

Cognition in Long-Term Survival of Acute Lymphoblastic Leukemia

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Aim of the Work: The event free survival (EFS) after treatment of childhood acute lymphoblastic leukemia. ALL reached more than 90%. The number of survivor patients is increasing. Therefore, the primary purpose of the present study is to assess the neuropsychological functions following Modified BFM and CCG protocols for central nervous system (CNS) negative long term survivors.

Patient and Method: A cross sectional multi center study of 30 long term survival (15 subjects treated with prophylactic systemic and intrathecal Methotrexate MTX and another 15 subjects prophylactically received cranial radiotherapy (RT). Long-term ALL survivors were compared by pairwise matched healthy control (HC) subjects (no=15) for age, gender, and educational level. Intellectual and cognitive abilities of these groups were evaluated using standardized age-Appropriate Wechsler Intelligence scale, Modified Mini Mental state examination and freedom from Distractibility.

Results: The Rt group exhibited a lower score in full IQ scores than both MTX group and HC group (Rt 91.6+ 9.1, MTX 109.7 + 11.3 , HC 125.06 + 11.6: $t = 4.15$ (Rt Vs MTX); $t = 9.9$ (RT VS HC). The Kaufman Factor Freedom from Distractibility scores were lower in both RT group and MTX groups compared with HC group (RT= 94.4+ 2.84; MTX 106.87, 1.78; HC 123.7+ 9.51: $t = 11.55$ (MTX Vs RT); $t = 9.2$ (RT/Vs HC).

Conclusion: Both CNS prophylactic therapy whether cranial radiotherapy or methotrexate was associated with deficits in attention, concentration and ability of sequencing and processing measured by Kaufman Factor Freedom from Distractibility which is more evident in RT group. Our results support the strategy of avoiding CNS irradiation when possible and recommend carefully follow up of ALL survivors, cognitive abilities to detect early signs of cognitive impairment and early interventions.

Keywords: Cognition - lymphoblastic leukemia - survivors

Abbreviations:

MTX: Methotrexate and systemic chemotherapy

Rt: Cranial irradiation therapy

CNS: central nervous system

IQ: intelligence quotient

CT: computerized tomography

ALL: acute lymphoblastic leukemia

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INTRODUCTION

Childhood malignancies are justifiably a frequent cause of big concern of parents and physicians because they become the second leading cause of death in children after accidents (Wolfe, et al. 2000). Hallbook (2006) reported that several studies emphasized a more favorable outcome for teenagers and young adults. With intensive ALL chemotherapy but no local radiotherapy an event free survival rate of 90% can be achieved.

Vora (2002) in India emphasized that after substantial improvements in cure rates for childhood ALL obtained with intensified treatment strategies in 1970s and 1980s, the last decade has seen late treatment related adverse effects and focused attention on risk targeted therapy to minimize adverse effect.

Meanwhile, long term neuropsychologic sequelae following CNS prophylaxis have been investigated marginally in children cured from ALL (Iuvone, et al. 2002). Some long-term survivors of childhood cancer

experience changes in cognitive functioning and have learning difficulties in school (Peckham, 1991).

Prevention of meningeal recurrence achieved by intrathecal methotrexate and systemic chemotherapy (MTX) is part of standard ALL treatment. Cranial irradiation therapy (Rt) has been a routine part of past protocol treatment but is currently reserved only for selected subsets of patients central nervous system (CNS) prophylaxis which may cause brain abnormalities such as intracerebral calcifications, cerebral atrophy, and white matter alterations (Iuvone, et al. 2002).

Cognitive impairment was found to be transient in children who did not manifest somnolence and were under 5 years at the time of diagnosis. Despite having normal IQ and normal CT scans 9 of 18 survivors in continuous complete remission were having learning problems at school 5 years after diagnosis (Jannoun and Chessells, 1987).