Prophylactic Cranial Irradiation for Acute Lymphoblastic Leukemia in Childhood

In Ah Kim M.D., Ihl Bhong Choi M.D., Ki Mun Kang M.D.
Kyung Sub Shinn M.D., Hack Ki Kim M.D.*

Department of Radition Oncology & Pediatrics, St. Mary's Hospital, Catholic University, Medical College*

= Abstract =

Purpose : This report is the result of retrospective analysis for children who received prophylactic cranial irradiation combined with intrathecal chemotherapy.

Materials and Methods : Ninety children with ALL who had got bone marrow remission after induction chemotherapy received PCI. All but 3 children were treated with a dose of 1800 cGy as a standard regimen. While the PCI was given, all patients received intrathecal chemotherapy.

Results : Nine of 90 patients experienced CNS relapse during the duration of follow-up ranged from 36 to 96 months (median 60 months). Three children experienced BM relapse prior to CNS relapse. Therefore, CNS relapse rate as the first adverse event was 6.7 %. Median time interval of CNS relapse was 16 months from the first day of hematologic complete remission. Eighty-nine percent of patients who had CNS relapse were associated with hematologic relapse, and 78 % of CNS relpase occurred during maintenance chemotherapy (on-therapy relapse).

The CNS RFS at 2 and 5 years are 68 % and 42 %, respectively with median of 43 months. The prognostic factors affecting CNS RFS are initial WBC count (cut-off point of 50,000/μl), FAB subtype and CALGB risk criteria. The DFS at 2 and 5 years are 61 and 39 %, respectively with median of 34 months. The prognostic factors affecting DFS are initial WBC count (cut-off point of 50,000/μl), FAB subtype, POG and CALGB risk criteria.

Conclusions : In our study, 6.7 % of CNS relapse rate as a first adverse event was comparable with other studies. Various risk criteria was based on age at diagnosis and initial WBC count such as POG and CALGB criteria, had prognostic significance for CNS RFS and DFS. Prospective randomized trial according to prognostic subgroup based on risk criteria and systematic study about neuropsychologic function for long term survivors, are essential to determine the most effective and least toxic form of CNS prophylaxis.

Key Words : Acute lymphoblastic leukemia, Prophylactic cranial irradiation, Intrathecal chemotherapy

본 논문은 1996년 2월 1일 접수하여 1996년 3월 29일 채택되었음.

INTRODUCTION

The recognition that central nervous system (CNS) relapse constituted a major obstacle to overall treatment success stimulated efforts to prevent CNS disease. About 50 - 70 % of patients would experience CNS relapse if not given adequate prophylaxis.[1, 2] Since the first report from St Jude Children's Research Hospital on the efficacy of presymtomatic radiation therapy (RT) in preventing CNS relapse, cranial RT in combination with intrathecal chemotherapy has become a standard part of the treatment of childhood ALL[3].

Presented in this report are the results of retrospective analysis for the childrens who received prophylactic cranial irradiation (PCI) combined with intrathecal (IT) chemotherapy. The objective of this study was to analyze the efficacy of PCI with intrathecal chemotherapy for prevention of CNS relapse in childhood ALL.

MATERIALS AND METHODS

Ninety children with ALL who had got bone marrow remission after inducton chemotherapy received PCI at Department of Radiation Oncology, St. Mary's Hospital between July, 1987 and June, 1992. The duration of follow-up ranged from 36 to 96 months (median of 60 months).

Age ranged from 1 and 8/12 years to 15 years old. Fourty-nine children were male and 41 were female. Morphologically 62, 26 and 2 ALL were L1, L2 and L3, respectively, according to French-American-British (FAB) classification.

In our institution, remission induction chemotherapy included vincristine, doxorubicine, L-asparaginase and prednisolone. Remission status was evaluated on day 28 of induction therapy and patients achieving M1 marrow status (blast < 5%) received PCI. Consolidation and maintenence therapy were different regimen and dose-schedule in between standard risk group and high risk group. The criteria for high risk group included age at diagnosis(younger than 2 years or older than 10 years), initial WBC count (above 100,000/$\mu\ell$), absence of CALLA (common ALL antigen) in flow- cytometric analysis. Five patients referred from outside hospital received systemic chemotherapy according to CCSG protocol.

When the patients were categorized by criteria of CCSG, high and intermediate risk group were indicated for PCI. The good risk group were treated till 1989. But we excluded this group of patients from 1990.

The PCI was delivered with 6 MV photon beam (SAD 100). The target volume included the entire intracranial subarachnoid space. Especially for encompassing the extension of the subarachnoid space along the optic nerves, posterior retina and orbital apex were included. By convention, the caudal margin of field extended to the bottom of the second cervical vertebra. All patients except 3 children were treated with a dose of 1800 cGy in 10 fractions as a standard regiemen. One patient younger than 2 years received with a dose of 1260 cGy. Other two patients were treated with dose of 1980 cGy and 2160 cGy to compensate interruption of treatment.

While the PCI was given, all patients received intrathecal chemotherapy; 76 with intrathecal methotrexate alone (4-5 times), 14 with methtrexate, cytosine arabinoside and hydrocortisone. From July, 1987 to June 1988, this triple intrathecal chemotherapy was combined for patients with high risk criteria that were mentioned above.

