations of this genetically heterogeneous entity are needed to confirm these results.

PMID:

19530250

[PubMed - indexed for MEDLINE]

Related citations

20. Blood. 2009 Jun 11;113(24):6077-84. Epub 2009 Feb 17.

Methotrexate/6-mercaptopurine maintenance therapy influences the risk of a second malignant neoplasm after

childhood acute lymphoblastic leukemia: results from the NOPHO ALL-92 study.

Schmiegelow K, Al-Modhwahi I, Andersen MK, Behrendtz M, Forestier E, Hasle H, Heyman M, Kristinsson J, Nersting J, Nygaard R, Svendsen AL, Vettenranta K, Weinshilboum R; Nordic Society for Paediatric Haematology and Oncology.

Collaborators: Schmiegelow K, Hejl M, Østergård M, Schrøder H, Pihkala U, Ilanmaa E, Antila K, Korpela K, Vuorinen O, Perkkiö M, Kojo N, Nyman R, Pere M, Lanning M, Niemi A, Vuoristo A, Niemi S, Isotalo J, Laapas H, Mäkipernaa A, Salmi T, Varsamäki T, Kristinsson J, Zeller B, Danielsen O, Madsen B, Nielsen B, Stensvold K, Lund JH, Danielsen K, Brekke P, Stamnes O, Glomstein A, Widing E, Hapnes C, Stokland T, Kolmannskog S, Halvorsen B, Spangen S, Carlsson G, Bergkvist M, Skanka N, Korlén B, Dimberg A, Adrian BA, Mellander L, Aronson S, Jensen D, Winiarski J, Lagerwall A, Jonsson NO, Cervin T, Samuelsson U, Berg A, Nilsson H, Behrendtz M, Wiebe T, Ljung R, Tessin I, Ljungren CG, Dohlwitz A, Christensen HO, Ronge E, Berglund M, Björk O, Fransson D, Eriksson M, Forestier E, Kreuger A, Blomgren M, Rönnblad B, Eriksson B, Berg T, Hedling L, Forsberg T, Lindquist B, Kristrom B, Hjalmars U.

Source

Faculty of Medicine, Institute of Gynecology, Obstetrics, and Pediatrics, University of Copenhagen, Copenhagen, Denmark. kschmiegelow@rh.dk

Comment in

- Blood. 2009 Jun 11;113(24):6258; author reply 6258-9.
- Blood. 2009 Jun 11;113(24):6041-2.

Abstract

Among 1614 children with acute lymphoblastic leukemia (ALL) treated with the Nordic Society for Paediatric Haematology and Oncology (NOPHO) ALL-92 protocol, 20 patients developed a second malignant neoplasm (SMN) with a cumulative risk of 1.6% at 12 years from the diagnosis of ALL. Nine of the 16 acute myeloid leukemias or myelodysplastic syndromes had monosomy 7 (n = 7) or 7q deletions (n = 2). In Cox multivariate analysis, longer duration of oral 6-mercaptopurine (6MP)/methotrexate (MTX) maintenance therapy (P = .02; longest for standard-risk patients) and presence of high hyperdiploidy (P = .07) were related to increased risk of SMN. Thiopurine methyltransferase (TPMT) methylates 6MP and its metabolites, and thus reduces cellular levels of cytotoxic 6-thioguanine nucleotides. Of 524 patients who had erythrocyte TPMT activity measured, the median TPMT activity in 9 patients developing an SMN was significantly lower than in the 515 that did not develop an SMN (median, 12.1 vs 18.1 IU/mL; P = .02). Among 427 TPMT wild-type patients for whom the 6MP dose was registered, those who developed SMN received higher average 6MP doses

than the remaining patients (69.7 vs 60.4 mg/m2; P = .03). This study indicates that the duration and intensity of 6MP/MTX maintenance therapy of childhood ALL may influence the risk of SMNs in childhood ALL.

PMCID: PMC2699230

Free PMC Article
PMID:

19224761

[PubMed - indexed for MEDLINE]
Related citations

21. Pediatr Blood Cancer. 2009 Apr;52(4):491-6.

Demographic data, natural history, and prognostic factors of idiopathic thrombocytopenic purpura in children: a multicentered study from Argentina.

Donato H, Picón A, Martinez M, Rapetti MC, Rosso A, Gomez S, Rossi N, Bacciedoni V, Schvartzman G, Riccheri C, Costa A, Di Santo J.

Source

Consultorios de Hematología Infantil, Buenos Aires, Argentina. hugodonato@aol.com

Abstract

BACKGROUND:

Demographics, outcome, and management of idiopathic thrombocytopenic purpura (ITP) in children present differences between countries. Although several factors influence outcome, it is impossible to predict at diagnosis which patients will have acute or chronic disease. High rates of spontaneous remission in chronic ITP have been reported.

PROCEDURE:

Data concerning 1,683 patients with ITP diagnosed from 1981 to date are presented; outcome was evaluated in 1,418 children.

RESULTS:

Remarkable presenting features were an incidence peak in the first 2 years of age and male predominance in patients <24 months of age. Three age groups with different recovery rates ($P < 0.001$) were established (2-12 months: 89.8%; 1-8 years: 71.3%; 9-18 years: 49.0%). Platelet count <10 x 10(9)/L and history of previous illness were associated with higher remission rates only in patients >12 months of age. The score developed by the NOPHO Group showed a predictive value of 83.9% for acute ITP. Spontaneous remission between 6 months and 11 years from diagnosis was achieved by 107 of 325 (32.9%) non-splenectomized children with chronic ITP, and in 44.9% of them between 6 and 12 months from diagnosis.

CONCLUSIONS:

Age and score were main prognostic factors. Infants <1 year of age are a special group with a brief course and very high recovery rate that are not influenced by other prognostic factors. Definition of groups based on age and scoring could be useful to establish differential management guidelines. The cut-off value to define chronic ITP should be changed to 12 months.

PMID:

19058214

[PubMed - indexed for MEDLINE]
Related citations

22. Leukemia. 2009 Mar;23(3):557-64. Epub 2008 Nov 6.

Thiopurine methyltransferase activity is related to the risk of relapse of childhood acute lymphoblastic leukemia: results from

the NOPHO ALL-92 study.

Schmiegelow K, Forestier E, Kristinsson J, Söderhäll S, Vettenranta K, Weinshilboum R, Wesenberg F; Nordic Society of Paediatric Haematology and Oncology.

Source

The Institute of Gynecology, Obstetrics, and Pediatrics, The Faculty of Medicine, University of Copenhagen, Copenhagen, Denmark. kschmiegelow@rh.dk

Abstract

Myelotoxicity during thiopurine therapy is enhanced in patients, who because of single nucleotide polymorphisms have decreased activity of the enzyme thiopurine methyltransferase (TPMT) and thus more thiopurine converted into 6-thioguanine nucleotides. Of 601 children with acute lymphoblastic leukemia (ALL) who were treated by the NOPHO ALL-92 protocol, 117 had TPMT genotype determined, whereas for 484 patients only erythrocyte TPMT activity was available. The latter were classified as heterozygous, if TPMT activity was <14 IU/ml, or deficient (<1.0 IU/ml). 526 patients had TPMT wild type, 73 were presumed heterozygous, and two were TPMT deficient. Risk of relapse was higher for the 526 TPMT wild type patients than for the remaining 75 patients (18 vs 7%, P=0.03). In Cox multivariate regression analysis, sex (male worse; P=0.06), age (higher age worse, P=0.02), and TPMT activity (wild type worse; P=0.02) were related to risk of relapse. Despite a lower probability of relapse, patients in the low TPMT activity group did not have superior survival (P=0.82), possibly because of an excess of secondary cancers among these 75 patients (P=0.07). These data suggest that children with ALL and TPMT wild type might have their cure rate improved, if the pharmacokinetics/-dynamics of TPMT low-activity patients could be mimicked without a concurrent excessive risk of second cancers.

PMID:

18987654

[PubMed - indexed for MEDLINE]

Related citations

23. Haematologica. 2008 Aug;93(8):1161-8. Epub 2008 Jun 12.

Acute lymphoblastic leukemia in

adolescents and young adults in Finland.

Usvasalo A, Räty R, Knuutila S, Vettenranta K, Harila-Saari A, Jantunen E, Kauppila M, Koistinen P, Parto K, Riikonen P, Salmi TT, Silvennoinen R, Elonen E, Saarinen-Pihkala UM.

Source

Hospital for Children and Adolescents, University of Helsinki, P.O. Box 281, 00029 HUS, Helsinki, Finland. anu.usvasalo@helsinki.fi

Comment in

- Haematologica. 2008 Aug;93(8):1124-8.

Abstract

BACKGROUND:

Interest has recently been paid to adolescents and young adults with acute lymphoblastic leukemia, particularly because all reports so far published indicate that these patients have a better outcome when treated with pediatric rather than adult therapeutic protocols. There are different biological subtypes of acute lymphoblastic leukemia with distinct features and prognoses; the distribution of these subtypes is not well known among adolescents. We, therefore, studied acute lymphoblastic leukemia in adolescents and young adults aged 10 to 25 years in Finland.

DESIGN AND METHODS:

This population-based study included 225 consecutive patients aged 10-25 years diagnosed with acute lymphoblastic leukemia during 1990-2004. One hundred and twenty-eight patients (10-16 years) were treated with pediatric Nordic (NOPHO) protocols, and 97 patients (17-25 years) with Finnish Leukemia Group National protocols. We characterized the biological subtypes, clinical features and outcome of these patients.

RESULTS:

For the whole cohort, the remission rate was 96%, 5-year event-free survival 62% and overall survival 72%. The 5-year event-free survival was 67% for the pediatric treatment group and 60% for the adult treatment group (p=n.s.). Patients with inferior outcome were those with a white blood cell count >or= 100 x 10(9)/L, the Philadelphia chromosome and MLL. Good prognostic features were TEL-AML1, hyperdiploidy, and pediatric intermediate risk stratification.

CONCLUSIONS:

Unlike all previous studies, we found that the outcome of adolescents and young adults with acute lymphoblastic leukemia treated with pediatric or adult therapeutic protocols was comparable. The success of the adult acute lymphoblastic leukemia therapy emphasizes the benefit of central referral of patients to academic centers and adherence to research protocols.

Free Article

PMID:

18556413

[PubMed - indexed for MEDLINE]

Related citations

24. Br J Haematol. 2008 Mar;140(6):665-72. Epub 2008 Feb 1.

Outcome of ETV6/RUNX1-positive childhood acute lymphoblastic leukaemia in the NOPHO-ALL-1992 protocol: frequent late relapses but good overall survival.

Forestier E, Heyman M, Andersen MK, Autio K, Blennow E, Borgström G, Golovleva I, Heim S, Heinonen K, Hovland R, Johannsson JH, Kerndrup G, Nordgren A, Rosenquist R, Swolin B, Johansson B; Nordic Society of Paediatric Haematology, Oncology (NOPHO); Swedish Cytogenetic Leukaemia Study Group (SCLSG); NOPHO Leukaemia Cytogenetic Study Group (NLCSG).

Source

Department of Clinical Sciences, Paediatrics, University of Umeå, Umeå, Sweden. erik.forestier@pediatri.umu.se

Abstract

The prognostic impact of t(12;21)(p13;q22) [ETV6/RUNX1 fusion] in paediatric acute lymphoblastic leukaemia (ALL) has been extensively debated, particularly with regard to the

frequency of late relapses and appropriate treatment regimens. We have retrospectively collected 679 ALLs with known ETV6/RUNX1 status, as ascertained by fluorescence in situ hybridization or reverse-transcription polymerase chain reaction, treated according to the Nordic Society of Paediatric Haematology and Oncology -ALL-1992 protocol. The assigned risk groups/treatment modalities for the 171 (25%) patients with t(12;21)-positive ALLs were 74 (43%) standard risk, 71 (42%) intermediate risk and 26 (15%) high risk. The 5- and 10-year event-free survival (EFS) of the 171 patients was 80% and 75% respectively, with no significant differences among the three risk groups. Most of the relapses occurred in boys and were late, with almost 50% of all relapses occurring > or = 5 years after diagnosis. Of all relapses after 6 years, 80% occurred in the t(12;21)-positive group. The overall survival was 94% at 5 years and 88% at 10 years; thus, the treatment of patients in second or later remission is usually successful. As yet, there is no reliable plateau in the EFS curve, a fact that raises the question as to when the prognostic ramifications of ALLs harbouring ETV6/RUNX1 should be evaluated.

PMID:

18241254

[PubMed - indexed for MEDLINE]

Related citations

25. Genes Chromosomes Cancer. 2008 Feb;47(2):149-58.

Clinical and cytogenetic features of pediatric dic(9;20)(p13.2;q11.2)-positive B-cell precursor acute lymphoblastic leukemias: a Nordic series of 24 cases and review of the literature.

Forestier E, Gauffin F, Andersen MK, Autio K, Borgström G, Golovleva I, Gustafsson B, Heim S, Heinonen K, Heyman M, Hovland R, Johannsson JH, Kerndrup G, Rosenquist R, Schoumans J, Swolin B, Johansson B, Nordgren A; Nordic Society of Pediatric Hematology and Oncology; Swedish Cytogenetic Leukemia Study Group; NOPHO Leukemia Cytogenetic Study Group.

