Clinical Studies on the Pituitary ACTH Secretory Capacity in Children by use of an Adrenocortical 11-β-Hydroxylase Inhibitor (Metopirone)

1. Studies on the fractionation of urinary 17-ketogenic steroids (17-KGS) (using periodate oxidation) and some fundamental aspects of the Metopirone test in children

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A modified Few's method of the urinary 17-KGS determination, by which urinary direct 17-KGS was fractionated into 2 parts of 11-deoxy-KGS and 11-oxy-17-KGS, was applied in examining the pituitary ACTH secretion capability in children in whom adrenocortical 11-β-hydroxylase inhibitor (Metopirone, SU-4885 CIBA) was administered. Several fundamental coditions were studied with the following results.

Metopirone capsules, 250 to 500mg a dose, were administered 6-8 times for one day to a daily dosage of 2g. in children with body weight of 20kg or less, and 3g. in those over 20kg.

1. Changes in urinary 11-deoxy and 11-oxy 17-KGS, 17-OHCS (Porter-Silber Chromogen PSC) and pregnanetriol before and after administration of Metopirone were studied; both 11-deoxy and 11-oxy 17-KGS seemed to show changes in level of 11-deoxy-cortisol and cortisol secretion. (Fig. 2 and 3).

2. Increase in urinary 17-KGS and 17-OHCS (by Reddy, Jenkins and Torn's methods) after administration of Metopirone in 25 children of various conditions were compared. The author belives that the increase in 17-KGS excretion is a better index in evaluting the response to Metopirone than 17-OHCS which often showed a low increase and would thus give a false negative interpretation (Fig. 4, Table 1).

3. Calculating the 17-KGS increment per unit body suface after administration of Metopirone in 10 cases of normal children of 3 to 14 years of age, it was noted that no differences were seen in relation to the age, and 11-deoxy was 5.57-20.87 mg/day/m² while the total (11-deoxy+11-oxy) was 4.49-21.44 mg/day m²; 11-deoxy/11-oxy ratio increased to the maximum of 3.48±1.10, Mean (M)±Standard Deviation (SD). Using this level as the standard, the responses were classified as normal, hyporeactive (limited pituitary reserve, frank insufficiency) and hyper-reactive. Urinary total 17-KS was also determined at the same time; the increase were less than 1 mg/day·m² in chidren under 10 years of age, and the author thinks that this level cannot be used as a criteria in evaluating the response (Fig. 5, 6 and Table 2, 3).
4. As for the Metopirone administration method, its effect by divided doses and development of side effects were studied. Doses of 250 to 500mg for 6 to 12 times for one day were suitable in children. Administration of 90 to 140 mg/day/kg body weight was necessary in order to maintain the 11-deoxy/11-oxy ratio children of various diseases over the M-1·SD of the normal children, and the admistration method which satisfies both is considered to be suitable in younger children (Fig. 7 and 8).

5. A case which showed dissociation between the elevation of 11-deoxy-17-KGS and total 17-KGS after the administration of Metopirone is described. Differences in the ratio of 11-deoxy/11-oxy was noted in cases which showed inhibition of response to pituitary irraadiation and thyroid treatment (Fig. 9, 10, and 11).

6. Literature on basic conditions of Metopirone test in children is reviewed on the abovementioned various points (Table 4). (pp. 756~775)