After CNS prophylaxis, CSF was periodically studied during and after maintenance chemotherapy. Diagnostic criteria for CNS relapse were based on the report from Rome workshop in 1985; 5 or more mononuclear leukocyte/μl in of CSF and morphologically unequivocal lymphoblast in cytocentrifuge samples.

The end points of analyses were CNS relapse rate, pattern of CNS relapse, CNS relapse free survival rate (CNS RFS), disease free survival rate (DFS) and prognostic factors affecting CNS RFS and DFS.

The CNS RFS and DFS was calculated according to method of Kaplan and Meier. To identify the

prognostic factors, univariate analyses using log rank test and multivariate analyses using Cox's regression model for concomitant variables were performed.

RESULTS

1. CNS relapse

Nine of 90 patients experienced CNS relapse. Three patients experienced BM relapse prior to CNS relapse. Therefore, Six of 90 patients developed CNS relapse as the first adverse event (6.7 %). Early relapse within 1 year after CNS prophylaxis were noted in 4 children. Interval of CNS relapse ranged from 7 to 43 months from the first day of hematologic complete remission (median of 16

Table 1. CNS Relapse Rate by Pretreatment Factors

Pretreatment Factors	CNS Relapse/N* (%)
Initial WBC Count (per μl)	
≥20,000	6/38 (15.7)
< 20,000	3/52 (7.7)
≥50,000	5/48 (10.4)
< 50,000	4/42 (9.5)
Age at Diagnosis (years old)	
< 3 or > 9	3/19 (15.8)
3 - 9	6/71 (8.5)
FAB Subtype	
L1	6/62 (9.6)
L2	3/26 (11.5)
L3	0/ 2 (0.0)

* N; number of patients

Table 2. CNS Relapse Rate by Various Risk Criteria

Study	Prognostic Group*	No of patients (%)	Relapse Rate (%)
CCG	Good Prognosis Initial WBC < 10000 Age at Dx 3-6 Yrs old	8 (8.8)	0/8 (0)
	Intermediate Prognosis WBC 10000 - 50000 & Any Age WBC < 10000 & Age < 3 or > 6	34 (37.7)	4/34 (11.8)
	Poor Prognosis WBC > 50000 & Any Age	48 (53.5)	5.48 (10.4)
POG	Good Prognosis Initial WBC < 10000 Age at Dx 2-9 Yrs old	22 (24.4)	1/22 (4.6)
	Average Prognosis WBC 10000 - 90000 & Any Age WBC < 10000 & Age < 2 or > 9	45 (50.0)	4/45 (8.9)
	Poor Prognosis WBC > 100000 & Age < 3 or > 5	23 (25.6)	4/23 (17.4)
CALGB	Standard Risk Initial WBC < 30000 Age at Dx 3-7 Yrs old	31 (34.4)	2/31 (6.5)
	Increased Risk Initial WBC > 30000 Age at Dx < 3 or > 7	59 (65.6)	7/59 (12.0)
St. Jude XI	Better Prognosis Initial WBC < 25000 Age at Dx 2-9 Yrs old	33 (36.6)	2/33 (6.1)
	Worse Prognosis Initial WBC > 25000 Age at Dx < 2 or > 9	57 (63.4)	7/57 (12.3)
Rome Workshop	Good Prognosis Initial WBC < 50000 Age at Dx 1-9 Yrs old	43 (47.7)	4/43 (9.3)
	Poor Prognosis Initial WBC > 50000 Age at Dx < 1 or > 9	47 (52.3)	5/47 (10.6)

* 15), 16)

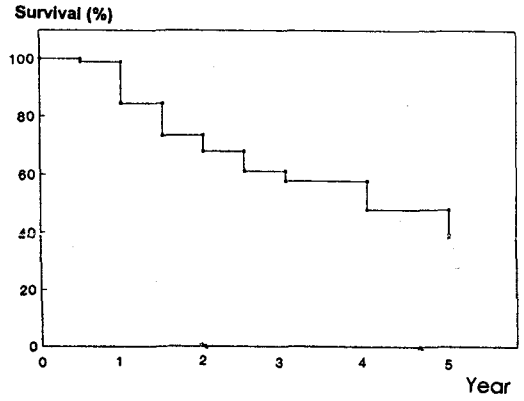

Fig. 1. CNS relapse free survival (RFS).

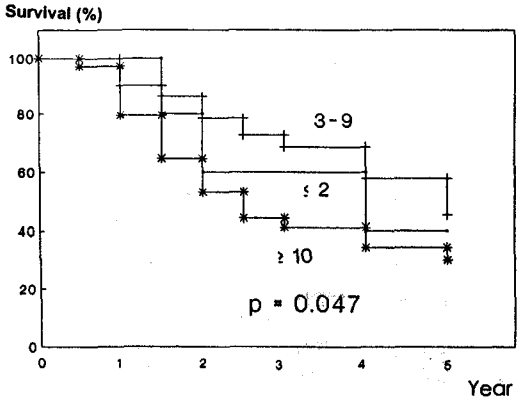

Fig. 3. CNS RFS by age at diagnosis.