Source

Department of Clinical Sciences, Pediatrics, University of Umeå, Umeå, Sweden.
ann.nordgren@ki.se

Abstract

Although dic(9;20)(p13.2;q11.2) is a characteristic abnormality in childhood B-cell precursor acute lymphoblastic leukemias (BCP ALL), little is known about its clinical impact or the type and frequency of additional aberrations it may occur together with. We here review the clinical and cytogenetic features of a Nordic pediatric series of 24 patients with dic(9;20)-positive BCP ALL diagnosed 1996-2006, constituting 1.3% of the BCP ALL, as well as 47 childhood cases from the literature. Consistent immunophenotypic features of the Nordic cases included positivity for HLA-DR, CD10, CD19, CD20, and CD22 and negativity for T-cell and myeloid markers; no detailed immunophenotypes were reported for the previously published cases. In the entire cohort of 71 cases, the modal chromosome distribution was 45 (62%), 46 (21%), 47 (7%), 48 (4%), 49 (3%), 44 (1%), and 50 (1%). Additional changes were present in 63%, the most frequent of which were homozygous loss of CDKN2A (33%) and gains of chromosomes 21 (28%) and X (10%). The median patient age was 3 years, the female/male ratio was 2.0, the median white blood cell count was 24 x 10(9)/l, 11% had central nervous system involvement, and 5% had a mediastinal mass at diagnosis. Risk group stratification was nonstandard risk in 79%. The event-free survival and overall survival at 5 years for the 24 Nordic cases was 0.62 and 0.82, respectively. Thus, although relapses are quite common, postrelapse treatment of many patients is successful.

PMID:

17990329

[PubMed - indexed for MEDLINE]
Related citations

26. Br J Haematol. 2007 Aug;138(4):513-6. Epub 2007 Jun 29.

A clinical score predicting a brief and uneventful course of newly diagnosed idiopathic thrombocytopenic purpura in

children.

Edslev PW, Rosthøj S, Treutiger I, Rajantie J, Zeller B, Jonsson OG; NOPHO ITP Working Group.

Source

Department of Paediatrics, Aalborg Hospital, Aalborg, Denmark.

Abstract

The Nordic idiopathic thrombocytopenic purpura study data showed that morbidity occurred mainly in children with thrombocytopenia lasting >3 months, whereas, the risk period with platelet counts <20 x 10(9)/l was short and the number of bleeding events low in children with shorter disease duration. These brief, uneventful courses were predicted by developing a scoring system based on six clinical features: abrupt onset (weight 5), age <10 years (3), preceding infection (2), platelet count <5 x 10(9)/l, wet purpura (1) and male gender (1). The score was derived and validated in two different cohorts of children. High scores (10-14) clearly identified low-risk patients. The score provides valid prognostic information and may be useful in clinical decision-making.

PMID:

17608764

[PubMed - indexed for MEDLINE]

Related citations

27. Tidsskr Nor Laegeforen. 2007 May 31;127(11):1493-5.

[Childhood acute lymphoblastic leukemia in Norway 1992-2000].

[Article in Norwegian]

Kolmannskog S, Flaegstad T, Helgestad J, Hellebostad M, Zeller B, Glomstein A.

Source

Barne- og ungdomsklinikken, Institutt for laboratoriemedisin, barne- og kvinnesykdommer, St. Olavs Hospital, 7006 Trondheim. svein.kolmannskog@ntnu.no

Abstract

BACKGROUND:

Acute lymphoblastic leukemia is the most common malignancy in childhood. The survival rate has increased steadily over the last 40 years.

MATERIAL AND METHODS:

All children aged 0-15 years and diagnosed in Norway in the period 1992-2000, were included in the study (n = 301). The patients were followed up until 1.1. 2005.

RESULTS AND INTERPRETATION:

The diagnosis was made in 301 children, 33 new cases per year (range 24 to 40) on average. The peak incidence was between 2 and 5 years. Four of 6 infants with acute lymphoblastic leukemia and all 4 with mature B-cell leukemia are alive. Two of the remaining 291 children died before treatment was started. 289 were all treated according to the common Nordic NOPHO-ALL 1992 protocol. All children achieved remission (99.7%), except for one who died before remission was achieved. 55 children (19%) relapsed. Radiation to the brain as part of central nervous system prophylaxis was given to just 10% of the children. The 10-year event-free survival (p-EFS) was 76%, and 244 of 289 (84%) were alive 4-13 years after the diagnosis was made. The data are comparable with the best international results.

Free Article
PMID:

17551551

[PubMed - indexed for MEDLINE]
Related citations

28. Arch Dis Child. 2007 Aug;92(8):704-7. Epub 2007 Apr 25.

Does treatment of newly diagnosed idiopathic thrombocytopenic purpura

reduce morbidity?

Treutiger I, Rajantie J, Zeller B, Henter JI, Elinder G, Rosthøj S; NOPHO ITP Study Group.

Source

Sachs' Children's Hospital, Stockholm, Sweden.

Abstract

AIM:

To explore whether early treatment of children with idiopathic thrombocytopenic purpura (ITP) with immunoglobulin and/or corticosteroids reduces subsequent morbidity.

METHODS:

Centres participating in a Nordic ITP study were divided according to whether they had treated more than 2/3, from 1/3 to 2/3, or less than 1/3 children within 14 days of diagnosis. The course of disease from 15 days to 6 months after diagnosis was compared for children managed at the three centre categories. The comparison was restricted to children in whom at least one platelet count <20x10(9)/l was measured, numbering 156, 143 and 84 in the three different categories, respectively.

RESULTS:

The three groups of children were clinically similar but were managed with initial treatment rates of 89%, 57% and 14%, respectively. By day 15, the platelet count had stabilised to >20x10(9)/l in 67%, 67% and 52% ($p<0.05$) and to >150x10(9)/l in 38%, 29% and 29% ($p<0.20$). At 1 month after diagnosis there was no difference in recovery rates. Chronic ITP developed in 27%, 22% and 25% in the three groups. During follow-up, one or more disease-related events occurred in 23%, 22% and 19%, with no difference in the average numbers of episodes with mucosal bleeding. Treatment courses were administered to 19%, 13% and 11%, respectively.

CONCLUSION:

Active treatment policies accelerated platelet recovery in children with short-lasting ITP but did not avert the development of chronic ITP and did not cause a reduction in morbidity during follow-up.

PMCID: PMC2083887

Free PMC Article

PMID:

17460024

[PubMed - indexed for MEDLINE]
Related citations

29. Genes Chromosomes Cancer. 2007 May;46(5):440-50.

Cytogenetic patterns in ETV6/RUNX1-positive pediatric B-cell precursor acute lymphoblastic leukemia: A Nordic series of 245 cases and review of the literature.

Forestier E, Andersen MK, Autio K, Blennow E, Borgström G, Golovleva I, Heim S, Heinonen K, Hovland R, Johannsson JH, Kerndrup G, Nordgren A, Rosenquist R, Swolin B, Johansson B; Nordic Society of Pediatric Hematology and Oncology (NOPHO); Swedish Cytogenetic Leukemia Study Group (SCLSG); NOPHO Leukemia Cytogenetic Study Group (NLCSG).

Source

Pediatrics Unit, Department of Clinical Sciences, University of Umeå, Umeå, Sweden. erik.forestier@pediatri.umu.se

Abstract

Between 1992 and 2004, 1,140 children (1 to<15 years) were diagnosed with B-cell precursor acute lymphoblastic leukemia (ALL) in the Nordic countries. Of these, 288 (25%) were positive for t(12;21)(p13;q22) [ETV6/RUNX1]. G-banding analyses were successful in 245 (85%); 43 (15%) were karyotypic failures. The modal chromosome numbers, incidence, types, and numbers of additional abnormalities, genomic imbalances, and chromosomal breakpoints in the 245 karyotypically informative cases, as well as in 152 previously reported cytogenetically characterized t(12;21)-positive ALLs in the same age group, were ascertained. The most common modal numbers among the 397 cases were 46 (67%), 47 (16%), 48 (6%), and 45 (5%). High-hyperdiploidy, triploidy, and tetraploidy were each found in approximately 1%; none had less than 40 chromosomes. Secondary chromosomal

abnormalities were identified by chromosome banding in 248 (62%) of the 397 ALLs. Of these, 172 (69%) displayed only unbalanced changes, 14 (6%) only balanced aberrations, and 26 (10%) harbored both unbalanced and balanced abnormalities; 36 (15%) were uninformative because of incomplete karyotypes. The numbers of secondary changes varied between 1 and 19, with a median of 2 additional aberrations per cytogenetically abnormal case. The most frequent genomic imbalances were deletions of 6q21-27 (18%), 8p11-23 (6%), 9p13-24 (7%), 11q23-25 (6%), 12p11-13 (27%), 13q14-34 (7%), loss of the X chromosome (8%), and gains of 10 (9%), 16 (6%), and 21 (29%); no frequent partial gains were noted. The chromosome bands most often involved in structural rearrangements were 3p21 (2%), 5q13 (2%), 6q12 (2%), 6q14 (2%), 6q16 (2%), 6q21 (10%), 6q23 (6%), 6q25 (3%), 9p13 (2%), 11q13 (2%), 11q23 (2%), 12p11 (6%), 12p12 (7%), 12p13 (25%), 21q10 (6%), and 21q22 (6%). Considering that the t(12;21) is known to arise in utero and that the postnatal latency period is protracted, additional mutations are most likely necessary for overt ALL. The frequently rearranged chromosome regions may harbor genes of importance for the transformation and/or progression of an initial preleukemic t(12;21)-positive clone.

PMID:

17285576

[PubMed - indexed for MEDLINE]
Related citations

30. Br J Haematol. 2007 Jan;136(2):229-236.

Improved outcome after relapse in children with acute myeloid leukaemia.

Abrahamsson J, Clausen N, Gustafsson G, Hovi L, Jonmundsson G, Zeller B, Forestier E, Heldrup J, Hasle H; Nordic Society for Paediatric Haematology and Oncology (NOPHO).

Source

Department of Clinical Sciences, Queen Silvia's Childrens Hospital, Gothenburg, Sweden. jonas.abrahamsson@vgregion.se

Abstract

In the Nordic Society for Paediatric Haematology and Oncology paediatric study acute myeloid leukaemia (AML) 93, event-free survival was 50% and overall survival was 66%, indicating that many patients were cured following relapse. Factors influencing outcome in children with relapsed AML were investigated. The study included all 146 children in the Nordic countries diagnosed with AML between 1988 and 2003, who relapsed. Data on disease characteristics and relapse treatment were related to outcome. Sixty-six percentage achieved remission with survival after relapse (5 years) 34 +/- 4%. Of 122 patients who received re-induction therapy, 77% entered remission with 40 +/- 5% survival. Remission rates were similar for different re-induction regimens but fludarabine, cytarabine, granulocyte colony-stimulating factor-based therapy had low treatment-related mortality. Prognostic factors for survival were duration of first complete remission (CR1) and stem cell transplantation (SCT) in CR1. In early relapse (<1 year in CR1), survival was 21 +/- 5% compared with 48 +/- 6% in late relapse. For children receiving re-induction therapy, survival in early relapse was 29 +/- 6% and 51 +/- 6% in late. Patients treated in CR1 with SCT, autologous SCT or chemotherapy had a survival of 18 +/- 9, 5 +/- 5 and 41 +/- 5%, respectively. Survival was 62 +/- 6% in 64 children given SCT as part of their relapse therapy. A significant proportion of children with relapsed AML can be cured, even those with early relapse. Children who receive re-induction therapy, enter remission and proceed to SCT can achieve a cure rate of 60%.

PMID:

17278259

[PubMed - indexed for MEDLINE]

Related citations

31. Vaccine. 2007 Feb 26;25(10):1838-40. Epub 2006 Nov 9.

Vaccination associated thrombocytopenic purpura in children.

Rajantie J, Zeller B, Treutiger I, Rosthöj S; NOPHO ITP working group and five national study groups.

Source

Helsinki University Central Hospital, Jorvi Hospital, Finland. jukka.rajantie@hus.fi

Abstract

Patients who presented with purpura and blood platelets <30x10(9)/l within 1 month after vaccination were collected from a population based material of 506 consecutive pediatric patients with newly diagnosed ITP. Of the 35 such patients, 24 had thrombocytopenia after MMR vaccination giving an estimated ITP risk of approximately 1 in 30,000 MMR inoculations. Symptoms of the 35 patients were nearly always acute. Thrombocytopenia disappeared within a month in 74% of the study patients and lasted longer than 6 months in only 10%. Bleeding episodes were uncommon during the follow-up period. We conclude that the incidence of symptomatic thrombocytopenia after vaccinations is much lower than that after respective natural infections and that the outcome in most cases is excellent.

PMID:

17126957

[PubMed - indexed for MEDLINE]

Related citations

32. Leukemia. 2006 Nov;20(11):1955-62. Epub 2006 Sep 21.

High leucovorin doses during high-dose methotrexate treatment may reduce the cure rate in childhood acute lymphoblastic leukemia.

Skärby TV, Anderson H, Heldrup J, Kanerva JA, Seidel H, Schmiegelow K; Nordic Society of Paediatric Haematology and Oncology (NOPHO).

Source

Department of Pediatrics, Lund University Hospital, Lund, Sweden. tor.skarby@med.lu.se

Abstract

We explored the relationship between time to relapse and different exposure variables (serum methotrexate (S-MTX) 23, 36 and 42 h after start of administration, MTX elimination time and leucovorin (LV) dose) during high-dose MTX (HDM) treatment of 445 children with acute lymphoblastic leukemia. MTX was infused at 5 g/m2 (non-high risk) or 8 g/m2 (high risk) over 24 h, 2-9 times per patient. LV rescue dose was adjusted according to the S-MTX

concentration. Time from end of the last HDM to relapse was analyzed by Cox regression analysis with the logarithms of S-MTX and LV dose as exposures. The combined results from all risk groups suggest that high LV dose is related to higher risk for relapse. Doubling of the LV dose increased the relapse risk by 22% (95% confidence interval 1-49%, P = 0.037). High LV doses correlated with high MTX levels at 23, 36 and 42 h and longer elimination time. The results suggest that high doses of LV increase the risk for relapse despite the fact that they were correlated with high MTX levels and longer MTX elimination time. The choice of MTX and LV doses may be regarded as an intricate balance between effect and counter-effect.

