ABSTRACT

Analysis of Adrenal Suppression After High Dose and Long Term Dexamethasone Therapy in Pediatric Patient with High Risk Acute Lymphoblastic Leukemia in Induction and Consolidation Phases
(Study at In-Patient, Child Health Department – Dr. Soetomo Teaching Hospital Surabaya)

Background – Glucocorticoids are essential in the treatment of acute lymphoblastic leukemia (ALL) but high doses may cause adrenal suppression that leads to impairment of body response against infection which is the major cause of morbidity and mortality. Dexamethasone has more effect on the adrenal suppression. The incidence of adrenal suppression during the induction and consolidation phases of pediatric ALL is unclear.
Objective – To analyze the effect of high dose and long term dexamethasone on cortisol levels during induction and consolidation phases of chemotherapy in pediatric ALL.
Method – A longitudinal, observational prospective method was conducted in this study. The study protocol was approved by Dr. Soetomo Teaching Hospital Surabaya Ethics Committee and informed consent was obtained. Patients were given dexamethasone for 49 days according to the 2013 Indonesian ALL Chemotherapy Protocol for high risk children. Morning serum cortisol levels were measured on weeks 0, 4, 5, 6, 7, 8, 10, and 12 during induction until consolidation phases then determined by chemiluminescence immunoassay with a detection limit of 0.50 µg/dL. Adrenal suppression was defined as serum cortisol level below 3.00 µg/dL.
Results – A total of 11 children with high risk ALL were recruited. There were significant decreases in the cortisol levels during 4^{th}–6^{th} weeks of induction phase (p=0.003). The mean cortisol levels during 4^{th}–6^{th} weeks were 1.33 ± 1.04 µg/dL (0.00–3.73 µg/dL); 1.05 ± 0.59 µg/dL (0.00–1.96 µg/dL) and 1.51 ± 1.47 µg/dL (0.00–5.48 µg/dL with mean decrease percentages of 76.72%; 81.72%; and 75.58% respectively. The adrenal function was starting to recover during dexamethasone tapering off with elevated cortisol level of ±6.7 times than in the induction phase. The mean cortisol levels during 7^{th}, 8^{th}, 10^{th}, and 12^{th} weeks were 10.29 ± 10.84 µg/dL (0.61–29.29 µg/dL); 16.48 ± 14.83 µg/dL (3.27–46.54 µg/dL); 15.64 ± 13.79 µg/dL (4.24–45.66 µg/dL); and 21.81 ± 13.71 µg/dL (5.02–46.08 µg/dL) with elevated cortisol levels of 6.7; 14.8; 14.1; and 21.6 times respectively. Adrenal suppression was experienced by 5 patients after tapering off dexamethasone but none was found after 1 week of cessation (consolidation phase).
Conclusion - High dose and long term use of dexamethasone caused adrenal suppression in the induction phase and may persist after tapering off therapy but none was observed during consolidation phase (reversible adrenal suppression). Cortisol level test and intensive clinical monitoring may be indicated.

Keywords: Dexamethasone, Acute Lymphoblastic Leukemia (ALL), Cortisol, Adrenal Suppression, Induction Phase, Consolidation Phase, High Dose Dexamethasone, Long Term Dexamethasone