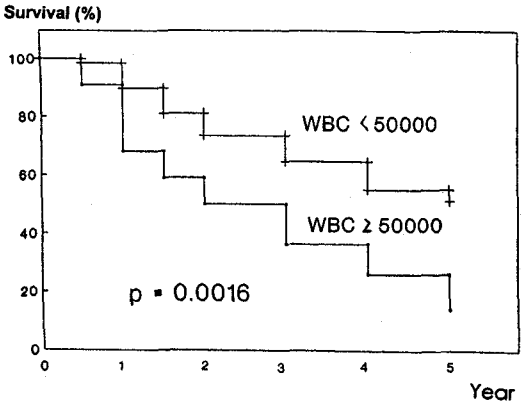

Fig. 2. CNS RFS by initial WBC count.

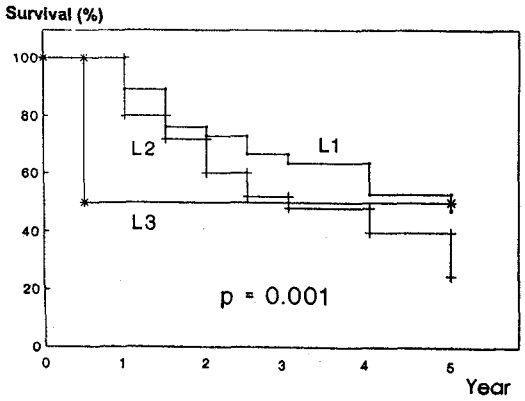

Fig. 4. CNS RFS by FAB classification.

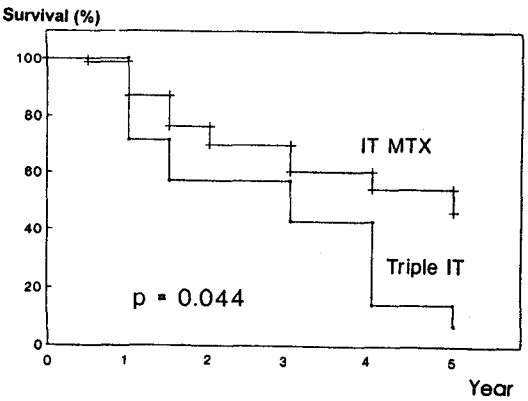

Fig. 5. CNS RFS by IT chemotherapy.

months). Three patients had a symptoms at that time of diagnosis for CNS relapse between periodic CSF examinations.

The 89 % of patients who had CNS relapse were associated with bone marrow relapse. In contrast, 42 % of patients with CNS remission experienced bone marrow relapse. Testicular relapse rate in patients with CNS relapse was approximately 2 fold higher than that in patients with CNS remission (11% vs 6%). Seven of 9 CNS relapses (78 %) occurred during maintenence chemotherapy (on-therapy relapse). All of two off-therapy relapses were combined with BM or testicular relapse. One patient had BM and testicular relapse and then subsequently developed CNS relapse 1 month later.

Table 1 shows the CNS relapse rates according

to pretreatment factors such as initial WBC count, age at diagnosis and FAB subtype. The CNS relapse rate of the patients treated with triple intrathecal chemotherapy had higher CNS relapse rate than that of IT MTX alone group (8 % vs 21 %).

Table 2 shows the CNS relapse rate according to risk criteria of CCG, POG, CALGB, St. Jude Children's Hospital Study XI and Rome Workshop.

2. CNS relapse free survival

The CNS relapse free survival (CNS RFS) rate at 2 and 5 years were 68 %, 42 %, respectively with median time of 43 months (Fig. 1). CNS RFS