PMID:

16990760

[PubMed - indexed for MEDLINE]

Related citations

33. Br J Haematol. 2006 Nov;135(3):352-4. Epub 2006 Sep 11.

High incidence of the ETV6/RUNX1 fusion gene in paediatric precursor B-cell acute lymphoblastic leukaemias with trisomy 21 as the sole cytogenetic change: a Nordic series of cases diagnosed 1989-2005.

Karrman K, Forestier E, Andersen MK, Autio K, Borgström G, Heim S, Heinonen K, Hovland R, Kerndrup G, Johansson B; Nordic Society of Paediatric Haematology and Oncology (NOPHO) and the NOPHO Leukaemia Cytogenetic Study Group (NLCSG).

Source

Department of Clinical Genetics, Lund University Hospital, Lund, Sweden. kristina.karrman@med.lu.se

Abstract

Trisomy 21 is common in ETV6/RUNX1-positive acute lymphoblastic leukaemia (ALL);

both these aberrations are associated with a favourable outcome. The prognostic impact of +21 as a sole cytogenetic change could be due to a cryptic t(12;21)(p13;q22). The occurrence of ETV6/RUNX1 was determined in 66 childhood ALLs with an acquired +21 and a chromosome number <51. ETV6/RUNX1 was found in 45% of cases and in the majority (10/18; 56%) of ALLs with sole +21. Event-free survival did not differ between the t(12;21)-positive and -negative cases. Thus, the prognostic impact of +21 is not attributable to cryptic ETV6/RUNX1.

PMID:

16965388

[PubMed - indexed for MEDLINE]

Related citations

34. Cancer. 2006 Oct 1;107(7):1551-61.

Treatment outcome in young adults and children >10 years of age with acute lymphoblastic leukemia in Sweden: a comparison between a pediatric protocol and an adult protocol.

Hallböök H, Gustafsson G, Smedmyr B, Söderhäll S, Heyman M; Swedish Adult Acute Lymphocytic Leukemia Group; Swedish Childhood Leukemia Group.

Source

Department of Hematology, Uppsala University Hospital, Uppsala, Sweden.

Abstract

BACKGROUND:

Several studies have reported a more favorable outcome for teenagers and young adults with acute lymphoblastic leukemia (ALL) when they were treated in pediatric oncology departments compared with adult hematology departments. However, biased risk grouping

and high treatment-related mortality have hampered some of those comparisons.

METHODS:

In Sweden during the 1990s, adolescents with ALL were treated in a pediatric oncology unit or in an adult hematologic unit, depending on the initial referral. In the current national, comparative, retrospective study, patients with ALL aged 10 years to 40 years who were treated either according to the Nordic Society of Pediatric Hematology and Oncology (NOPHO) ALL protocol (1992-2000) (NOPHO-92 protocol) or according to the Swedish Adult ALL Group protocol (1994-2000) (Adult protocol) were included. None of the protocols had age as a high-risk criterion.

RESULTS:

In total, 243 patients with B-precursor and T-cell ALL were treated according to the protocols. There was a significant difference in the remission rate between the NOPHO-92 protocol (99%; n = 144 patients) and the Adult protocol (90%; n = 99 patients; $P < .01$), and the event-free survival (EFS) was also superior for the NOPHO-92 protocol compared with the Adult protocol ($P < .01$). However, EFS was higher for patients aged 15 years to 25 years compared with patients aged 26 years to 40 years within the Adult protocol group ($P = .01$). The treatment protocol itself was identified as an independent risk factor.

CONCLUSIONS:

The NOPHO-92 protocol resulted in a better outcome than the Adult protocol; therefore, adolescents may benefit from the pediatric protocol treatment strategy. Prospective trials are warranted to determine whether young adults would benefit from similar treatment.

Free Article

PMID:

16955505

[PubMed - indexed for MEDLINE]

Related citations

35. J Pediatr Hematol Oncol. 2006 Aug;28(8):486-95.

The incidence peaks of the childhood acute leukemias reflect specific cytogenetic aberrations.

Forestier E, Schmiegelow K; Nordic Society of Paediatric Haematology and Oncology NOPHO.

Source

Department of Clinical Sciences, Pediatrics, University of Umeå, Sweden, and Pediatric Clinic II, The University Hospital Rigshospitalet, Copenhagen, Denmark.

Abstract

The correlation between age and karyotype was studied in 1425, 0 to 14.9 years old children who were diagnosed with acute lymphoblastic leukemia (ALL) or acute myeloblastic leukemia. Almost 80% of the non-Down B-cell precursor ALL cases in the 2 to 7 years frequency peak group who had aberrant cytogenetic results had either a high-hyperdiploid clone (51 to 61 chromosomes) or a translocation t(12;21)(p13;q22). Among B-cell precursor ALL cases, high white blood cell counts correlated with earlier age at diagnosis (rS=-0.23; P<0.001) being most evident for 11q23/MLL-aberrations, translocation t(12;21)(p13;q22), and high-hyperdiploidy. Among acute myeloblastic leukemia patients, frequency peaks were found for those with MLL/11q23 rearrangements (peak: first year), Down syndrome (peak: second to third year), or cytogenetic abnormalities other than translocations t(8;21), t(15;17), and inv(16)/t(16;16) (peak: first to third year). The epidemiology of the cytogenetic subsets of acute leukemias questions whether age as a disease-related prognostic parameter has any relevance in childhood leukemia clinical research beyond being a surrogate marker for more important, truly biologic features such as cytogenetic aberrations and white cell count at diagnosis. Further research is needed to explore whether the 2 to 7 years age incidence peak in childhood ALL harbor yet unidentified cytogenetic subsets with the same natural history as the high-hyperdiploid and t(12;21)-positive leukemias.

PMID:

16912588

[PubMed - indexed for MEDLINE]

Related citations

36. Ugeskr Laeger. 2006 Jun 26;168(26-32):2554-8.

[Acute lymphoblastic leukaemia in Danish children and young people 10 to 19 years of age. Should young adults with acute lymphoblastic leukaemia be treated in the same way as children?].

[Article in Danish]

Schrøder H, Kjeldstad M, Boesen AM, Nielsen OJ, Schmidt KG, Johnsen HE, Gregersen H, Gustafsson G.

Source

Arhus Universitetshospital, Skejby Sygehus, Børneafdelingen, DK-8200 Arhus. hsa@sks.aaa.dk

Abstract

INTRODUCTION:

Data seem to indicate that young adults with acute lymphoblastic leukemia (ALL) have a better survival rate when treated with paediatric protocols than with adult ALL protocols. The purpose of this study was to report the clinical characteristics and outcome of all children and young adults 10-19 years of age diagnosed with ALL in Denmark between 1992 and 2001.

MATERIALS AND METHODS:

The study included 99 patients 10-19 years of age with ALL in Denmark during a 10-year period found in the complete NOPHO (Nordic Society of Pediatric Hematology and Oncology) registry and through the Danish Cancer Registry and local pathology databases. Data were retrieved by reviewing patients' medical charts. 61 children (10-14 years) were treated on paediatric protocols, and 38 young adults (15-19 years) were diagnosed with ALL. Data were reported as of 1 January 2005.

RESULTS:

There were no differences between the two groups with respect to the distribution of T-ALL, CNS leukemia, total WBC and high-risk chromosomal abnormalities. There was a statistically significant lower event-free survival rate (EFS) ($p < 0.01$) and lower overall

survival rate ($p < 0.01$) in young adults than in 10-14-year-old children (0.38 vs. 0.60 and 0.47 vs. 0.67). There were more transplant-related deaths in the young adults. The higher treatment intensity in children may be an explanatory factor. Children were given more prednisone, vincristine and high-dose methotrexate than were the young adults.

CONCLUSION:

Young adult patients with ALL might benefit from therapy with paediatric NOPHO ALL protocols.

PMID:

16824410

[PubMed - indexed for MEDLINE]

Related citations

37. Dan Med Bull. 2006 Feb;53(1):76-9.

Acute lymphoblastic leukemia in adolescents between 10 and 19 years of age in Denmark--secondary publication.

Schrøder H, Kjeldahl M, Boesen AM, Nielsen OJ, Schmidt K, Johnsen HE, Gregersen H, Heyman M, Gustafsson G.

Source

Department of Pediatrics, University Hospital of Aarhus, Skejby Hospital, Aarhus, Denmark. hsa@sks.aaa.dk

Abstract

INTRODUCTION:

Data seem to indicate that young adults with acute lymphoblastic leukemia (ALL) have a better survival when treated with pediatric protocols compared with adult ALL protocols. The purpose of the study was to report the clinical characteristics and outcome of all children and young adults 10-19 years of age diagnosed with ALL in Denmark between 1992 and 2001.

MATERIAL:

The study includes 99 patients 10-19 years of age with ALL in Denmark during a ten year period found in the complete NOPHO (Nordic Society of Pediatric Hematology and Oncology) registry and through the Danish Cancer Registry and local pathology databases. Data were retrieved by reviewing medical charts of the patients. A total of 61 children (10-14 years) treated on pediatric protocols and 38 young adults (15-19 years) were diagnosed with ALL. Data were reported as of January 1st 2005.

RESULTS:

There were no difference with respect to the distribution of T-ALL, CNS-leukemia, total white blood count and high risk chromosomal abnormalities between the two groups. There was a statistical significant lower event free survival ($p<0.01$) and lower overall survival ($p<0.01$) in young adults compared with 10-14 year-old children (0.38 vs 0.60 and 0.47 vs 0.67). There were more transplant-related deaths in the young adults. Higher treatment intensity in children may be an additional explanatory factor. Children received more prednisone, vincristine and high-dose methotrexate than young adults.

CONCLUSION:

Young adult patients with ALL might benefit from therapy with pediatric NOPHO ALL protocols.

PMID:

16761337

[PubMed - indexed for MEDLINE]

Related citations

38. Ann Hematol. 2006 May;85(5):275-80. Epub 2006 Mar 4.

Optimal treatment intensity in children with Down syndrome and myeloid leukaemia: data from 56 children treated on NOPHO-AML protocols and a review of the

literature.

Abildgaard L, Ellebaek E, Gustafsson G, Abrahamsson J, Hovi L, Jonmundsson G, Zeller B, Hasle H.

Source

Department of Paediatrics, Skejby Hospital, 8200, Aarhus N, Denmark.

Abstract

Children with Down syndrome (DS) and myeloid leukaemia have a significantly higher survival rate than other children, but they also experience considerable treatment-related toxicity. We analysed data on 56 children with DS who were treated on the Nordic Society for Paediatric Haematology and Oncology-acute myeloid leukaemia (NOPHO-AML)88 and NOPHO-AML93 protocols and reviewed the literature. In the dose-intensive NOPHO-AML88 protocol, 8 out of 15 patients (53%) experienced an event. In the less dose-intensive NOPHO-AML93 protocol, 7 out of 41 patients (17%) had an event. Therapy was reduced in 29 patients (52%) with in average 75% and 67% of the scheduled dose of anthracycline and cytarabine, respectively. Treatment-related death occurred in seven who all received full treatment. Relapse and resistant disease occurred at a similar rate in those receiving full and reduced treatment. Review of major series of myeloid leukaemia of DS showed no clear relationship between dose and survival; however, it appears that both a reduction in treatment dose and a less intensively timed treatment regimen improved the outcome. Further studies are needed to define the optimal regimen for treating myeloid leukaemia of DS.

PMID:

16518605

[PubMed - indexed for MEDLINE]

Related citations

39. Pediatr Hematol Oncol. 2006 Apr-May;23(3):207-16.

Thrombotic effects of asparaginase in two acute lymphoblastic leukemia protocols (NOPHO ALL-1992 versus NOPHO ALL-

2000): a single-institution study.

Ruud E, Holmstrøm H, de Lange C, Natvig S, Albertsen BK, Wesenberg F.

Source

Department of Paediatrics, National Hospital, Oslo, Norway. ellen.ruud@rikshospitalet.no

Abstract

Asparaginase is essential in the treatment of lymphoproliferative malignancies, but it is associated with several side effects. The objective of this study was to compare asparaginase-induced alterations of the coagulation inhibitors and the impact on central line-associated thrombosis in children treated according to 2 different asparaginase regimens. The study enrolled 30 children treated for acute lymphoblastic leukemia, and they were divided into 2 groups with respect to asparaginase preparation and protocol (NOPHO ALL-1992 versus NOPHO ALL-2000). The coagulation inhibitors antithrombin, protein C, and proteins S were measured prior to and during asparaginase therapy, and incidence of central line-associated thromboses was compared to evaluate the protocols' thrombogenicity. Thirteen children received Erwinia asparaginase and 17 children received E. coli asparaginase. Independent of protocol, the coagulation inhibitors were significantly reduced during asparaginase therapy ($p < .001$), and central line-associated thromboses were frequent. Four children developed thrombosis in the course of asparaginase therapy, and there was a correlation between asparaginase-induced fall of antithrombin and occurrence of new thromboses ($p = .01$).

PMID:

16517537

[PubMed - indexed for MEDLINE]

Related citations

40. Leukemia. 2005 Dec;19(12):2090-100.

Long-term results in children with AML: NOPHO-AML Study Group--report of three consecutive trials.

Lie SO, Abrahamsson J, Clausen N, Forestier E, Hasle H, Hovi L, Jonmundsson G, Mellander L, Siimes MA, Yssing M, Zeller B, Gustafsson G; Nordic Society of Pediatric Hematology and Oncology (NOPHO); AML Study Group.

Source

Department of Pediatrics, University Hospital, Rikshospitalet, Oslo, Norway.

