Polytransfused Children with Beta Thalassemia Major have Wider Endocrine Dysfunction

We read with interest the brief report entitled "Assessment of adrenal endocrine function in Asian Thalassemics"(1). A large number of children in India undergo long term transfusions and are therefore at risk of hypothalamo-pituitary dysfunction. The paper makes an important observation of detecting biochemical evidence of adrenal hypofunction in polytransfused patients.

The authors describe a low dose (1 microgram) and a standard dose (250 microgram) ACTH stimulation test to assess adrenal function. However neither test discriminates between primary (adrenal gland) and secondary (hypothalamus, pituitary gland) adrenal hypofunction. Given that children with beta thalassaemia are more likely to have pituitary malfunction, serum ACTH estimation should be an additional useful test.

A significant proportion of thalassemics have hypogonadotrophic hypogonadism and therefore remain prepubertal in sexual maturation. Delayed puberty itself may partly account for the reduction in weight for age. Of course, other variables such as nutrition, socio-economic status, parental build and ethnic background may also be responsible for small body size. Puberty is an important process not only for sexual maturation but also for bone mineralisation. Puberty should therefore be assessed in all children and the gonadotrophin releasing hormone test performed in those with poor progression.

Iron overload from polytransfusions is well known to cause pituitary failure. The authors measured serum ferritin as an index of iron overload but found no significant correlation with basal cortisol concentrations. It may be noted that thalassaemics who are growth hormone deficient from pituitary iron deposition, have relatively low ferritin levels(2) and this may account for the lack of association.

We should be alert to the real possiblity of growth hormone deficiency, hypogonadotrophic hypogonadism, hypothyroidism and hypoparathyroidism in all beta thalassaemia children undergoing regular transfusions. In addition to basal cortisol and ACTH, it is important to assess thyroid function, parathyroid hormone and insulin like growth factor-1(IGF-1) in these children. Dual energy *X*-ray absorptiometry (DXA) scans may be performed where there are adequate resources to assess bone mineral density. Children in growth failure should have a low threshold for undergoing pituitary function tests. Those complaining of tiredness or fatiguability should be investigated with the low dose ACTH test for adrenal reserve. A pituitary magnetic resonance scan may be considered as an investigation to visualize pituitary iron overload(3).

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Reply

We agree entirely with Dr. Banerjee that multitransfused patients of beta thalassemia are susceptible to multiple endocrine dysfunctions of clinical import and hence need comprehensive evaluation. Cost considerations largely dictate the extent of evaluation especially in a country like ours. Regarding serum ACTH levels for diagnosis of secondary adrenal insufficiency, we beg to differ from Dr. Banerjee. A large overlap of ACTH levels, between normal and proven secondary adrenal insufficiency, has been documented in literature(1) and hence the test has limited value. The more discriminant CRH stimulation test is not routinely used in clinical practice because of cost and non-availability. We concur with the views on pituitary MR imaging as an index of iron overload. In addition to T2 relaxation rate, the pituitary to fat signal intensity ratio (P/F) has been used as another marker of iron overload. The degree of reduction of P/F ratio correlates well with presence of hypogonadotropic hypogonadism, with a sensitivity of 90%, specificity of 89% and an overall accuracy of 89%(2).

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Fluid Resuscitation in Septic Shock

In reference to recent article(1) on this subject, we have the following comments to offer:

1. In the study, authors have compared the efficacy of saline with degraded gelatin in saline. So they have compared the crystalloid with colloid in crystalloid. The study would have been more authenticated if comparison would have been made between crystalloid and pure colloid as 5% albumin, fresh frozen plasma, synthetic colloid solutions (heta starch, dextran 40, dextran 60).
2. Authors have used fluid boluses even after 6 hours up to 24 hours of fluid resuscitation. Ideally, if the administration of 60mL/kg of crystalloid results in no improvement in septic shock, myocardial dysfunction should be considered. That needs the inotropic support in the form of dopamine or epinephrine(2).

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