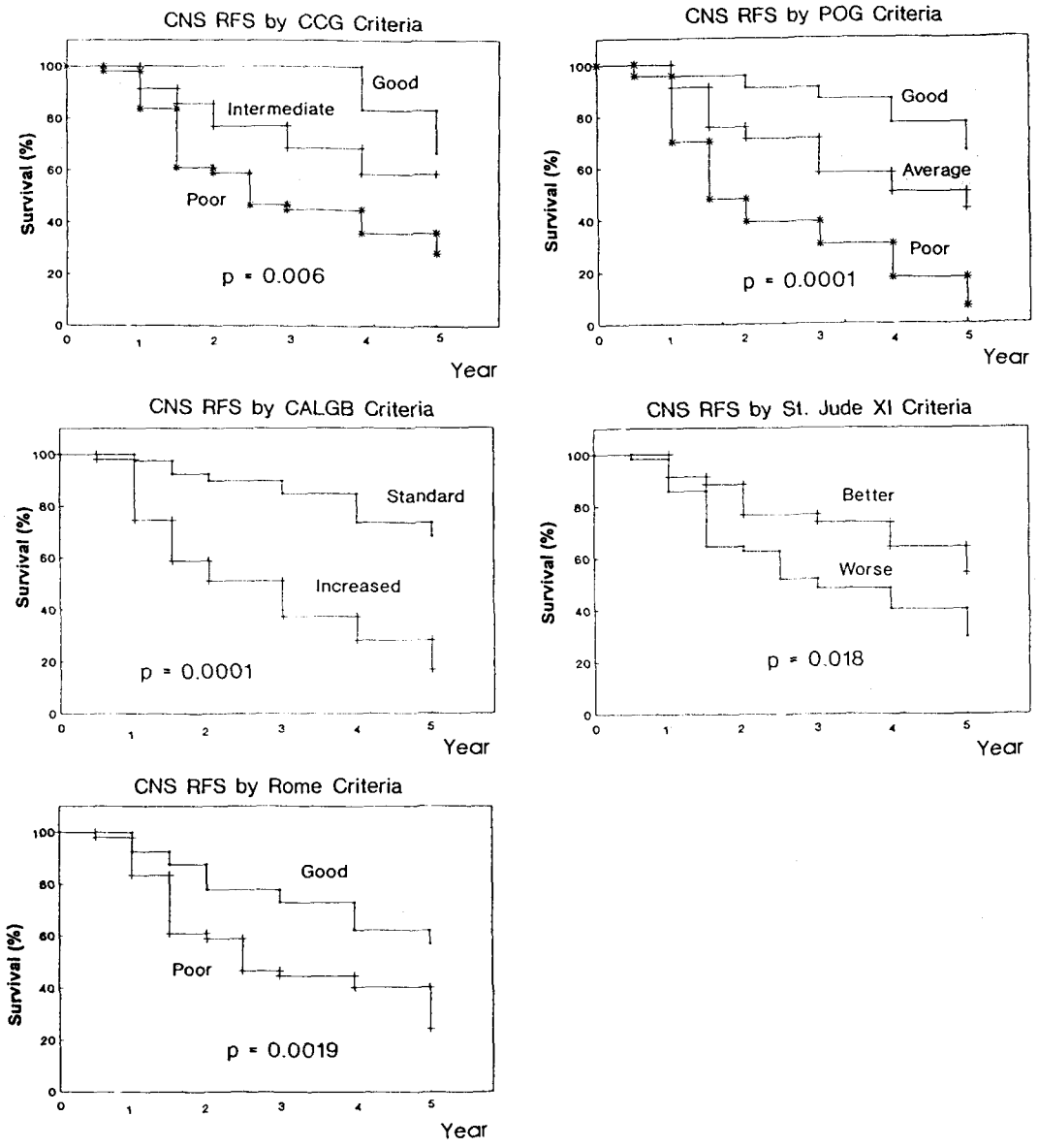

Fig. 6. CNS RFS by various risk criteria.

according to initial WBC count had significant difference at a cut-off point of 50000/μl (Fig. 2). CNS RFS of who are 3-9 years old at the age at diagnosis had significantly higher than that of who were below 3 years old or above 9 years old (Fig. 3). CNS RFS according to FAB classification had significant difference (Fig. 4). The triple intrathecal chemotherapy group had significantly inferior CNS RFS compared with intrathecal MTX alone group (Fig. 5).

Fig. 6 shows CNS RFS according to various risk criteria by CCG, POG, CALGB, St. Jude XI study and Rome Workshop. All criteria had prognostic significance by univariate analysis. In multivariate analysis by Cox regression model, the factors affecting CNS RFS were initial WBC count (cut-off point of 50000/μl), FAB subtype and CALGB risk criteria (Table 3).

Table 3. Prognostic Factors for CNS RFS

Prognostic Factors	p-value	Risk Ratio
Initial WBC (20000)	0.379	0.667
Initial WBC (50000)*	0.002	1.950
Age at Dx (2, 10 Yrs)	0.086	0.837
FAB Subtype (L1, 2, 3)*	0.007	1.950
IT MTX vs Triple IT	0.078	0.112
CCG Risk Criteria	0.347	1.743
POG Risk Criteria	0.063	1.647
CALGB Risk Criteria*	0.009	3.020
St. Jude XI Risk Criteria	0.450	0.682
Rome Workshop Criteria	0.917	1.035

* statistically significant factors by Cox's regression model

3. Disease free survival

The disease free survival (DFS) rate at 2 and 5 years are 61 % and 39 %, respectively with median time of 34 months (Fig. 7). The DFS accoding to initial WBC count had significant difference at cut-off point of 50000/μl (Fig. 8). The DFS of who were 3-9 years old at the age at diagnosis had significantly higher than that of who were below 3 years old or above 9 years old (Fig. 9). The DFS according to FAB classification had significant difference (Fig. 10).

The triple intrathecal chemotherapy group had significantly inferior DFS compared with intrathecal MTX alone group (Fig. 11).

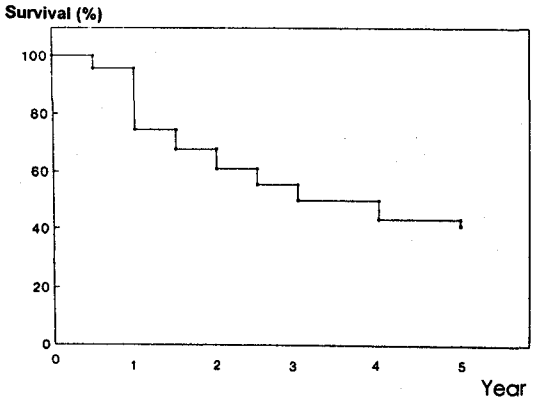

Fig. 7. Disease free survival (DFS).