Abstract

In all, 447 children with acute myeloid leukaemia (AML) have been treated on three consecutive NOPHO studies from July 1984 to December 2001. NOPHO-AML 84 was of moderate intensity with an induction of three courses of cytarabine, 6-thioguanine and doxorubicin followed by four consolidation courses with high-dose cytarabine. The 5-year event-free survival (EFS), disease free survival (DFS) and overall survival (OS) were 29, 37 and 38%. NOPHO-AML 88 was of high intensity with the addition of etoposide and mitoxantrone in selected courses during induction and consolidation. The interval between the induction courses should be as short as possible, that is, time intensity was introduced. The 5-year EFS, DFS and OS were 41, 48 and 46%. In NOPHO-AML 93, the treatment was stratified according to response to first induction course. The protocol utilised the same induction blocks as NOPHO-AML 88, but after the first block, children with a hypoplastic, nonleukaemic bone marrow were allowed to recover before the second block. Consolidation was identical with NOPHO-AML 88. The 5-year EFS, DFS and OS in NOPHO-AML 93 were 48, 52 and 65%. The new NOPHO-AML protocol has been based on experiences from previous protocols with stratification of patients with regard to in vivo response and specific cytogenetic aberrations.

PMID:

16304571

[PubMed - indexed for MEDLINE]

Related citations

41. Br J Haematol. 2005 Oct;131(1):50-8.

Treatment-related death in childhood acute lymphoblastic leukaemia in the Nordic

countries: 1992-2001.

Christensen MS, Heyman M, Möttönen M, Zeller B, Jonmundsson G, Hasle H; Nordic Society of Paediatric Haematology and Oncology (NOPHO).

Source

Department of Paediatrics, Skejby Hospital, Aarhus, Denmark.

Abstract

Despite continuously more successful treatment of childhood acute lymphoblastic leukaemia (ALL), 2-5% of children still die of other causes than relapse. The Nordic Society of Paediatric Haematology and Oncology-ALL92 protocol included 1652 patients < or =15 years of age with precursor B- and T-cell ALL diagnosed between 1992 and 2001. Induction deaths and deaths in first complete remission (CR1) were included in the study. A total of 56 deaths (3%) were identified: 19 died during induction (1%) and 37 in CR1 (2%). Infection was the major cause of death in 38 cases. Five patients died of early death before initiation of cytotoxic therapy. Five patients died because of toxicity of inner organs and one of accidental procedure failures. Seven patients died of complications following allogenic haematopoietic stem cell transplantation (HSCT) in CR1. Girls were at higher risk of treatment-related death (TRD) [relative risk (RR) = 2.2; 95% confidence interval (CI(95%)): 1.2-4.0, P < 0.01], mostly because of infections. Risk of TRD was also higher in children with Down syndrome (RR = 4.5; CI(95%): 2.0-10.2, P < 0.00). In conclusion, 3% of children with ALL died of TRD, with bacterial infections as the most common cause of death. Girls and Down syndrome patients had a higher risk of TRD. Infections still remain a major challenge in childhood ALL.

PMID:

16173962

[PubMed - indexed for MEDLINE]

Related citations

42. Acta Paediatr. 2005 Feb;94(2):178-84.

Childhood idiopathic thrombocytopenic purpura in the Nordic countries:

epidemiology and predictors of chronic disease.

Zeller B, Rajantie J, Hedlund-Treutiger I, Tedgård U, Wesenberg F, Jonsson OG, Henter JI; NOPHO ITP.

Source

Paediatric Department of National Hospital of Norway, Oslo, Norway.
bem.zeller@rikshospitalet.no

Abstract

AIM:

To describe the epidemiology of idiopathic thrombocytopenic purpura (ITP) in the Nordic countries, to define clinical subgroups and to investigate factors predicting chronic disease.

METHODS:

A prospective registration was done from 1998 to 2000, including all children with newly diagnosed ITP aged 0-14 y and at least one platelet count <30 x 10(9)/l.

RESULTS:

506 children were registered and 423 followed for 6 mo. The incidence was 4.8/10(5) per year. Most children were aged 0-7 y (78%), with a predominance of boys, while patients aged 8-14 y had equal representation of the two sexes. There were seasonal variations determined by variations in postinfectious cases with sudden onset. The platelet count was <10 x 10(9)/l in 58%, but bleeding manifestations were mild or moderate in 97%. The insidious form (symptoms for more than 2 wk) was more frequent in older children and girls, showed little seasonal variation, had milder manifestations and ran a chronic course in more than half the cases. Intracranial haemorrhages did not occur in the first 6 mo after diagnosis. Chronic ITP developed in 25%. The strongest predictor of chronic disease was insidious onset of symptoms (OR 5.97).

CONCLUSION:

In the Nordic countries, ITP mainly affects children aged 0-7 y, with a winter bulk of postinfectious cases superimposed on a steady occurrence of non-infectious cases. Clinically, it may be useful to distinguish between children with sudden versus insidious onset of symptoms rather than between different age groups.

PMID:

15981751

[PubMed - indexed for MEDLINE]
Related citations

43. Br J Haematol. 2005 Mar;128(6):797-804.

Acute leukaemia in children with Down syndrome: a population-based Nordic study.

Zeller B, Gustafsson G, Forestier E, Abrahamsson J, Clausen N, Heldrup J, Hovi L, Jonmundsson G, Lie SO, Glomstein A, Hasle H; Nordic Society of Paediatric Haematology and Oncology (NOPHO).

Source

Department of Paediatrics, National Hospital of Norway, N-0027 Oslo, Norway. bem.zeller@rikshospitalet.no

Abstract

To determine the epidemiology and outcome of children with Down syndrome (DS) diagnosed with acute leukaemia in the Nordic countries, data registered in the Nordic Society of Paediatric Haematology and Oncology (NOPHO) population-based leukaemia registry were analysed. Of 3494 children with acute leukaemia diagnosed between July 1984 and December 2001, 136 patients (3.9%) with DS were identified. 2.1% of the children with acute lymphoid leukaemia (ALL) and 14.0% of the children with acute myeloid leukaemia (AML) had DS. In ALL, DS patients had similar age and sex distribution and no major differences in blood counts compared with non-DS children. None of the DS patients had T cell leukaemia. Outcome was inferior to that of non-DS children and treatment results did not improve over time. In AML, DS patients showed a significant female predominance and all but one were <5 years old. DS patients with AML had significantly lower platelet and white blood cell counts and two-thirds were type M7 as according to the French-American-British classification. None of the patients <5 years of age had typical AML cytogenetic aberrations. Outcome was far better in the DS group. DS patients treated for AML after 1992 had an excellent outcome (probability of event-free survival, 83 +/- 6%). The high proportion of female DS patients with AML is unexplained. The differing treatment results in AML versus ALL need further evaluation and represent a challenge for the coming years.

PMID:

15755283

[PubMed - indexed for MEDLINE]
Related citations

44. Pediatr Blood Cancer. 2005 May;44(5):461-8.

Immune reconstitution after childhood acute lymphoblastic leukemia is most severely affected in the high risk group.

Ek T, Mellander L, Andersson B, Abrahamsson J.

Source

Department of Paediatrics, Goteborg University, Goteborg, Sweden. torben.ek@medfak.gu.se

Abstract

OBJECTIVE:

The aim was to examine the immune reconstitution after current chemotherapy for childhood ALL, with a special focus on finding immunologic variables that predict a poor immune response to vaccinations.

PROCEDURE:

In a cross-sectional study of 31 children after treatment with the NOPHO ALL-1992 protocol peripheral blood lymphocyte subsets, T- and B-cell function in vitro and serum immunoglobulins (Ig) were measured. All patients were examined once, at 1 or at 6 months after cessation of chemotherapy, immediately before vaccination with DT and Hib.

RESULTS:

Lymphocytes, T-cells, and CD4+ T-cells were low at 6 months after treatment. Naive T-cell subsets were more reduced than memory subsets. In the high risk (HR) ALL group, CD8+ T-

cells were reduced at 6 months. NK-cells were low at 1 month, but normal at 6 months; however, the CD3+CD56+ (NKT) subset was reduced at both time points. Total B-cell number was low at 1 month, but normal at 6 months. A relative increase of CD5+ B-cells (B-1 cells) was evident, particularly in the HR group. Antigen-independent T- and B-cell function in vitro were affected at 1 month, but virtually normalized at 6 months. Serum IgM level was decreased at 1 month and IgG3 level was increased at 1 and 6 months.

CONCLUSIONS:

This study shows that immune reconstitution after childhood ALL is slower than previously reported and emphasizes the influence of treatment intensity. The most intensively treated patients still have persistent abnormalities in T-, B-, and NK-cell subsets at 6 months post therapy and show a poor response to immunization with T-cell dependent antigens. In the HR group, routine re-immunizations before this time point are of limited benefit, and the effect of repeated vaccinations should be evaluated.

PMID:

15558707

[PubMed - indexed for MEDLINE]
Related citations

45. J Pediatr Hematol Oncol. 2004 Nov;26(11):727-34.

Intensive treatment for childhood acute lymphoblastic leukemia reduces immune responses to diphtheria, tetanus, and Haemophilus influenzae type b.

Ek T, Mellander L, Hahn-Zoric M, Abrahamsson J.

Source

Department of Pediatrics, Goteborg University, Goteborg, Sweden. torben.ek@medfak.gu.se

Abstract

OBJECTIVES:

Immunity to diphtheria toxoid (D), tetanus toxoid (T), and Haemophilus influenzae type b (Hib) is affected in children with acute lymphoblastic leukemia (ALL). The aims were to examine immunity and to compare the response to immunization at 1 or 6 months after treatment.

METHODS:

Thirty-one patients were immunized with DT and conjugated Hib vaccine (ActHib) at 1 month or 6 months after treatment of ALL with the NOPHO 92 protocol. Antibody levels were determined before and 3 weeks after vaccination. Specific T and Hib antibody-secreting cells of IgG/IgA/IgM isotypes were analyzed in peripheral blood using an ELISPOT technique.

RESULTS:

All specific antibody levels decreased during ALL treatment, and protective levels after treatment were noted for 17% against D, 33% against T, and 100% against Hib. No high-risk patient had full D or T protection after treatment. After vaccination all the standard- and intermediate-risk patients achieved full protection against D, T, and Hib. The high-risk group showed insufficient immune response (full protection after vaccination: D 56%, T 22%, Hib 78%). No difference was found between vaccination at 1 month or 6 months after treatment. The poor antibody production in the high-risk group correlated to low numbers of antibody-secreting cells.

CONCLUSIONS:

Nonprotective antibody levels against D, T, and Hib after childhood ALL are more common than previously thought. Insufficient immune response was restricted to the high-risk group and was related to a low number of memory B cells in this study. Immunizations should be included in follow-up after childhood ALL, and the policy should be adapted to treatment intensity.
PMID:

15543007

[PubMed - indexed for MEDLINE]
Related citations

46. Leukemia. 2004 Jul;18(7):1270-7.

Prediction of immunophenotype, treatment response, and relapse in childhood acute lymphoblastic leukemia using DNA microarrays.

Willenbrock H, Juncker AS, Schmiegelow K, Knudsen S, Ryder LP.

Source

Center for Biological Sequence Analysis, Technical University of Denmark, Lyngby, Denmark.

Abstract

Gene expression profiling is a promising tool for classification of pediatric acute lymphoblastic leukemia (ALL). We analyzed the gene expression at the time of diagnosis for 45 Danish children with ALL. The prediction of 5-year event-free survival or relapse after treatment by NOPHO-ALL92 or 2000 protocols resulted in a classification accuracy of 78% and a Matthew's correlation coefficient of 0.59 independently of immunophenotypes. The sensitivity and specificity for prediction of relapse were 87% and 69% respectively. Prediction of high vs low levels of the minimal residual disease (MRD) on day 29 (>/=0.1% or </=0.01%) resulted in an accuracy of 100% for precursor-B samples. The classification accuracy of precursor-B- vs T-lineage immunophenotypes was 100% even in samples with as little as 10% leukemic blast cells, and the immunophenotype classifier constructed in this study was able to classify 131 of 132 samples from a previous study correctly. Our study indicates that the Affymetrix Focus Array GeneChip may be used without loss of classification performance compared to previous studies using the far more extensive U133A+B GeneChip set. Further studies should focus on prediction of MRD, as this prediction would relate strongly to long-term outcome and could thus determine the intensity of induction therapy.

PMID:

15152267

[PubMed - indexed for MEDLINE]

Related citations

47. Pediatr Blood Cancer. 2004 Jan;42(1):8-23.

Outcome of children with high-risk acute lymphoblastic leukemia (HR-ALL): Nordic results on an intensive regimen with restricted central nervous system irradiation.

Saarinen-Pihkala UM, Gustafsson G, Carlsen N, Flaegstad T, Forestier E, Glomstein A, Kristinsson J, Lanning M, Schroeder H, Mellander L; Nordic Society of Pediatric Hematology and Oncology.

Source

Hospital for Children and Adolescents, University of Helsinki, Helsinki, Finland. ulla.pihkala@hus.fi

Abstract

BACKGROUND:

Improvement in outcome of childhood high-risk (HR) ALL was sought with a very intensive Nordic protocol leaving most patients without CNS-RT.

METHODS:

A total of 426 consecutive children entered the NOPHO-92 HR-ALL program. HR criteria included WBC > or =50 x 10(9)/L, CNS or testicular involvement, T-cell, lymphomatous features, t(9;22), t(4;11), or slow response. Of these, 152 children had very high risk (VHR) with special definitions. CNS consolidation was based on high-dose MTX (8 g/m2) and ARA-C (12 g/m2) alternating. VHR patients also received cranial RT.

RESULTS:

The 9-year EFS was 61 +/- 3%, OS 74 +/- 2%, and EFS for T-ALL 62 +/- 4%. Cumulative incidence of isolated CNS relapse was 4.7 +/- 1%, and CNS relapse in total 9.9 +/- 2%. Poor prognostic factors were WBC > or =200 x 10(9)/L and a very slow response.

CONCLUSIONS:

HR-ALL was successfully treated on the NOPHO-92 regimen, with a relatively low CNS relapse rate for non-irradiated children. WBC > or =200 x 10(9)/L and very slow response emerged as strong poor prognostic factors.

