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STUDIES ON THYROID AND HYPOPHYSARY THYROTROPHIC HORMONE (TSH) IN DOWN SYNDROME

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Thyroid function in children with Down syndrome has been a point of controversy in medical literature. Authors such as Benda and Bixby [1], Kurland et al [5], Pearse et al [6], Saxena and Pryles [8] described a series of abnormalities in thyroid function in mongoloids. On the other hand Cottino [2], Kearns & Hutson [4], Rimoin [7] and Simon et al [9] reported patients with this syndrome but with normal thyroid function.

In a previous report, the authors (Schmidt et al [10]), studying children with Down syndrome and controls, concluded that uptake of ^{131}I after 2 hours of ingestion was significantly lower in the mongoloid children when compared to normals, although no difference in the ^{131}I uptake was noticed between the two groups of children after 24 hours.

The purpose of the present study was to complement the previous report and reach a better understanding of the hypothalamus-hypophysis-thyroid axis in Down syndrome.

MATERIAL AND METHODS

22 children, clinically and cytogenetically diagnosed as affected by Down sindrome, aged from 4 to 15 years (16 males and 6 females), were studied. The Hypophysary

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Trabalho apresentado nos Congressos Pediátricos 1975: IX Panamericano, IV Latino-Americano e XIX Brasileiro, São Paulo. Realizado no Centro de Habilitação da APAE de São Paulo, em colaboração com a Escola Paulista de Medicina (EPM) e o Centro de Medicina Nuclear da Faculdade de Medicina da Universidade de São Paulo (FMUSP) com o auxílio da Comissão Nacional de Energia Nuclear (SP): * Professor Adjunto do Departamento de Pediatria da EPM (Professor A. A. Carvalho); ** Diretor Clínico do Centro de Medicina Nuclear da FMUSP; *** Diretor Técnico do Centro de Habilitação da APAE de São Paulo; **** Médicos do Centro de Habilitação da APAE de São Paulo; ***** Farmacêutica-Bioquímica do Centro de Habilitação da APAE de São Paulo.

Thyrotrophic Hormone (TSH) stimulation test was performed in 6 patients with IM injection of 10 International Units of Bovine thyroid stimulating hormone * 24 hours before ingestion of 20-30 mC of ^{131}I.

Uptake of the radioisotope was assessed after 2 and after 24 hours. The readings of the radioiodine were made through sparkling detectors supplied with thallium activated sodium iodide cristal, measuring 3,5 × 5cm, in order to reduce to a minimum the iodine quantity which should be administered to the patient. The technique employed followed the norms recommended by the International Agency of Atomic Energy 3. The tracing doses varied from 20 to 30 mC of ^{131}I. The serum TSH concentration was assayed by radioimmuneassay ** in all 22 patients. The normal values are from 0,0 to 10 μU/ml.

RESULTS

A general view of the results is presented in tables 1 and 2. Table 1 shows the iodine uptake after 24 hours of ingestion, as well as the clearance rate before and after the TSH stimulus. It can be noticed that in 4 of the 6 patients (cases number 7,8,9 and 18) the ^{131}I uptake after 2 hours was below the normal values and that clearance rates were decreased in all six. After TSH stimulus, the ^{131}I uptake after 2 hours was increased in all but one (case number 3). Case 7 had a slight increase in the uptake, from 3,0 to 5,92% D. Case 8 had an increase from 1,60% D to 5,24% D. In spite of the uptake, in these 2 patients the values are below normal. Cases number 9 and 18 had an increase in the radioiodine uptake from 5,25% D and 7,46% D to 16,14% D and 11,62% D respectively, reaching normal values. Case number 12, with normal values of iodine uptake after 2 hours (9,98% D) had, after TSH stimulus an uptake of 22,34% D. The clearance rate after TSH was increased in all patients reaching normal values in cases number 9,12 and 18.

The serum TSH was studied in all 22 cases (Table 2). Cases number 15 and 17 had borderline values (10 μU/ml). Cases 4, 8 and 22 had slightly increased values (11 μU/ml), and two cases had abnormally increased values: cases 11 had 18 μU/ml and case 16 had 21,0μU/ml.