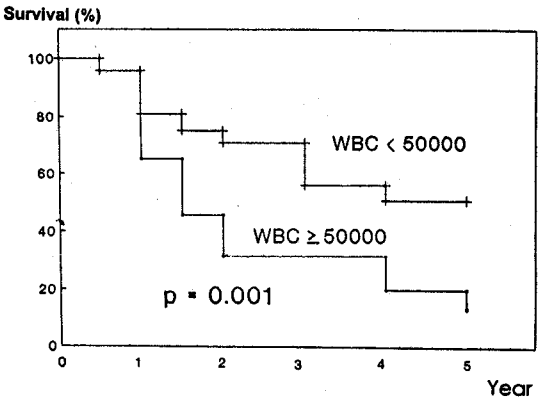

Fig. 8. DFS by initial WBC count.

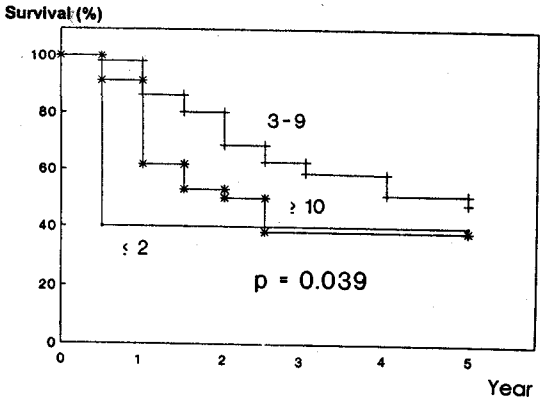

Fig. 9. DFS by age at diagnosis.

Fig. 12 shows DFS according to various risk criteria by CCG, POG, CALGB, St. Jude XI study and Rome Workshop. All criteria had prognostic significance by univariate analysis. In multivarite analysis by Cox regression model, the factors affecting DFS are initial WBC count (cut-off point of 50000/μl), FAB subtype, POG and CALGB risk criteria(Table 4).

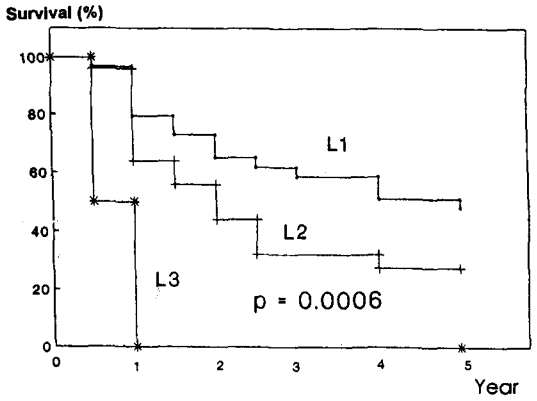

Fig. 10. DFS by FAB classification.

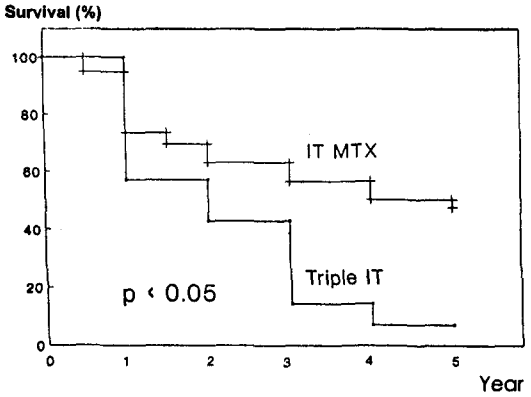

Fig. 11. DFS by IT chemotherapy.

Table 4. Prognostic Factors for DFS

Prognostic Factors	p-value	Risk Ratio
Initial WBC (20000)	0.229	0.613
Initial WBC (50000)*	0.001	2.543
Age at Dx (2, 10 Yrs)	0.086	0.913
FAB Subtype (L1, 2, 3)*	0.003	1.988
IT MTX vs Triple IT	0.071	0.114
CCG Risk Criteria	0.404	1.651
POG Risk Criteria	0.018	1.894
CALGB Risk Criteria*	0.011	2.867
St. Jude XI Risk Criteria	0.422	0.676
Rome Workshop Criteria	0.814	1.079

* statistically significant factors by Cox's regression model

DISCUSSIONS

In the era prior to the institution of CNS preventive therapy, the CNS became the most frequent site of initial relapse in children with ALL. In some studies, the incidence of this complication was as high as 75 %[1, 2]. With the use of intensive multiagent chemotherapy in early 1960s, remission was most often terminated by CNS leukemia. Clinical trials at St Jude children's Hospital established the efficacy of prophylactic cranial irradiation given early in the course of therapy. Protocol regimens using PCI (at dose levels of 24 Gy) and IT-MTX repeated intermittently throughout continuation of therapy have reported rates of initial CNS relapse below 5 %[3]. In this era, usually accepted dose is 24 Gy because of unacceptable results reported for 5 Gy and conflicting results with 12 Gy[4].

D'Angio et al reported that reduction of dose (18 Gy) did not result in significantly increase in overall incidence of CNS relapse, BM relapse or death rate in CCG study 101/143. They also confirmed that PCI (18 Gy)/IT-MTX provided effective CNS protection and seems superior to more extended fields[5].