PMID:

14752789

[PubMed - indexed for MEDLINE]
Related citations

48. J Natl Cancer Inst. 2003 Oct 15;95(20):1539-44.

Age- and sex-specific incidence of childhood leukemia by immunophenotype in the Nordic countries.

Hjalgrim LL, Rostgaard K, Schmiegelow K, Söderhäll S, Kolmannskog S, Vettenranta K, Kristinsson J, Clausen N, Melbye M, Hjalgrim H, Gustafsson G.

Source

Department of Epidemiology Research, Danish Epidemiology Science Centre, Statens Serum Institut, Copenhagen, Denmark. lih@ssi.dk

Abstract

BACKGROUND:

Studies from various countries have found an increasing incidence of childhood leukemia in recent decades. To characterize time trends in the age- and sex-specific incidence of childhood acute leukemia during the last 20 years in the Nordic countries, we analyzed a large set of population-based data from the Nordic Society of Paediatric Haematology and Oncology (NOPHO) in their acute leukemia database covering a population of approximately

5 million children aged 0-14 years.

METHODS:

Temporal trends in acute myeloid leukemia and acute lymphoblastic leukemia incidence rates overall and for acute lymphoblastic leukemia immunophenotypes and for specific age groups were analyzed by Poisson regression adjusting for age, sex, and country. All statistical tests were two-sided.

RESULTS:

We identified 1595 girls and 1859 boys diagnosed with acute lymphoblastic leukemia between January 1, 1982, and December 31, 2001, and 260 girls and 224 boys diagnosed with de novo acute myeloid leukemia between January 1, 1985, and December 31, 2001. No statistically significant change was seen in the overall incidence rate for acute lymphoblastic leukemia during the 20-year study (annual change = 0.22%, 95% confidence interval [CI] = -0.36% to 0.80%). The incidence rate of B-precursor acute lymphoblastic leukemia remained unchanged (annual change = 0.30%, 95% CI = -0.57% to 1.18%) from January 1, 1986, through December 31, 2001. A somewhat lower incidence in the first years of the study period indicated an early increasing incidence of B-precursor acute lymphoblastic leukemia that corresponded to a simultaneous decreasing incidence of unclassified acute lymphoblastic leukemia. Incidences of T-cell acute lymphoblastic leukemia (annual change = 1.55%, 95% CI = -1.14% to 4.31%) and acute myeloid leukemia (annual change = 0.58%, 95% CI = -1.24% to 2.44%) were stable during the study period.

CONCLUSION:

Incidences of acute myeloid leukemia overall, acute lymphoblastic leukemia overall, and specific acute lymphoblastic leukemia immunophenotypes have been stable in the Nordic countries over the past two decades.

Free Article

PMID:

14559876

[PubMed - indexed for MEDLINE]

Related citations

49. J Pediatr. 2003 Sep;143(3):302-7.

Duration and morbidity of newly diagnosed idiopathic thrombocytopenic purpura in children: A prospective Nordic study of an unselected cohort.

Rosthøj S, Hedlund-Treutiger I, Rajantie J, Zeller B, Jonsson OG, Elinder G, Wesenberg F, Henter JI; NOPHO ITP Working Group.

Source

Pediatric Department, Aalborg Hospital, Denmark. rosthoej@aas.nja.dk

Comment in

- J Pediatr. 2003 Sep;143(3):287-9.

Abstract

OBJECTIVE:

To determine the duration of the risk period with platelet counts <20 x 10(9)/L and the frequency of bleeding episodes in unselected children with idiopathic thrombocytopenic purpura (ITP).

STUDY DESIGN:

We established a registry for patients with newly diagnosed ITP in the five Nordic countries, enrolling children aged 0 to 14 years with platelet counts <30 x 10(9)/L. Treatment centers prospectively reported presenting features, management details, and disease-related events during the first six months after diagnosis.

RESULTS:

At presentation (n=501), more than half of the children had a platelet count <10 x 10(9)/L, but only 15 (3.0%) had a hemorrhage requiring blood transfusion. During follow-up of 409 patients, thrombocytopenia resolved uneventfully in 277. A risk period was present in 376 cases. Among 283 with self-limiting ITP, 26 were at risk >1 month and 25 had 30 events. Among 93 patients with chronic ITP, 73 were at risk >1 month and 44 had 111 events. Events occurred with an average frequency of 0.39 per month at risk. Life-threatening hemorrhages did not occur in the first six months after diagnosis.

CONCLUSION:

Most children with ITP are at risk for serious bleeding for less than one month. Continuing severe thrombocytopenia is associated with little morbidity, bleeding episodes being infrequent and very rarely serious.

PMID:

14517509

[PubMed - indexed for MEDLINE]

Related citations

50. Br J Haematol. 2003 Jul;122(2):217-25.

Treatment stratification based on initial in vivo response in acute myeloid leukaemia in children without Down's syndrome: results of NOPHO-AML trials.

Lie SO, Abrahamsson J, Clausen N, Forestier E, Hasle H, Hovi L, Jonmundsson G, Mellander L, Gustafsson G.

Source

Department of Paediatrics, University Hospital, Rikshospitalet, Oslo, Norway.

Abstract

Three consecutive protocols for childhood acute myeloid leukaemia (AML) have been used in the Nordic countries since 1984: the Nordic Society for Paediatric Haematology and Oncology (NOPHO)-AML84 was of moderate intensity, NOPHO-AML88 of high intensity with upfront loading and aggressive consolidation. NOPHO-AML93 utilized the same treatment blocks as NOPHO-AML88, but after the first block those children with a hypoplastic non-leukaemic bone marrow were allowed to recover from aplasia. Poor responders received intensified induction therapy. Between January 1993 and December 2000, 219 children without Down's syndrome were entered on NOPHO-AML93. Compared with NOPHO-AML88, the event-free survival (EFS) at 7 years increased from 41% to 49%

(P = 0.06) and 7-year overall survival increased from 47% to 64% (P < 0.01). Toxic death during induction was reduced from 10% to 3%. Survival was similar in patients receiving stem cell transplantation or chemotherapy only in first remission. The major prognostic factors in NOPHO-AML93 were response to therapy and cytogenetics. A total of 67% of patients achieved remission after the first induction course and showed an EFS of 56% compared with 35% in those not in remission (P < 0.01). Cytogenetic results were obtained in 95% of patients. Patients with t(9;11) (p22;q23) (n = 16) experienced a significantly better EFS (86%) than other cytogenetic groups. The overall outcome was improved by employing the previous toxic protocol with different timings, and through individualizing therapy according to the initial response of the patient.

PMID:

12846889

[PubMed - indexed for MEDLINE]

Related citations

51. Br J Haematol. 2003 May;121(4):566-77.

Cytogenetic abnormalities in childhood acute myeloid leukaemia: a Nordic series comprising all children enrolled in the NOPHO-93-AML trial between 1993 and 2001.

Forestier E, Heim S, Blennow E, Borgström G, Holmgren G, Heinonen K, Johannsson J, Kerndrup G, Andersen MK, Lundin C, Nordgren A, Rosenquist R, Swolin B, Johansson B; Nordic Society of Paediatric Haematology and Oncology (NOPHO); Swedish Cytogenetic Leukaemia Study Group (SCLSG); NOPHO Leukaemia Cytogenetic Study Group (NLCSG).

Source

Departments of Clinical Sciences, Paediatrics, University of Umeå, Sweden. erik.forestier@pediatri.umu.se

Abstract

Between 1993 and 2001, 318 children were diagnosed with acute myeloid leukaemia (AML) in the Nordic countries. The patient group comprised 237 children < 15 years of age with de novo AML, 42 children < 15 years with Down syndrome (DS) and de novo AML, 18 adolescents 15-18 years of age with de novo AML, and 21 children < 15 years with treatment-related AML (t-AML). The first group was all-inclusive, yielding an annual childhood de novo AML incidence of 0.7/100 000. Cytogenetic analyses were successful in 288 cases (91%), and clonal chromosomal abnormalities were detected in 211 (73%). The distribution of ploidy levels were pseudodiploidy (55%), hyperdiploidy (34%) and hypodiploidy (11%). The most common aberrations (> 2%) were + 8 (23%) (as a sole change in 6.2%), 11q23-translocations, including cryptic MLL rearrangements (22%) [t(9;11)(p21-22;q23) in 11%], t(8;21)(q22;q22) (9.0%), inv(16)(p13q22) (6.2%), -7/7q- (5.2%), and t(15;17)(q22;q12) (3.8%). Except for +8, these abnormalities were rare in group 2; only one DS patient had a t(8;21) and none had 11q23-translocations, t(15;17) or inv(16). In the t-AML group, three cases displayed 11q23-rearrangements, all t(9;11); and there were no t(8;21), t(15;17) or inv(16). Overall, the observed frequencies of t(8;21) and t(15;17) were lower, and frequencies of trisomy 8 and 11q23-translocations higher, than in previous studies. Furthermore, seven abnormalities that were previously reported as only single AML cases were also seen, meaning that der(4)t(4;11)(q26-27;q23), der(6)t(1;6)(q24-25;q27), der(7)t(7;11)(p22;q13), inv(8)(p23q11-12), t(11;17)(p15;q21), der(16)t(10;16)(q22;p13) and der(22)t(1;22)(q21;q13) are now classified as recurrent abnormalities in AML. In addition, 37 novel aberrations were observed, 11 of which were sole anomalies.

PMID:

12752097

[PubMed - indexed for MEDLINE]

Related citations

52. Cancer Chemother Pharmacol. 2003 Apr;51(4):311-20. Epub 2003 Mar 28.

High-dose methotrexate: on the relationship of methotrexate elimination time vs renal function and serum methotrexate levels in 1164 courses in 264 Swedish children with acute lymphoblastic leukaemia (ALL).

Skärby T, Jönsson P, Hjorth L, Behrentz M, Björk O, Forestier E, Jarfelt M, Lönnerholm G,

Höglund P.

Source

Department of Clinical Pharmacology, Lund University Hospital, 221 85 Lund, Sweden. tor.skarby@klinfarm.lu.se

Abstract

PURPOSE:

The objectives of the present study were to determine the relationship between methotrexate (MTX) elimination time and various aspects of renal function and to evaluate the prognostic value of elevated serum MTX and creatinine for delayed MTX elimination.

PATIENTS AND METHODS:

The majority of the 264 children were being treated for ALL. According to the NOPHO-92 protocol, 5 or 8 g MTX/m(2) was administered over 24 h. Serum creatinine was assessed daily. In 11 patients from one centre, renal function was studied in more detail using serum cystatin C, iohexol clearance, and urinary albumin, IgG and protein HC.

RESULTS:

Increased serum creatinine correlated significantly with the elimination time of MTX, whereas no indications were found of tubular or barrier function damage. Of the 1164 courses, 44 had delayed elimination of MTX (>/=120 h). Serum MTX >150 microM at the end of infusion had a sensitivity of 0.27 and a specificity of 0.94 to predict delayed MTX elimination, and >/=50% increase in serum creatinine during the first treatment day (creatinine ratio) had a sensitivity of 0.32 and a specificity of 0.99. The corresponding risk ratios were 5 and 19 for MTX >150 micro M and creatinine ratio, respectively. In courses with a normal elimination time (<72 h), 99% of the courses had a rise in serum creatinine of less than 50%.

CONCLUSIONS:

Elevation of serum creatinine by more than 50% is a better predictor of delayed elimination than the level of serum MTX at the end of MTX infusion, especially if information on previous creatinine measurements is used to reduce the impact of an occasionally low serum creatinine value before the start of the MTX infusion.

PMID:

12721759

[PubMed - indexed for MEDLINE]

Related citations

53. Leukemia. 2003 Jan;17(1):138-48.

Flow cytometric follow-up of minimal residual disease in bone marrow gives prognostic information in children with acute lymphoblastic leukemia.

Björklund E, Mazur J, Söderhäll S, Porwit-MacDonald A.

Source

Department of Pathology, Karolinska Hospital and Institutet, Stockholm, Sweden.

Abstract

Using flow cytometry (FC) and live gate (LG) analysis we have followed levels of minimal residual disease (MRD) in the bone marrow (BM) of 70 consecutive patients with childhood acute lymphoblastic leukemia (59 B precursor ALL and 11 T-ALL) treated according to the Nordic (NOPHO-92) protocols. Thorough studies of B and T cell antigen expression patterns in normal BM performed during BIOMED 1 Concerted Action on MRD, made it possible to tailor individual protocols of marker combinations for follow-up in 97% of patients. In 12% of LG analyses, the numbers of cells exceeded 10(6) and in 82% exceeded 10(5), giving the sensitivity level of MRD detection 10(-5) and 10(-4), respectively. The median follow-up time was 53 months. Patients with MRD levels > or = 0.01% at follow-up time-points during and after first induction, and at the end of treatment had significantly lower disease-free survival by comparison to patients with MRD values <0.01%. Seven of nine patient with recurrence in the BM showed under treatment persisting MRD levels > or = 0.01% of BM cells. This was also observed in another two patients with infant leukemia who relapsed. In conclusion, the investigation of levels and the dynamics of MRD by sensitive and quantitative FC can provide a basis for further clinical studies for at least upgrading of therapy.

PMID:

12529671

[PubMed - indexed for MEDLINE]

Related citations

54. Med Pediatr Oncol. 2003 Feb;40(2):82-7.

Post-induction residual disease in translocation t(12;21)-positive childhood ALL.

Seyfarth J, Madsen HO, Nyvold C, Ryder LP, Clausen N, Jonmundsson GK, Wesenberg F, Schmiegelow K.

Source

Department of Clinical Immunology, The National University Hospital, Rigshospitalet, Copenhagen, Denmark.

Abstract

BACKGROUND:

t(12;21)(p1 3;q22), the most frequent chromosomal translocation found in childhood acute lymphoblastic leukemia (ALL), occurs in approximately 25% of B-lineage ALL cases and has been claimed to carry a good prognosis.

