Treating Leukemia in a Resource-poor Setting

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ABSTRACT

Acute lymphatic leukemia (ALL) is the commonest childhood malignancy in India; most patients have no access to specialized health care. Our experience in treating such children who are unable to avail of facilities at specialized centers is described here. The case records of 79 patients with acute lymphatic leukemia, treated at a Government Medical College in Kerala over 15 years were analyzed. Of the 73 patients who completed treatment, 23 survived (36%); 20 had event-free survival more than 5 years after remission. The utilization of available resources is described. We suggest "twinning" between specialized centers in India and peripheral hospitals as a means to reach more children.

Key words: *India, Leukemia, Outcome.*

INTRODUCTION

Acute lymphatic leukemia (ALL) is the commonest malignancy in children. It is treatable with survival rates of more than 80% in the best of centers(1,2). Treatment of malignancy in developed countries is highly specialized. In India, although there are several oncology institutes and regional cancer centers, very few patients have access to specialized treatment. The reasons for this are low socio-economic status, distance from the treatment center and the financial burden of chemotherapy, supportive treatment and simultaneously supporting the family back home.

Our institution is a Government Medical College Hospital in central Kerala, serving the people of four districts. Many of the children with malignancy who come to us, refuse referral to the Regional Cancer Center (RCC) at Trivandrum (which is 300 km away), opting for treatment at our hospital. We have been treating children with leukemia since 1990, although overcrowding, shortage of staff and dearth of funds are perennial problems. We feel that this singular experience should be shared with everybody involved in the care of children. We present here a retrospective analysis of the case records of patients with acute lymphatic leukemia treated in our department from January 1990 to June 2006.

METHODS

Diagnosis of ALL was confirmed by blood and bone-marrow examination with Leishman stain, PAS and Sudan Black. Immunohistochemistry and cyto-genetics are not done at our institution. The treatment varied between 1990 and 2006, in accordance with protocols prescribed by standard textbooks and those advised by the RCC at Trivandrum (***Table* I**). Treatment was also affected by availability of drugs in the market as well as the capacity of the parent to purchase them. In 1990, the drugs available for induction of remission were vincristine and prednisolone. By 2000, all chemotherapeutic drugs were easily available. Colony-stimulating factor and blood component therapy became available in 2001.

Strict isolation was not possible in the period of study as an Isolation Ward was acquired only in 2006. The children were nursed in a curtained-off area of the general ward. Hand-washing by the relative and medical/nursing staff was enforced; patients wore face-masks; and personal hygiene was emphasized. Cotrimoxazole prophylaxis was given

TABLE I TREATMENT PROTOCOLS USED TO TREAT ALL OVER DIFFERENT PERIODS OF TIME

Year	1990-91 (*n*=10)	1991-2002 (*n*=59)	2003-2006 (*n*=10)
Induction drugs	Vincristine, prednisolone	Vincristine, prednisolone, L-asparaginase; PLUS adriamycin/cyclophosphamide in high-risk patients; no reinduction,	BFM Protocol IIIA-vincristine, prednisolone, L-asparaginase cyclophosphamide, cytarabine, daunorubicin,methotrexate, PLUS reinduction
CNS Prophylaxis	Cranial irradiation	Triple intrathecal with cytarabine, hydrocortisone,and methotrexate	Cranial irradiation and IT methotrexate
Maintenance	Daily mercaptopurine, weekly methotrexate, monthly vincristine and prednisolone, triple IT on alternate months	Daily mercaptopurine, weekly methotrexate, monthly vincristine and prednisolone, triple IT on alternate months	Daily mercaptopurine and weekly methotrexate, monthly vincristine and prednisolone

as a routine. Chemotherapy was administered on fixed days to avoid wastage of drugs.

Children who completed treatment were reviewed frequently in the first year, then once a year. An annual get-together of survivors and children on treatment, along with their parents, has regularly been held since 2000 to boost the morale of the families and ensure follow-up.

RESULTS

A total of 79 records were analyzed. Thirteen children are currently on treatment; 2 were lost to follow-up. Of the remaining 64 patients, 23(36%) survived; 20 have had event-free survival more than 5 years after remission.

The most frequent acute complication of therapy was bone-marrow suppression, which was experienced by every patient. Other complications were fatal neurotoxicity of intrathecal methotrexate in 2 patients (before the preservative-free preparation became available), L-asparaginase induced transient diabetes mellitus in 2 children, 2 cases of reversible peripheral neuropathy due to vincristine, pyogenic meningitis after intrathecal injection in 1 patient and 1 case of aspergilloma of the spinal cord.

Thirteen children died of leukemia during induction; 6 within one week of diagnosis. Of the 17 deaths following relapse, 11 were due to systemic relapse, 5 had CNS relapse and 1 had testicular relapse. Nine deaths were due to bone-marrow suppression, of whom 1 had massive hemop-tysis and 8 had neutropenic sepsis. Two died of neurological complications after intrathecal metho-trexate. Four of the children who died were below 2 years of age, 6 were above 10 years; 13 patients had TLC above 50,000/mm^3 at onset.

Of the survivors, 6 are now young adults; 1 is employed, 4 are married (of whom 3 have had normal babies) and 2 are college-students. All the younger ones attend school regularly. Three children have permanent disability; 1 has impaired vision following retinal hemorrhage, 1 has facial palsy and 1 child is paraplegic.

DISCUSSION

For the many reasons detailed above (not the least being poor categorization of disease) our results cannot be compared to treatment outcomes published from any other center. These drawbacks notwithstanding, we do have a survival rate of close to 40%. Had we not attempted to treat these children, the mortality would doubtless have been higher. Given the fact that leukemia in India has been reported to cause 30 to 50% of potential life lost due to cancer in every age group, it is well worth continuing the effort(3). As facilities for supportive care improve, survival rates will only be better. Difficulty in procuring drugs for chemotherapy has

WHAT THIS STUDY ADDS?

- Acute lymphoblastic leukemia may be managed in resource-poor centers with optimum utilization of resources, if referral to specialized centers is not feasible. The outcome however remains sub-optimal.

always been a great hurdle. Chemotherapeutic drugs, not being strictly 'life-saving drugs,' are never a priority on the purchase list of the administration, given the financial constraints of a government hospital. Funds are arranged through local donors, government-run relief funds and recently, through trust funds.

Our experience serves to highlight the fact that a very large number of children with curable malignancies have no access to adequate treatment. There is a need for easier access to specialized healthcare in the public sector, as well as for financial support of patients with cancer. It is hoped that this report will encourage more general pediatricians to treat malignancies and not regard it as fighting a lost cause.

"Twinning" between oncology centers in developed countries and hospitals in developing countries has been described as a strategy to improve cancer care(4,5). Such programs have been working in Central and South America, South-east Asia and Northern Africa in collaboration with western centers, with good results. We suggest "twinning" to be made possible between better centers within our country and smaller hospitals in the periphery so that a greater number of children can be reached.

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