The high continuous complete remission rates achieved in the Berlin-Frankfurt-Munster (BFM) group and Dana Faber Cancer Institute (DFCI) regimens include systematic use of PCI, confirming the low risk of meningeal relapse rate after PCI/IT-MTX[6, 7]. Kim et al reported the 14.2 % of initial total CNS relapse rate and 5.2 % of isolated CNS relapse rate[8]. In our study, 6.7 % of CNS relapse rate as a first adverse event is comparable with such data. The optimal CNS treatment is still controversial, and the number of patients who receive PCI varies greatly. Seventy percent of children on the BFM group protocols, 60 % of

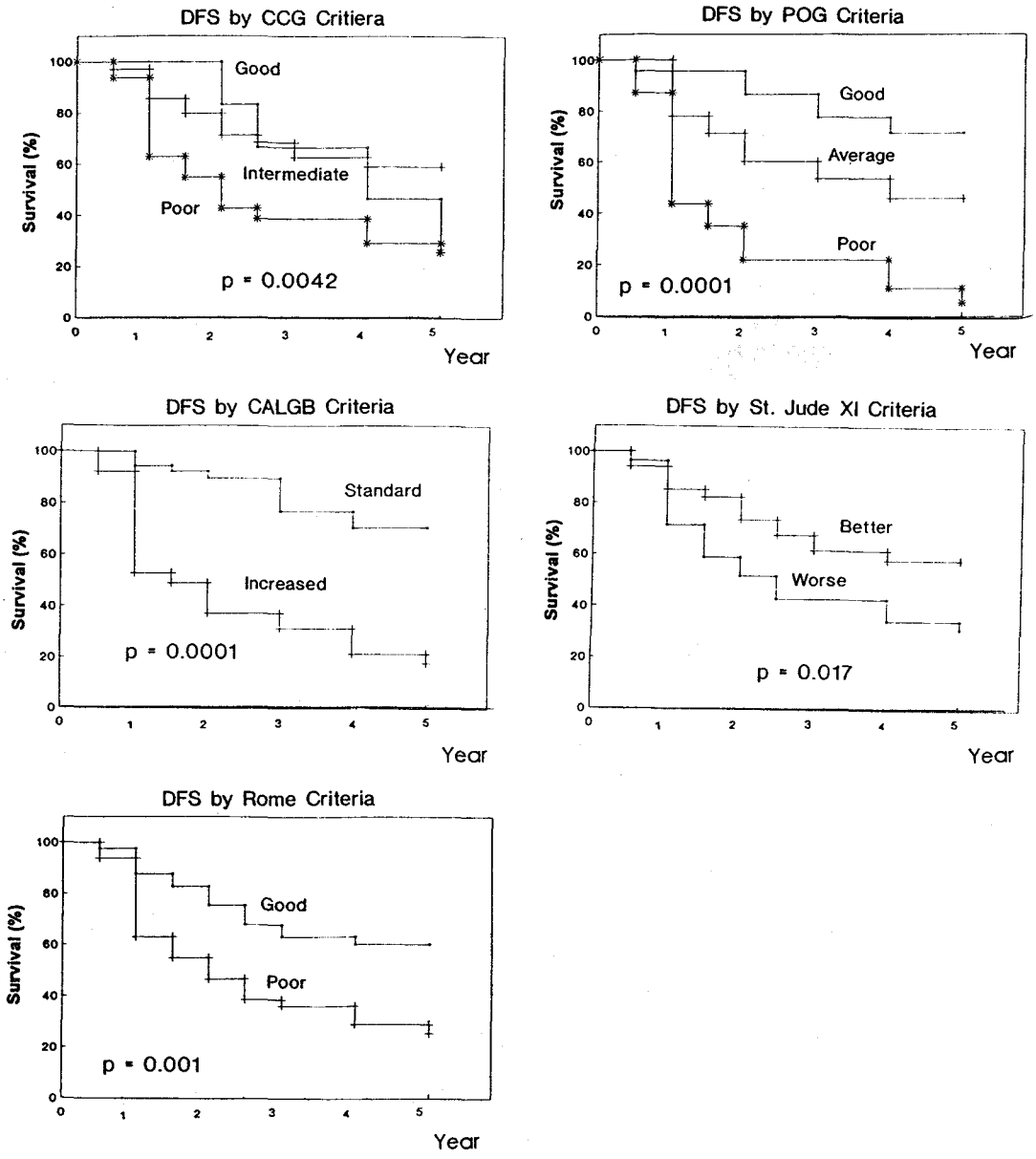

Fig. 12. DFS by various risk criteria.

patients treated on DFCI regiemens, 40 % of those at St. Jude Children's Research Hospital and 15 % of patients on Pediatric Oncology Group (POG) trial currently receive PCI. No children with newly diagnosed ALL receive PCI at the National Cancer Institute[9].

The use of IT-MTX alone early in the course of consolidative therapy has been ineffective. The Children's Cancer Study Group (CCSG) reported a 38% incidence of subsequent isolated CNS failure[10]. POG tested "triple IT" chemotherapy (MTX, cytosine arabinoside, prednisolone) given repeatedly throughout continuation therapy versus PCI plus limited duration IT-MTX[11]. At 4 years, the incidence of

primary CNS relapse was identical at 4 % with either form of therapy. The latter study has been criticized for lack of adequate follow-up or subsequent reporting and a relatively low rate of absolute survival and CCR, potentially masking a benefit from PCI in any of the prognostic groups[3].

