PREDICTORS OF DEXAMETHASONE-INDUCED NEUROPSYCHOLOGICAL SIDE EFFECTS IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Background

Dexamethasone is highly effective in the treatment of acute lymphoblastic leukemia (ALL), but may lead to serious **neuropsychological side effects**. Despite the standard dose, the severity of side effects varies widely between patients. We hypothesized that neuropsychological side effects are influenced by **glucocorticoid sensitivity** at the tissue level or by **dexamethasone serum levels**. In this study we determined whether neuropsychological side effects could be predicted by a very low dose dexamethasone suppression test (**DST**) as diagnostic test for glucocorticoid sensitivity or by dexamethasone trough levels.

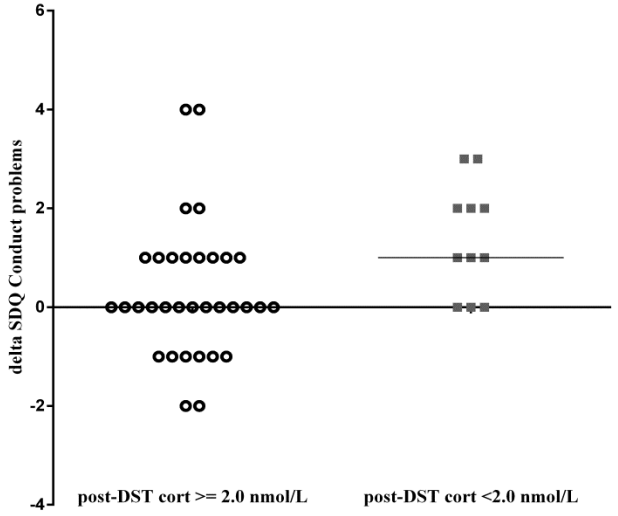
Methods

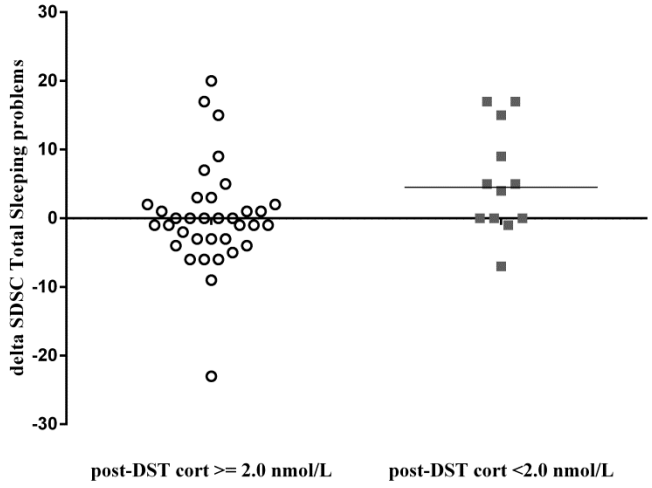
- Fifty patients (3-16 years) treated with dexamethasone courses (6mg/m^2) according to the maintenance phase of DCOG ALL protocols were included.
- In the **salivary very low dose DST**, which was performed in the week before a dexamethasone course, a post-dexamethasone cortisol level of <2.0 nmol/L was considered a hypersensitive response.
- Dexamethasone **trough levels** were measured after four days of dexamethasone.
- Neuropsychological endpoints consisted of the **parent-reported questionnaires**: Strengths and Difficulties Questionnaire (SDQ-Dut) and Sleep Disturbance Scale for Children (SDSC), which were completed before and during a dexamethasone pulse.

Conclusions and Relevance

The very low dose DST and dexamethasone trough levels could **not accurately predict** neuropsychological side effects.

However, patients with **glucocorticoid hypersensitivity** experienced significantly **more** dexamethasone-induced **depressive symptoms**. Future studies should further elucidate the glucocorticoid sensitivity dependent mechanisms by which neuropsychological side effects are influenced.





Results

48 of the 50 enrolled patients completed the salivary very low dose DST. The post-dexamethasone cortisol levels were significantly lower than baseline morning cortisol levels (median 3.7 (IQR:1.9-7.9) vs 11.2 (7.3-15.4), P<0.001). Patients with a **hypersensitive response** (N=13, 26%) had **more dexamethasone-induced behavioral problems** (median delta: 1.0 (inter quartile range: 0.0,2.0) vs 0.0 (-0.5,1.0), P=0.01), **sleeping problems** (4.5 (0.0, 13.5) versus 0.0 (-3.0, 2.0), P=0.03), and/or **somnolence** (3.0 (1.0, 6.0) vs 1.0 (-0.5, 2.5), P<0.05).
The positive predictive value of the DST for psychosocial problems and sleeping problems was 50% and 30% respectively. Dexamethasone levels were **not** associated with neuropsychological side effects.