PROCEDURE:

As part of the Nordic Society of Pediatric Hematology and Oncology (NOPHO) ALL-MRD 95 study, which includes children from Iceland, Norway, and Denmark diagnose d with ALL, patients were screened for the presence of t(12; 21) by reverse transcriptase-polymerase chain reaction (RT-PCR) at diagnosis, and their residual disease was quantified after 4 weeks of induction therapy (prednisolone, vincristine, doxorubicin, i.t. methotrexate) by a competitive, clone-specific, semi-nested PCR analysis.

RESULTS:

Among 96 children diagnosed with ALL, and quantified for post induction residual disease, 32 were t(12;21)-positive. The median residual disease was similar for B-precursor ALL patients with and without t(12;21) (0.009 vs. 0.03%, P = 0.12).

CONCLUSIONS:

Al though patients with t(12;21)-positive ALL have been claimed to have a good outcome, these data indicate that this does not reflect a high sensitivity to prednisolone, vincristine, and doxorubicin given during induction therapy.

PMID:

12461790

[PubMed - indexed for MEDLINE]
Related citations

55. Exp Hematol. 2002 Oct;30(10):1170-7.

Minimal residual disease quantification in childhood acute lymphoblastic leukemia by real-time polymerase chain reaction using the SYBR green dye.

Li AH, Forestier E, Rosenquist R, Roos G.

Source

Department of Medical Biosciences and Pathology, Umeå University, Umeå, Sweden.

Abstract

OBJECTIVE:

Clone specific immunoglobulin (Ig) and T-cell receptor (TCR) gene sequences can be used as molecular targets for detection of minimal residual disease (MRD) in acute lymphoblastic leukemia (ALL). Real-time quantitative PCR (RQ-PCR) with no need for post-PCR processing is an attractive approach for detection and quantification of specific DNA or RNA sequences. In the present study we evaluated a real-time PCR-based technology for MRD

quantification in children with precursor-B ALL.

MATERIALS AND METHODS:

DNA samples from 36 children with newly diagnosed precursor-B ALL were available for molecular analysis. All patients were uniformly treated according to the Nordic Society of Pediatric Hematology and Oncology (NOPHO) protocols from 1992. A real-time PCR assay was applied for MRD quantification using LightCycler technology and the SYBR green fluorescent dye for detection of clone-specific Ig and TCR gene rearrangements as target sequences. The specificity of the PCR products was verified by melting curve analysis.

RESULTS:

Thirty-four of the 36 children with precursor-B ALL (94%) displayed at least one clonal Ig heavy chain (IgH) or TCR gene sequence useful as a molecular target. These clone-specific targets were successfully applied for real-time PCR quantification in all but one patient. Melting curve analysis was important for identifying all specific PCR products. In 32 pediatric precursor-B-ALL patients an MRD level >/=10(-3) at day 29 during induction treatment was significantly correlated with later bone marrow relapse (p = 0.0025).

CONCLUSIONS:

Real-time PCR using clone-specific primers and the SYBR green dye for detection is a feasible technique for identifying patients at risk for relapse. This approach provides an easily applicable tool for detection of IgH/TCR gene rearrangements in the routine setting. Melting curve analysis allowed clear distinction between specific rearrangements and unspecific background signals.

PMID:

12384148

[PubMed - indexed for MEDLINE]

Related citations

56. Leukemia. 2002 Oct;16(10):2037-45.

Deletion of the Ink4-locus (the p16ink4a, p14ARF and p15ink4b genes) predicts

relapse in children with ALL treated according to the Nordic protocols NOPHO-86 and NOPHO-92.

Calero Moreno TM, Gustafsson G, Garwicz S, Grandér D, Jonmundsson GK, Frost BM, Mäkipernaa A, Rasool O, Savolainen ER, Schmiegelow K, Söderhäll S, Vettenranta K, Wesenberg F, Einhorn S, Heyman M.

Source

Research Laboratory of Radiumhemmet, CCK Karolinska Hospital, Stockholm, Sweden.

Abstract

Inactivation of the Ink4 gene locus locus on 9p comprising the tumour suppressor gene p16ink4a and its neighbours p14ARF and p15ink4b is common in childhood acute lymphoblastic leukaemia (ALL), but the prognostic significance is controversial. DNA from 230 patients was retrospectively analysed by Southern blotting, single strand conformation polymorphism (SSCP) and sequencing techniques. The results were correlated with clinical characteristics and outcome. One hundred and ninety-four fully analysed patients, similarly treated using the Nordic NOPHO-86 or the current NOPHO-92 protocols, were included in the outcome analysis. Deletions approached a minimally deleted region between the p16ink4a and p15ink4b genes, making the p14ARF gene the most commonly deleted coding sequence. Bi-allelic deletion was associated with high white blood cell count (WBC) ($P < 0.001$), T cell phenotype ($P < 0.001$) and mediastinal mass ($P < 0.001$). Patients with Ink4 locus bi-allelic deletions had an inferior pEFS ($P < 0.01$) and multivariate analysis indicated that bi-allelic deletion of the p16ink4a and the p14ARF genes was an independent prognostic risk factor ($P < 0.05$). Sub-group analysis revealed a pronounced impact of deletion status for high-risk patients, ie with high WBC. Deletion-status and clinical risk criteria (WBC) could thus be combined to further differentiate risk within the high-risk group. The analysis of the Ink4 locus adds independent prognostic information in childhood ALL treated by Nordic protocols and may help in selection of patients for alternative treatment.

Free Article
PMID:

12357355

[PubMed - indexed for MEDLINE]
Related citations

57. Ther Drug Monit. 2002 Aug;24(4):502-6.

Serious neutropenia in ALL patients treated with L-asparaginase may be avoided by therapeutic monitoring of the enzyme activity in the circulation.

Ylikangas P, Mononen I.

Source

Department of Clinical Chemistry, Päijät-Häme Central Hospital, Lahti, Finland.

Abstract

The antineoplastic enzyme L-asparaginase is commonly used for the induction of remission in acute lymphoblastic leukemia (ALL). L-Asparagine is an essential amino acid for many lymphoid tumor cells and L-asparaginase catalyzes its conversion to L-aspartic acid and ammonia. The dosage of this highly toxic drug is individualized based on the body surface area of the patient, but monitoring of L-asparaginase activity during the L-asparaginase therapy is not commonly used. We measured L-asparaginase activity in the serum of ten children (aged 3-13 y) with ALL (ALL NOPHO-92 standard or intermediate risk groups) during their L-asparaginase therapy. L-asparaginase was given 30,000 IU/m2 IM during days 37-46 of the induction therapy and no other chemotherapeutic drug except for prednisone was given at the same time. We observed that this dosage schedule resulted in almost 6-fold differences in the serum activity of L-asparaginase between the patients. There was also a relationship between the area under the L-asparaginase activity-time curve (AUC) and even peak L-asparaginase activity in serum during the enzyme therapy and neutropenia after the therapy in the patients: the higher the AUC or peak value was, the more severe was the neutropenia in the patients after treatment. Monitoring L-asparaginase in serum could be useful in optimization of the therapy with this toxic drug.

PMID:

12142634

[PubMed - indexed for MEDLINE]

Related citations

58. Br J Clin Pharmacol. 2001 Oct;52(4):433-7.

Monitoring of Erwinia asparaginase therapy in childhood ALL in the Nordic countries.

Albertsen BK, Schrøder H, Jakobsen P, Müller HJ, Carlsen NT, Schmiegelow K.

Source

Centre for Clinical Pharmacology, University of Aarhus, Aarhus, Denmark. bka@farm.au.dk

Abstract

AIMS:

Evaluation of L-asparaginase therapy in the NOPHO-92 ALL-protocol (treatment protocol of acute lymphoblastic leukaemia of the Nordic Society of Paediatric Haematology and Oncology, initiated in 1992) after intravenous and intramuscular administration of Erwinia asparaginase during induction and re-induction therapy.

METHODS:

Forty children with newly diagnosed acute lymphoblastic leukaemia received Erwinia asparaginase (30 000 IU/m2 i.v. or i.m.) during induction therapy (every day for 10 days), and 19 children received Erwinia asparaginase (30 000 IU/m2 i.v. or i.m.) during re-induction therapy (twice a week for 2 weeks). Within the treatment periods asparaginase trough activity (using a spectrophotometric assay) was determined on specific days. The goal of therapy is complete L-asparagine depletion, which asparaginase activities above 100 IU l(-1) have been shown to ensure. Therefore determination of L-asparagine (using a h.p.l.c. method) was performed only in plasma samples with asparaginase activities below 100 IU l(-1).

RESULTS:

During induction therapy 92.2% of the trough enzyme activities were above 500 IU l(-1) for the i.v.-treated patients, and 92.4% of the trough enzyme activities were above 500 IU l(-1) for the i.m.-treated patients. During re-induction therapy 64.7% of the trough enzyme activities were below 100 IU l(-1) in the i.v.-treated group, and 73.3% of the trough enzyme activities were below 100 IU l(-1) in the i.m.-treated group. For trough enzyme activities below 100 IU l(-1) L-asparagine depletion was complete in two thirds of the samples.

CONCLUSIONS:

In the NOPHO-92 ALL-protocol L-asparaginase treatment during induction therapy was unnecessarily intense, but during the re-induction phase it appeared inadequate.

PMCID: PMC2014586

Free PMC Article
PMID:

11678787

[PubMed - indexed for MEDLINE]
Related citations

59. Leukemia. 2000 Dec;14(12):2267-75.

Improving outcome through two decades in childhood ALL in the Nordic countries: the impact of high-dose methotrexate in the reduction of CNS irradiation. Nordic Society of Pediatric Haematology and Oncology (NOPHO).

Gustafsson G, Schmiegelow K, Forestier E, Clausen N, Glomstein A, Jonmundsson G, Mellander L, Mäkipernaa A, Nygaard R, Saarinen-Pihkala UM.

Source

Childhood Cancer Research Unit, Karolinska Institute, Stockholm, Sweden.

Abstract

In this population-based material from the five Nordic countries (Denmark, Finland, Iceland, Norway and Sweden), 2860 children below 15 years of age were diagnosed with acute

lymphoblastic leukemia (ALL) from July 1981 to June 1998. The annual incidence was 3.9/100,000 children and was stable throughout the study period. The development from regional or national protocols to common Nordic treatment protocols for all risk groups was completed in 1992 through a successive intensification with multidrug chemotherapy, including pulses of methotrexate in high doses and avoidance of cranial irradiation in most children. The overall event-free survival (EFS) at 5 years has increased from 56.5 +/- 1.7% in the early 1980s to 77.6 +/- 1.4% during the 1990s. The main improvements were seen in children with non-high risk leukemia. In high-risk patients, progress has been moderate, especially in children with high WBC (> or =100 x 10(9)/l) at diagnosis. During the last time period (January 1992-June 1998), only 10% of the patients have received cranial irradiation in first remission, while 90% of the patients have received pulses of high dose methotrexate (5-8 g/m2) isolated or combined with high-dose cytosine arabinoside (total dose 12 g/m2) plus multiple intrathecal injections of methotrexate as CNS-targeted treatment, not translating into increased cumulative incidence of CNS relapse.

PMID:

11187918

[PubMed - indexed for MEDLINE]

Related citations

60. Eur J Haematol. 2000 Mar;64(3):194-200.

Cytogenetic findings in a population-based series of 787 childhood acute lymphoblastic leukemias from the Nordic countries. The NOPHO Leukemia Cytogenetic Study Group.

Forestier E, Johansson B, Borgström G, Kerndrup G, Johansson J, Heim S.

Source

Department of Clinical Science, University of Umeå, Sweden.
Erik.Forestier@Pediatri.umu.se

Abstract

Different types of leukemia are characterized by different patterns of nonrandom chromosomal aberrations, but the frequencies with which the various karyotypic subtypes are seen differ among cytogenetic laboratories, countries, and geographic regions. During the 12-yr period 1986- 1997, a total of 2054 children (< 15 yr of age) were diagnosed with acute lymphoblastic leukemia (ALL) in the five Nordic countries (Denmark, Finland, Iceland, Norway, and Sweden). Cytogenetic analyses were successfully performed in 1372 patients, 787 (57%) of whom displayed clonal chromosomal abnormalities. ALL with > or = 47 chromosomes was the most frequent cytogenetic subgroup (63%), with massive hyperdiploidy (> or = 52 chromosomes) and chromosome numbers in the tri- and tetraploid range, constituting 46% of all abnormal cases. ALL-associated translocations were found at low frequencies [11q23 translocations in 3.7%, t(9;22)(q34;q11) or del(22q) in 2.2%, t(4;11)(q21;q23) in 2.0%, t(11;19)(q23;p13) in 1.40%, t(1;19)(q23;p13) in 1.3%, and t(8;14)(q24;q32) in 1%]. Two rearrangements not previously reported in childhood ALL, but recurrent in this population-based material, were identified: der(7;9)(q10;q10) and t(9;12)(q22;p11-12), the molecular genetic consequences of which are unknown. Hyperdiploid childhood leukemias, especially those with a high hyperdiploid modal number, thus seem to be more frequent and ALL-specific translocations less frequent in the Nordic countries than in other geographic regions. Although technical differences among laboratories cannot be ruled out as a cause of at least some of the frequency differences observed compared with previous studies, systematic differences in exposure to environmental oncogenic factors or in geographic/ethnic origin are an intriguing possibility.

PMID:

10997886

[PubMed - indexed for MEDLINE]

Related citations

61. Br J Haematol. 2000 Jul;110(1):147-53.

Prognostic impact of karyotypic findings in childhood acute lymphoblastic leukaemia: a Nordic series comparing two treatment periods. For the Nordic Society of

Paediatric Haematology and Oncology (NOPHO) Leukaemia Cytogenetic Study Group.