Of 1776 children studied by CCG-101/141, early CNS relapse occured more frequently in patients less than 2 years old or 8 to 18 years old or in those with an initial WBC count greater than 20,000/ml, with a lymphomatous presentation, mediastinal mass, marked lymph node involvement and splenomegaly or with thrombocytopenia[12]. In our study, both of age at diagnosis (cut-off point of 2 and 9 years old) and initial WBC count (cut-off point of 50000/μl) were significant impact on the CNS RFS and DFS by univariate analysis but age didn't have significance by multivariate analysis.

Indeed, the majority of patients who experienced a CNS relapse died, not as a result of the morbidity of CNS disease, but rather as consequence of their subsequent BM relapse. The risk of BM relapse in SJROH series was 74 % after CNS failure compared to 46 % without CNS failure[13]. Our data show that about 2 fold higher BM and testicular relapse rate in CNS relapse (+) group than CNS relapse (-) group. Of 31 patients with a CNS relapse after intensive chemotherapy and PCI from DFCI, only 4 patients were alive without disease at 25-71 months. The impact of effective CNS prophylaxis seems obvious[6].

Building upon the apperent efficacy of systemic MTX in prolonging hematologic remission and preventing extramedullary relapse outside the CNS, a prospective study of IV/IT MTX versus PCI/IT-MTX in favorable risk ALL was persued at SJROH between 1979 and 1983. In a liberally defined favorable risk ALL population with WBC count < 10,000/μl, disease free survival at 4 years favored the IV/IT MTX group: 67 versus 56 %. Improved survival in the former group reflects both hematologic and testicular control; the rate of isolated CNS relapse was 10 % with IV/IT-MTX and 4% following PCI[14].

Although confirming the efficacy of regimen combining high dose IV MTX/IV chemotherapy, further analysis of SJROH study indicates a substantial impact of CNS therapy in those who might be categorized as intermediate risk (WBC count 25,000-100,000/μl). The latter subset experienced a significantly higher rate of isolated CNS relapse following IV/IT MTX: 30 % at 4 years compared to 2 % following PCI. Within ther better risk subset with WBC count < 25000/μl, there was no statistically significant difference in CNS relapse in this study[15].

Overall, many of studies demonstrate the value of PCI in eradicating occult meningeal leukemia, especially in subpopulation of high risk group. In general, there is strong evidences that the survival rate has increased when CNS relapse is prevented, but this findng is not unanimous as demonstrated by CALGB-7111 and CCG study-101 studies[4, 16].

What is clear is that a single treatment regimen should not be applied to all children with ALL. Those with a good prognosis and a low risk of CNS relapse can be treated with IT MTX alone, provided it is given periodically throughout maintenence therapy (CCG-161 study). Multiple IT drugs are not necessary. In patients at intermediate risk of CNS relapse, PCI may be successfully replaced by maintenence triple IT chemothrapy (POG studies), a combination of IT and intermediate dose IV MTX (CALGB-7611 study), or by high dose IV MTX alone (CCG-191 & NCI-7702 studies)[17]. At the end of prognosis spectrum, children at high risk of CNS relapse should not be treated with either IT or high dose IV MTX therapy alone. They either require PCI, prolonged treatment with combination IT chemotherapy, or a combination of single agent IT chemothrapy and high dose IV chemotherapy (CCG-191 & NCI-7702). Not all patients require the same amount or type of CNS prophylaxis to prevent CNS relapse. Within various subgroups of patients intrathecal chemotherapy alone in adequate dosage may provide protection, thus possibly avoiding the risk of long-term adverse effects that have been associated with CNS irradiation.

The increased number of patients now achieving long-term disease free survival makes it especially

important to determine the most effective, yet least toxic, form of CNS prophylaxis.