COMMENTS

Of the group of 6 cases (3,7,8,9,12 and 18) in which radioiodine uptake and clearance rate before and after TSH stimulus were assessed, only case 8 had a slight increased in TSH level (11 μU/ml).

The decreased ^{131}I uptake after 2 hours but normal after 24 hours in Down syndrome, confirming previous data [10], raised the doubt either the pituitary stimulus was subnormal or that the thyroid gland had a slow response but compensated when analyzed after 24 hours. The pituitary function, expressed by serum TSH level showed abnormally high values for this hormone on 5 of our 22 patients, and normal values in the other 17. The results obtained on these patients with Down syndrome, suggest that there is a thyroid dysfunction in which a slow response to TSH stimulus seems to be the basic defect.

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* Organon Laboratories

** The analysis was performed by Bio-Science Laboratories, Van Nuys, California

Case	Age (years)	Sex	Before TSH injection			After TSH injection		
			Thyroid uptake of the ^{131}I (% D)		Depuration rate	Thyroid uptake of the ^{131}I (% D)		Depuration rate
			after 2 hours normal values 8 — 12	after 24 hours normal values 24 — 48	normal values 12.9 ± 2	after 2 hours normal values 8 — 12	after 24 hours normal values 24 — 48	normal values 12.9 ± 2
3	4	M	9.26	1.76	3.31	9.20	4.24	4.15
7	5	M	3.00	15.88	2.30	5.92	38.02	5.65
8	9	F	1.60	8.80	1.66	5.24	29.09	3.71
9	15	F	5.25	0.72	3.70	16.14	48.32	13.03
12	10	M	9.98	21.66	5.23	22.34	54.48	13.69
18	12	M	7.46	24.16	5.19	11.62	29.62	11.53

Table 1 — Thyroid function tests before and after stimulus with hypophysary thyrotrophic hormone (TSH — μI injected intramusculary).

Case	Age	Sex	TSH (μ U/ml)
1	8	M	7.1
2	6	M	6.4
3	4	M	4.5.
4	7	M	11.0
5	11	M	5.9
6	8	M	6.9
7	5	M	7.4
8	9	F	11.0
9	15	F	4.4.
10	15	F	7.9
11	13	M	18.0
12	10	M	6.3
13	4	M	7.3.
14	8	M	7.5.
15	8	M	10.0
16	8	M	21.0
17	10	F	10.0
18	12	M	7.3
19	10	M	9.3.
20	11	M	7.5
21	11	M	7.5
22	8	F	11.0

Table B — *Serum levels of bopophysary thyrotrophic hormone (TSH) in patients with Down's syndrome: determination of TSH made by RIE with normal ranging from 0.0 — 10 μ U/ml.*

SUMMARY

Serum TSH was studied in 22 patients with Down syndrome, from 4 to 15 years old. In 6 of these patients radioiodine uptake by thyroid gland after 2 and 24 hours of administration and clearance rates before and after TSH stimulus (10 μI-IM) were measured. Results show that serum TSH was normal in 17 patients and above normal limits in 5 patients. Thyroid uptake after 2 hours as well clearance rates, both below normal, had a response to TSH stimulus with normal or below values. These data along with previous reports, suggest, that in children with Down syndrome, there is a thyroid dysfunction in which a slow response no TSH stimulus seems to be the basic defect.

RESUMO

Estudo do hormônio tireotrófico hipofisário (TSH) na sindrome de Down

Em 22 pacientes com sindrome de Down, cuja idade variou de 4 a 15 anos, foi feita a determinação sérica do hormônio hipofisário. Em 6 destes casos

verificou-se a captação tireoidiana do ^{131}I com 2 e 24 horas após ingestão do radioisótopo, bem como a velocidade de depuração, antes e após um estímulo com TSH (10 μU-via intramuscular). Os resultados evidenciaram que os níveis séricos de TSH estavam normais ou aumentados (5 casos). A captação tireoidiana das primeiras duas horas, bem como a velocidade de depuração, ambas diminuídas no início, responderam ao estímulo com TSH, com valores normais ou abaixo do normal. Os resultados obtidos, aliados a estudos anteriores, sugerem, nos pacientes estudados, uma disfunção tireoidiana por lentidão de resposta ao estímulo pelo TSH.

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