Forestier E, Johansson B, Gustafsson G, Borgström G, Kerndrup G, Johannsson J, Heim S.

Source

Department of Paediatrics, University of Umeå, Sweden. erik.forestier@pedatri.umu.se

Abstract

The prognostic impact of acquired chromosome abnormalities was evaluated in a population-based consecutive series of 768 children (< 15 years of age) with acute lymphoblastic leukaemia (ALL). The study cohort included all cases of cytogenetically abnormal childhood ALL diagnosed between 1986 and 1997 in the five Nordic countries (Denmark, Finland, Iceland, Norway and Sweden). The probability of event-free survival (pEFS) for the total cohort was 0. 72 +/- 0.02. When comparing the two treatment periods of July 1986 to December 1991 and January 1992 to December 1997, a better survival was seen for the latter time period (pEFS of 0.69 +/- 0.02 vs. 0.76 +/- 0.02, P = 0.05). Hypodiploidy with less than 45 chromosomes, t(9;22)(q34;q11) and 11q23 translocations were associated with a dismal outcome during the whole study period (pEFS of 0.57 +/- 0.12, 0.41 +/- 0.14 and 0.37 +/- 0.10 respectively). The poor prognostic influence of 11q23 rearrangements seemed to be restricted to infants and older children (> 10 years), who differed significantly from children aged 1-10 years in this regard (P < 0. 01). Patients with t(9;22)-positive ALL seemed to benefit from allogeneic bone marrow transplantation in first remission (P = 0.05). The pEFS for children with t(1;19)(q23;p13)-positive ALL was intermediate (0.63 +/- 0.17), with a tendency to a better outcome for patients with the unbalanced variant der(19)t(1;19). Hyperdiploid ALL patients, subdivided into moderate hyperdiploidy (47-51 chromosomes), massive hyperdiploidy (52-60 chromosomes) and cases in the tri-/tetraploid range (> 60 chromosomes) had the best outcome in the last treatment period (pEFS of 0.81 +/- 0.06, 0.80 +/- 0.04 and 0.88 +/- 0.07 respectively), unless t(1;19), t(8;14), t(9;22) or 11q23 translocations were present. In a multivariate analysis including white blood cell (WBC) count, immunophenotype, age, mediastinal mass, central nervous system involvement and leukaemia karyotype, only WBC and modal chromosome number were shown to be significant independent risk factors (P < 0.01).

PMID:

10930992

[PubMed - indexed for MEDLINE]

Related citations

62. Acta Paediatr. 1998 Nov;87(11):1151-61.

Intensified treatment of acute childhood lymphoblastic leukaemia has improved prognosis, especially in non-high-risk patients: the Nordic experience of 2648 patients diagnosed between 1981 and 1996. Nordic Society of Paediatric Haematology and Oncology (NOPHO)

Gustafsson G, Kreuger A, Clausen N, Garwicz S, Kristinsson J, Lie SO, Moe PJ, Perkkiö M, Yssing M, Saarinen-Pihkala UM.

Source

Childhood Cancer Research Unit, Karolinska Hospital, Stockholm, Sweden.

Comment in

- Acta Paediatr. 1999 Apr;88(4):360-2.

Abstract

In a multinational, population-based study from the five Nordic countries (Denmark, Finland, Iceland, Norway and Sweden), 2648 children below 15 y of age were diagnosed with acute lymphoblastic leukaemia (ALL) in the years 1981-1996. The annual incidence was 3.9/100000 children and was stable throughout the study period. The development from regional or national protocols to common Nordic treatment protocols for all risk groups was completed in 1992 through a successive intensification of therapy, based on multidrug chemotherapy including pulses of methotrexate in high doses and avoidance of cranial irradiation in most children. For children with non-B-cell ALL (n=2602), the event-free survival (p-EFS) increased from 0.53+/-0.02 (diagnosed 7/81-6/86) to 0.67+/-0.02 (7/86-12/91) to 0.78+/-0.02 (1/92-12/96). The corresponding p-EFS values at 5 y were 0.57, 0.70 and 0.78, respectively. The main improvements were seen in the group of children with non-

high risk leukaemia, with 5-y p-EFS values increasing from 0.60 to 0.76 and 0.85 for the three periods. In high-risk patients, progress has been moderate, especially in children with high white blood cell values at diagnosis. During the last 5-y period, only 10% of the patients received cranial irradiation in first remission while 90% of the patients received high doses of cytostatic infusions (methotrexate isolated or combined with cytarabinoside) and multiple intrathecal injections of methotrexate as CNS-adjusted treatment without any indication of an increased CNS relapse rate.

PMID:

9846917

[PubMed - indexed for MEDLINE]

Related citations

63. J Pediatr Hematol Oncol. 1997 Mar-Apr;19(2):102-9.

Impact of morning versus evening schedule for oral methotrexate and 6-mercaptopurine on relapse risk for children with acute lymphoblastic leukemia. Nordic Society for Pediatric Hematology and Oncology (NOPHO).

Schmiegelow K, Glomstein A, Kristinsson J, Salmi T, Schrøder H, Björk O.

Source

Section of Clinical Hematology and Oncology, Juliane Marie Center, University Hospital, Copenhagen, Denmark.

Abstract

PURPOSE:

To study the risk of non-B-cell acute lymphoblastic leukemia (ALL) relapse in relation to the

routines of administration of oral methotrexate (MTX) and 6-mercaptopurine (6MP) and to the erythrocyte (E) levels of the intracellular cytotoxic metabolites, that is, MTX polyglutamates and 6-thioguanine nucleotides (E-MTX and E-6TGN).

PATIENTS AND METHODS:

E-MTX and E-6TGN levels were measured at least three times (medians, eight and nine) in 294 children with non-B-cell ALL during oral MTX and 6MP therapy. For each patient, we registered (a) the individual circadian schedule of drug administration and (b) the coadministration of food, and (c) calculated a mean (m) of all E-MTX and E-6TGN measurements and (d) the product of mE-MTX and mE-6TGN (mE-MTX*6TGN), due to their synergistic action.

RESULTS:

A total of 42 patients were on a morning schedule, 219 were on an evening schedule, and 33 had miscellaneous routines. A total of 149 patients took the drugs with meals, 106 took the drugs between meals, and 39 had varying routines. With a median follow-up of 78 months, ALL has recurred in 66 patients. The patients on an evening schedule had a superior outcome [probability of event-free survival (pEFS) = 0.82 +/- 0.03 vs. 0.57 +/- 0.08; p = 0.0002], whereas the coadministration of food did not significantly influence outcome. Patients with a mE-MTX*6TGN < 813 [product of median mE-MTX (4.7 nmol/mmol Hb) and mE-6TGN (173 nmol/mmol Hb)] had an inferior outcome (pEFS = 0.70 +/- 0.04 vs. 0.85 +/- 0.03; p = 0.003), even if only patients on an evening schedule were analyzed. Thus, 109 patients on the MTX/6MP evening schedule with an mE-MTX*6TGN < or = 813 (nmol/mmol Hb)2 had a pEFS of 0.89 +/- 0.03 and a probability of continuous hematopoietic remission of 0.91 +/- 0.03.

CONCLUSIONS:

An evening schedule should be recommended for oral MTX/6MP maintenance therapy. The value of individual dose adjustments by E-MTX and E-6TGN remains to be determined in prospective randomized trials.

PMID:

9149738

[PubMed - indexed for MEDLINE]

Related citations

64. J Pediatr Hematol Oncol. 1997 Jan-Feb;19(1):28-34.

Studies of cerebral blood flow in children with acute lymphoblastic leukemia: case reports of six children treated with methotrexate examined by single photon emission computed tomography.

Osterlundh G, Bjure J, Lannering B, Kjellmer I, Uvebrant P, Márky I.

Source

Department of Pediatrics, Göteborg University, Sweden.

Abstract

PURPOSE:

Cranial irradiation has been widely used in order to prevent central nervous system (CNS) relapse of acute lymphoblastic leukemia (ALL) in childhood. Owing to the risk of late side effects, the Nordic Society for Pediatric Hematology and Oncology (NOPHO) replaced CNS irradiation with systemic high-dose methotrexate (HDMTX) in 1992. A prospective study of the effects of HDMTX and intrathecal MTX on CNS function is in progress at our center.

PATIENTS AND METHODS:

Six ALL patients underwent (99m)Tc-HMPAO single-photon emission computed tomography (SPECT) examination of regional cerebral blood flow (rCBF): three owing to neurological symptoms during treatment for ALL and the other three as part of the study.

RESULTS:

All the patients had various degrees of disturbed rCBF, which was more pronounced in the patients with neurological symptoms. One patient had severe symptoms and impaired rCBF after three intrathecal injections of MTX but before administration of HDMTX.

CONCLUSIONS:

Impaired cerebral perfusion was found in patients with and without neurological symptoms during treatment for ALL. The impact of these findings is still unknown, from both the long- and the short-term perspective. The possibility that intrathecal MTX alone or in combination

with HDMTX may affect rCBF through vascular damage should be further investigated, in terms of both mechanisms and clinical significance.

PMID:

9065716

[PubMed - indexed for MEDLINE]

Related citations

65. Leukemia. 1996 Aug;10(8):1269-73.

Intensive chemotherapy in childhood myelodysplastic syndrome. A comparison with results in acute myeloid leukemia.

Hasle H, Kerndrup G, Yssing M, Clausen N, Ostergaard E, Jacobsen N, Jacobsen BB.

Source

Department of Pediatrics, Odense University Hospital, Denmark.

Abstract

Myelodysplastic syndrome (MDS) in children is often considered as a variant of acute myeloid leukemia (AML) and frequently treated as such. However, there are very few reported data on the outcome following AML treatment. We analyzed 20 consecutive cases of de novo MDS treated in Denmark according to the NOPHO AML protocols. The results were compared with those obtained in 31 children with de novo AML treated with the same protocols, and with the outcome in 10 children with MDS who received allogeneic bone marrow transplantation (BMT) without prior AML therapy. Distinction between MDS and AML was made morphologically according to the FAB criteria. All children were followed for at least 37 months. The proportion of complete remission in MDS and AML was 35 percent vs 74 percent. (P = 0.005), resistant disease 25 percent vs 10 percent (P = 0.14), death in cytopenia 40 percent vs 16 percent (P= 0.06), and 3-year survival 15 percent vs 35 percent. (P = 0.11), respectively. Duration of treatment-related cytopenia was similar in MDS and AML, except for a longer period of leukopenia in MDS following the second course of induction. Seven of 10 MDS children receiving BMT without prior chemotherapy are long-term survivors. Our data suggest that conventional AML regimens are associated with a low

rate of complete remission, a high risk of death in cytopenia, and a limited curative potential in childhood MDS. Allogeneic BMT was in contrast associated with a high survival rate. BMT may, at least in some patients, be performed successfully without prior induction chemotherapy. The different response to therapy in MDS and AML may reflect fundamental biological differences between the two conditions.

PMID:

8709630

[PubMed - indexed for MEDLINE]

Related citations

66. Br J Haematol. 1996 Jul;94(1):82-8.

A population-based study of 272 children with acute myeloid leukaemia treated on two consecutive protocols with different intensity: best outcome in girls, infants, and children with Down's syndrome. Nordic Society of Paediatric Haematology and Oncology (NOPHO).

Lie SO, Jonmundsson G, Mellander L, Siimes MA, Yssing M, Gustafsson G.

Source

Department of Paediatrics, National Hospital of Norway, Oslo, Norway.

Abstract

From July 1984 the five Nordic countries (Denmark, Finland, Iceland, Norway and Sweden) have registered all children with acute myeloid leukaemia (AML) and treated them on two consecutive protocols of different intensity (NOPHO-84 and NOPHO-88). We probably have information on every child with this diagnosis in our region. We found an annual incidence of AML of 0.7 new cases per 100,000 children < 16 years of age. We observed a distinct peak of

incidence in the first 2 years of life. Children with Down's syndrome accounted for 13% of all cases. Eighty of 105 cases treated on NOPHO-84 achieved remission (78%). In NOPHO-88, 100/118 patients entered remission (85%). The overall event-free survival (p-EFS) for the two studies was 0.32 for NOPHO-84 and 0.42 for NOPHO-88. The majority of relapses occurred within 2 years of diagnosis. When looking for prognostic factors the strongest significant adverse factor found was male sex. Children with Down's syndrome (n = 35) had a very favourable outcome if they received therapy according to protocol, and infants (n = 26) had a superior outcome compared to children 1-2 years or > 10 years of age at diagnosis.

PMID:

8757513

[PubMed - indexed for MEDLINE]

Related citations

67. Bone Marrow Transplant. 1996 Mar;17(3):357-63.

Allogeneic bone marrow transplantation in first remission for children with very high-risk acute lymphoblastic leukemia: a retrospective case-control study in the Nordic countries. Nordic Society for Pediatric Hematology and Oncology (NOPHO).

Saarinen UM, Mellander L, Nysom K, Ringden O, Schroeder H, Glomstein A, Gustafsson G.

Source

Division of Pediatric Hematology-Oncology, Children's Hospital, University of Helsinki, Finland.

Abstract

Among children with high-risk (HR) ALL there are subgroups with very-high-risk (VHR)

features and poor prognosis despite developments in conventional chemotherapy for childhood ALL. We evaluated the outcome of VHR-ALL in children receiving allogeneic BMT (allo-BMT) in first remission (1CR) in a retrospective case-control study. In the population-based ALL material of the five Nordic countries, 22 children with VHR-ALL have undergone allo-BMT in 1CR between 1981-1991. We compared the outcome in these 22 children with 44 closely matched control patients who received conventional chemotherapy on HR-ALL protocols, as well as with a group of 405 children representing the remaining HR-ALL patients in the Nordic ALL database. The disease-free survival at 10 years was 73% in children receiving allo-BMT in 1CR, 50% in the matched controls (P = 0.02), and 59% in the remaining HR-ALL patients. The good prognosis of the allo-BMT group was due to a low relapse rate of 9%, as opposed to 41% in the group of matched controls. The superiority of allo-BMT as therapy in 1CR was mainly apparent in those with a very high WBC of > or = 100 x 10(9)/I at diagnosis; in the allo-BMT group 9/10 survived, as opposed to 8/20 of the matched controls (P = 0.03). We conclude that allo-BMT in 1CR should be seriously considered for children with a matched sibling donor and a VHR-ALL with WBC of > or = 100 and other established VHR criteria.