REFERENCES

1. **Evans AE, Gilbert ES, Zandstra R.** The increasing incidence of central nervous system leukemia in children. Cancer 1970; 26:404-409
2. **Hardisty RM, Norman PM.** Meningeal leukemia. Arch Dis Child 1967; 42:441-447
3. **Halperin EC, Constine LS.** Leukemia In: Halperin EC, Constine LS et al eds. Pediatric Radiation Oncology. 2nd ed. New York: Raven Press 1994; 12-39
4. **Nesbit ME, Sather HN, Robison LL, Ortega J, Litterman PS, D'Angio GJ, Hammond GD.** Presymptomatic central nervous system therapy in previously untreated childhood acute lymphoblastic leukemia: A report from Children's Cancer Study Group. Lancet 1981; 28:461-465
5. **D'Angio GJ, Litterman P, Nesbit ME, Sather HN, Hittle R, Ortega J, Donaldson M, Hammond GD.** Evaluation of radiation therapy factors in prophylactic central nervous system irradiation for childhood leukemia. A report from the Children's Cancer Study Group. Int J Radiat Oncol Biol Phys 1981; 7:1031-1038
6. **Gelber R, Sallan SE, Cohen HJ et al.** Central nervous system treatment in childhood acute lymphoblastic leukemia. Cancer 1993; 72:261-270
7. **Riehm H, Gadner H.** Results and significance of six randomized trials in four consecutive ALL-BFM studies. In: Buchner T, Schllong G et al eds. Hematology and Blood Transfusion. Berlin: Springer-Verlag 1990; 439-450
8. **IH Kim, DH Choi, JH Kim et al.** Effect of prophylactic cranial irradiation in acute lymphoblastic leukemia in children. J Korean Soc Ther Radiol 1989; 7:269-277
9. **Poplack DG, Reaman GH.** Successful prevention of CNS leukemia without cranial irradiation. Proc Am J Clin Oncol 1989; 8:213-219
10. **Nesbit ME, Sather HN, Ortega J et al.** Sanctuary therapy; A randomized trial of 724 children with previously untreated acute lymphoblastic leukemia. Cancer Res 1982; 42:674-680
11. **Sullivan MP, Humphery GB, Vietti TJ et al.** Superiority of conventional intrathecal methotrexate therapy, unmaintained, or radiotherapy in treatment for meningeal leukemia. Cancer 1975; 35:1066-1073
12. **Bleyer WA.** Central Nervous System Leukemia In: Gunz F and Henderson ES : Leukemia. 4th ed. New York: Grune & Stratton 1982; 865-911
13. **George SL, Och JJ, Mauer AM, Simone JV.** The importance of an isolated central nervous system relapse in children with acute lymphoblastic leukemia. J Clin Oncol 1985; 3:776-781
14. **Aboromowitch M, Och J, Pui CH et al.** High dose methotrexate improves clinical outcome in children with ALL: St. Jude Total Therapy Study X. Med Pediat Oncol 1988; 16:297 -230
15. **Aboromowitch M, Och JJ, Pui CH, Fairclough D, Murphy SB, Rivera GK.** Efficacy of high dose methotrexate in childhood acute lymphocytic leukemia; Analysis by contemporary risk classification. Blood 1988; 71:866-869
16. **Freeman AI, Weinberg V, Brecher ML et al.** Comparison of intermediate dose methotrexate with cranial irradiation for the post-induction treatment of acute lymphocytic leukemia in children. N Engl J Med 1984; 308:477-484
17. **Bleyer WA, Poplack DG.** Prophylaxis and treatment of leukemia in central nervous system leukemia and other sanctuaries. Semin Oncol 1985; 12:131-148

국문초록 =

소아 급성 림프모구성 백혈병의 예방적 전뇌 방사선조사

가톨릭의대 성모병원 방사선 종양학과, 소아과*

김인아 · 최일봉 · 강기문 · 신경섭 · 김학기*

목 적 : 소아 급성임파모구성 백혈병 환자에 있어 예방적 전뇌방사선조사 및 척수강내화학요법후 중추신경계 재발율, 재발양상, 중추신경계 무병생존율, 전체무병생존율및 이에 영향을 미치는 예후인자들을 알아보고자 하였다.

대상 및 방법 : 1987년 7월부터 1992년 6월까지 예방적 전뇌 방사선조사를 받은 급성 임파구성 백혈병 환아 90예를 대상으로 후향적 분석을 시행하였다. 3명을 제외한 모든 환자들이 일일 180 cGy 씩 총 1800 cGy의 전뇌방사선치료를 받았고, 방사선 치료중 척수강내 화학요법이 병행되었다.

결 과 : 추적관찰기간 36-96 개월 (중앙값 60 개월)동안 90명의 환아중 9례에서 중추신경계 재발을 보였으나, 골수재발이 선행되었던 3례를 제외하면 중추신경계 재발율은 6.7 %로 나타났다. 중추신경계 재발환자의 89 % 에서 골수재발이 동반되었으며, 11 % 에서 고환재발이 동반되었다. 골수완전관해로부터 중추신경계 재발까지의 경과기간은 16 개월 (중앙값) 이었고, 78 %의 중추신경계 재발이 관해유지요법중에 발생하였다.

2년 및 5년 중추신경계 무병생존율은 각각 68 %, 42 % 였고, 중앙값은 43 개월이었다. 중추신경계 무병생존율에 영향을 미치는 예후인자는 진단당시의 백혈구수 (5만 기준), FAB 분류군, CALGB 위험분류기준으로 나타났다. 2년 및 5년 전체무병생존율은 각각 61 %, 39 %였고 중앙값은 34 개월이었다. 전체무병생존율에 영향을 미치는 예후인자는 진단당시의 백혈구수 (5만 기준), FAB 분류군, CALGB 및 POG 위험분류군으로 나타났다.

결 론 : 본 연구에서 중추신경계 재발율은 6.7 % 로 다른 연구들에서 보고하는 범위에 속하여 효과적인 중추신경계 예방요법으로 판단 되었다. 진단당시의 나이및 백혈구수를 기준으로한 위험분류기준 중 POG 및 CALGB 위험분류기준이 중추신경계 무병생존율 및 전체무병생존율에 유의한 예후인자로 나타났다. 부작용을 최소화하면서도 효과적인 중추신경계예방요법을 알아내기 위해서는 각 위험분류군에 따른 중추신경계 예방요법의 차별화에 대한 전향적인 연구및 장기 생존자들에 대한 체계적인 신경 심리학적 추적 조사가 필요할 것으로 사료된다.