PMID:

8704687

[PubMed - indexed for MEDLINE]

Related citations

68. Med Pediatr Oncol. 1995 Nov;25(5):372-8.

Outcome after first relapse in children with acute lymphoblastic leukemia: a population-based study of 315 patients from the Nordic Society of Pediatric Hematology and Oncology (NOPHO).

Schroeder H, Garwicz S, Kristinsson J, Siimes MA, Wesenberg F, Gustafsson G.

Source

Department of Pediatrics, University Hospital of Aarhus, Denmark.

Abstract

This study reports the outcome after relapse of acute lymphoblastic leukemia (ALL) in a population-based study of 809 children over 1 year of age diagnosed July 1981 through June 1986 and with non-B acute lymphoblastic leukemia in the five Nordic countries. By January 1994, 315 children had suffered at least one relapse. The bone marrow was involved in 216 cases. There were 69 isolated CNS relapses, 25 isolated testicular recurrences and five relapses in other extramedullary sites. Of the 315 children with relapse, 94 are still in a second complete remission 12-138 (median: 78) months after relapse. The overall probability of a second event free survival (P-2.EFS) and survival after relapse was 0.28 and 0.33 respectively. The probability of remaining in second remission at 11 years was significantly correlated to the duration of first remission ($P < 0.001$), the site of relapse ($P < 0.001$) and gender ($P = 0.004$). The P-2.EFS for early, intermediate, and late bone marrow involved relapses were 0.08, 0.19, and 0.50 respectively. For early, intermediate and late isolated CNS relapses the P-2.EFS were 0.21, 0.38 and 0.61, respectively. The P-2.EFS for boys with isolated testicular relapses was 0.69. Girls with isolated CNS relapse ($P < 0.001$) and with bone marrow involved relapse ($P = 0.04$) had a significantly better prognosis than boys. Children with initial high risk criteria, especially T-ALL and mediastinal mass who relapsed, had a very poor prognosis. Conclusion: In this population-based study, about 30% of children with ALL obtained a long second remission and possible cure.

PMID:

7674994

[PubMed - indexed for MEDLINE]

Related citations

69. J Pediatr Hematol Oncol. 1995 May;17(2):163-6.

Childhood non-Hodgkin's lymphoma in the five Nordic countries. A five-year population-based study from the Nordic Society of Pediatric Hematology and Oncology.

Márky I, Schmiegelow K, Perkkiö M, Jónsson OG, Storm-Mathiesen I, Gustafsson G,

Kreuger A, Langmark F.

Source

Nordic Society of Pediatric Hematology and Oncology (NOPHO), Sweden.

Abstract

PURPOSE:

The comparable health-care organizations and common Cancer Registry for childhood malignancies in the five Nordic countries offered an opportunity to conduct an epidemiological study on a reasonable number of childhood non-Hodgkin's lymphoma (NHL) cases collected in a population-based manner.

MATERIAL AND METHODS:

All childhood cases (0-14.9 years at diagnosis) reported during the 5-year period of 1985-1989 to the Nordic Society of Pediatric Hematology and Oncology (NOPHO) Cancer Registry for childhood malignancies were reviewed and analyzed according to age, Murphy's stage, gender, site, and survival.

RESULTS:

The annual incidence of NHL is 0.7 per 100,000 children in the five Nordic countries, constituting 5% of all childhood malignancies. Age distribution was even; the male/female ratio was 3:1. Age and stage were shown by Cox regression analysis to be independent prognostic factors. Older age and lower stage affected outcome favorably. The stage and site distribution was similar to previous reports. Survival data were in accordance with those expected with modern treatment protocols.

CONCLUSIONS:

The incidence and relative frequency of NHL in childhood in the five Nordic countries is in agreement with previously reported data, but the even distribution of cases throughout childhood is a new finding. Older age at onset and stage of disease affect outcome favorably, whereas male gender contrary to acute lymphoblastic leukemia was not found to affect outcome.

PMID:

7749767

[PubMed - indexed for MEDLINE]

Related citations

70. J Clin Oncol. 1995 Feb;13(2):345-51.

Risk of relapse in childhood acute lymphoblastic leukemia is related to RBC methotrexate and mercaptopurine metabolites during maintenance chemotherapy. Nordic Society for Pediatric Hematology and Oncology.

Schmiegelow K, Schrøder H, Gustafsson G, Kristinsson J, Glomstein A, Salmi T, Wranne L.

Source

Nordic Society for Pediatric Hematology and Oncology, Copenhagen.

Abstract

PURPOSE:

During maintenance chemotherapy for childhood acute lymphoblastic leukemia (ALL), the cytotoxic metabolites of methotrexate (MTX polyglutamates) and mercaptopurine (6MP) (thioguanine nucleotides [6TGN]) accumulate intracellularly, including in erythrocytes (E-MTX and E-6TGN) with large interindividual variations. In the present Nordic Society for Pediatric Hematology and Oncology (NOPHO) study, the relation of E-MTX and E-6TGN to relapse risk was explored.

PATIENTS AND METHODS:

Two hundred ninety-seven patients with non-B-cell ALL, aged 1 to 14 years, on oral MTX and 6MP had E-MTX and E-6TGN levels measured three to 35 (median, eight) and three to 75 (median, nine) times, respectively. For each patient, a mean of all E-MTX (mE-MTX) and E-6TGN (mE-6TGN) measurements was calculated, as well as the product of mE-MTX and mE-6TGN (mE-MTX-6TGN), since MTX and 6MP may have synergistic action.

RESULTS:

For patients in remission, the median mE-MTX and mE-6TGN values were 4.7 nmol/mmol hemoglobin (Hgb) (range, 0.4 to 10.3) and 173 nmol/mmol Hgb (range, 58 to 846). With a

median follow-up duration of 66 months for patients in remission, 64 patients relapsed. Cox regression analysis identified mE-MTX-6TGN and sex to be the most significant parameters to predict relapse (global P = .001). Factors that predicted a better prognosis were high mE-MTX 6TGN and female sex. Patients who had a mE-MTX-6TGN less than the product of the median mE-MTX and median mE-6TGN (813 [nmol/mmol Hgb]2) had a significantly poorer event-free survival (EFS) than did patients with higher values (5-year probability of EFS [pEFS5y], 0.70 v 0.86; P = .001).

CONCLUSION:

The pharmacokinetics of MTX and 6MP may have significant influence on the risk of relapse. The value of dose adjustments by E-MTX and E-6TGN remains to be determined.

PMID:

7531219

[PubMed - indexed for MEDLINE]

Related citations

71. Ann Med. 1992 Oct;24(5):319-23.

Progress in the treatment of childhood leukaemias.

Lie SO, Gustafsson G.

Source

Department of Pediatrics, University Hospital, Oslo, Norway.

Abstract

The Nordic Society for Pediatric Hematology and Oncology (NOPHO) has run a population-based registry on all cases of acute leukaemias in the Nordic countries since 1981. Data on close to 2000 children with these diagnoses are presented and used as a background for a general discussion of progress in the therapy of these challenging conditions. Our material is unique in that it is population based. The results obtained are comparable to those obtained by all other major cooperative groups. Since January 1992, the treatment protocols for all types of acute leukaemias in childhood have been harmonized in the Nordic countries.

PMID:

1418912

[PubMed - indexed for MEDLINE]
Related citations

72. Acta Paediatr. 1992 Jan;81(1):66-8.

Superior treatment results in females with high-risk acute lymphoblastic leukemia in childhood.

Lanning M, Garwicz S, Hertz H, Jonmundsson G, Kreuger A, Lie SO, Moe PJ, Salmi TT, Schröder H, Siimes MA, et al.

Source

Nordic Society of Pediatric Hematology and Oncology (NOPHO), Finland, Sweden.

Abstract

In this population-based study, 808 children aged 1-15 years from Denmark, Finland, Iceland, Norway and Sweden, were diagnosed between July 1981 and June 1986 as suffering from non-B-cell acute lymphoblastic leukemia (ALL). The total population was 4.5 million children. Remission was achieved in 770/808 of the patients (95%). No sex difference in the remission rate was observed. The event free survival (EFS) at 102 months was 0.47 for males and 0.62 for females (p less than 0.001). There was no difference in EFS between males and females with standard-risk (0.58 and 0.60) or intermediate-risk (0.47 and 0.60) ALL, respectively. The EFS for females with high-risk ALL (0.68) was superior to that of males with high-risk ALL (0.31). Cox multivariant analysis showed that white blood cell count, sex, age and thrombocyte count were significant prognostic factors in all children. The intensified treatment according to the prognostic factors used in this study led to equal EFS for females with ALL from all risk groups. Males with high-risk ALL, however, did not benefit from the intensified treatment.

PMID:

1600307

[PubMed - indexed for MEDLINE]
Related citations

73. Acta Paediatr Scand. 1991 Dec;80(12):1220-8.

Second malignant neoplasms in patients treated for childhood leukemia. A population-based cohort study from the Nordic countries. The Nordic Society of Pediatric Oncology and Hematology (NOPHO).

Nygaard R, Garwicz S, Haldorsen T, Hertz H, Jonmundsson GK, Lanning M, Moe PJ.

Source

Department of Paediatrics, University Hospital of Trondheim, Norway.

Abstract

Among a cohort of 981 children who were followed up 4.3-26.5 years after cessation of antileukemic therapy, eight patients in remission of acute lymphoblastic leukemia (ALL) developed a distinctively new malignant disease. The second malignant neoplasms (SMN) included brain tumors, basal cell carcinomas, thyroid cancer, leiomyosarcoma and finally rhabdomyosarcoma in a patient who also had suffered from Hodgkin's disease while still on antileukemic treatment. Cranial radiation had been given to 58.4% of the patients in the study group, which consisted of 895 ALL patients who had completed various chemotherapy protocols. With one exception, the SMN appeared after 7.5-16.5 years at a location previously exposed to radiotherapy (RT). The estimated cumulative risk of SMN appearing within 20 years after diagnosis was 2.9%, and the corresponding risk for cases with RT was 8.1% compared to 0.3% for those without ($p = 0.05$). In a Cox regression analysis, the incidence rate ratio of SMN between patients with and without RT was 6.7 (95% CI = 0.8, 57.7). Based on age-, year- and sex-specific cancer incidence figures for Norway, the overall standardized incidence rate ratio (SIR) of SMN after treatment for ALL was 5.9 (95% CI = 2.2, 12.9). The number of brain tumors among patients who had received cranial radiation was nearly 27 times greater than expected, whereas no such tumors were seen after chemotherapy.

Individuals treated for childhood ALL are at increased risk of a new malignancy, and this seems mainly to be associated with previous irradiation.

PMID:

1785295

[PubMed - indexed for MEDLINE]

Related citations

74. Acta Paediatr Scand. 1989 Jan;78(1):104-9.

A population-based study of children with standard risk acute lymphoblastic leukemia in the five Nordic countries. A follow-up of 230 patients.

Gustafsson G, Berglund G, Garwicz S, Hertz H, Jonmundsson G, Moe PJ, Salmi TT, Seip M, Siimes MA, Yssing M.

Source

Nordic Society of Pediatric Hematology and Oncology (NOPHO), Sweden.

Abstract

Two hundred and thirty children with standard risk acute lymphoblastic leukemia (ALL) were diagnosed during a period of 3 years from July 1, 1981 to June 30, 1984 in the five Nordic countries. Criteria for standard risk ALL were age above 2.0 and below 10 years, WBC less than or equal to 20 x 10(9)/l, no evidence of CNS-involvement, mediastinal mass or T- or B-cell leukemia. The children were treated without prophylactic CNS irradiation, the majority (200 patients) according to two treatment programs. Follow-up of the entire group after a minimum of 30 months showed 64% of the children living in complete continuous remission with a probability of event-free survival of 0.60. The treatment results are not entirely satisfactory and intensification of therapy is required. A subgroup of patients with WBC between 10 and 20 x 10(9)/l and with adverse prognosis was identified, justifying a change of the present criteria for risk grouping.

PMID:

2919509

[PubMed - indexed for MEDLINE]
Related citations

75. Med Pediatr Oncol. 1989;17(2):127-30.

Radio-iodobenzylguanidine scintigraphy of neuroblastoma: conflicting results, when compared with standard investigations.

Schmiegelow K, Simes MA, Agertoft L, Berglund G, Storm-Mathisen I, Andreassen M, Salmi TT, Nygård R, Wiebe T, Kreuger A, et al.

Source

Nordic Society of Paediatric Hematology and Oncology (NOPHO).

Abstract

Seventy-one patients with neuroblastoma (NB) and 25 patients with other neoplastic or nonneoplastic diseases were studied with MIBG scintigraphy. Sensitivity and specificity at diagnosis were 94% and 88%, respectively. Of 52 patients with NB studied during follow-up, 14 had on one or several occasions conflicting results, when the findings at MIBG scintigraphy were compared to standard investigations (SI: CT scan, bone scan, x-ray, and ultrasound). The correlation of MIBG scintigraphy and SI to clinical outcome were in these 14 patients not significantly different. Adding VMA-excretion measurements did not significantly improve the predictive value of MIBG scintigraphy or SI. Patients with tumor-suspected lesions only at MIBG scintigraphy should be followed closely and the nature of the lesions should be explored through biopsy.

PMID:

2649775

[PubMed - indexed for MEDLINE]