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Short Report

Thyroid function in haemodialysed patients of Gassim, Saudi Arabia: TRH stimulation

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Summary

To study the hypophysical-pituitary-thyroid axis in Saudi patients on (RDT), 200 units of TRH were given intravenously predialysis to each of 21 such subjects. As expected (TSH) rose promptly within 30 minutes followed by a gentle decline at 60 minutes. A more gentle rise was also noted in T3 which continued for the 60 minutes of observation. Rather unexpectedly, T4 level was noted to show a reciprocal decline. To our knowledge, this pattern has not been defined in literature. In 12 patients (GH) was noted to rise promptly within 30 minutes followed by a gentle decline at 60 minutes. (LH) and (FSH) did not follow any definite pattern as observed for T3 and T4. Since the oral preparation of TRH is now available, can (TRH) be effectively used to treat renal dwarfism?

Résumé

Pour étudier l'axe tyroidiene hypophysiale, pituitaire chez les patients Saoudiens subissant le traitement RDT, deux cents unités de TRH ont été données par voie intraveineuse, à chacun des 21 sujets avant la dialyse. Comme prévu TSH est vite monté dans l'espace de 30 minutes suivi par un déclin lent pendant les 60 minutes d'observation. Une montée plus lente a été observée dans T3, laquelle a continué pour 60 minutes d'observation. Le niveau T4 a démontré un déclin déclin réciproque non-prévu. Nous ignorons une telle tendance en littérature. Chez 12 patients GH est monté promptement pendant 30 minutes suivi d'un lent déclin à 60 minutes. LH et FSH n'ont pas manifesté de tendance particulière Sililaire à T3 ou T4. Puisque la forme orale de TRH est disponible, peut-on l'employer effectivement dans le traitement de nanisme rénal?

Introduction

Many aspects of thyroid function patients on regular dialysis treatment (RDT) in the Saudi population remain unexplored. A number of our recent findings do not conform to those of authors from other parts of the world (Khandekar, Soyanwo *et al.* (1993). We therefore decided to study, in a preliminary effort, the hypophyseal-pituitary-thyroid (H-P-T) axis in our patients currently on RDT. To our knowledge, such a study has not been carried out before in the Saudi population.

Patients and methods

In 21 patients who were at the time of study (September 1991) current on RDT, the H-P-T axis was studied. Informed consent was obtained from all patients as result of which the 22nd patient declined to participate in the study. Investigation was carried out immediate to predialysis, irrespective of the time of the day. Before giving 200 units of TRH intravenously to each patient, venous blood sample was obtained and again after 30 minutes and 60 minutes of the injection. Samples were analyzed for T3, T4, and TSH in all the patients. In 12 of the patients it was possible to determine in addition, GH, LH, and FSH. Hormone levels were done by radioimmunoassay using Beckman gamma counter and the Amersham kits by only one of us (MK).

All results were fed into a computer, STATITIX 3.1 (SX) programme, descriptive statistics, the Student's *t* test for parametric data and Wilcoxin rank test for non-parametric data were used to determine levels of statistical significance and degrees of correlation. The Havard graphic programme was used to plot the graphs.

Results

Table 1 shows the effect of intravenous injection of TRH after 30 and 60 minutes on T3, T4, and TSH.

Table 1: Effect of I.V. TRH on T3, T4 and TSH.

	T3 nmol/l	T4 nmol/l	TSH FIU/ml
n	21	21	21
Predial mean	0 76	66 25	1 48
± S D	0 24	24 96	0 96
30-Min mean	0 765	63 85	5 35
± S D	0.25	22 9	3 63
P	NS	NS	< 0 0001
60-Min mean	0 82	61 6	5 32
± S.D.	0.24	21.42	31.36
P	NS	< 0 03	< 0 001

Figure 1 demonstrates the percentage increase in these parameters after TRH stimulation. TSH is seen to rise promptly by more than 250 percent (from mean of 1.48 ± 0.96 to 5.35 ± 3.63 mic.IU/ml) within 30 minutes and to remain sustained up to 60 minutes (5.32 ± 3.36 mic.IU/ml). Such a pattern was not seen in T3 and T4. Rather, a gentle rise of less than one percent (from mean of 0.76"0.24 to 0.765 ± 0.25 mmol/l) was observed at 30 minutes with a further rise (up to 0.82 ± 0.24nmol/l) at 60 minutes. On the other hand T4 moved in the opposite direction, decreasing by 3.6 percent (from a mean of 66.25 ± 24.96 to 63.85 ± 22.9 nmol/l) at 30 minutes and a further decrease to 61.6 ± 21.42 nmol/l at 60 minutes. The rather compelling suggestion is that TRH stimulation produces these changes by facilitating in some way, the dissociation of T4 to T3, an observation which to our knowledge, has not been reported.

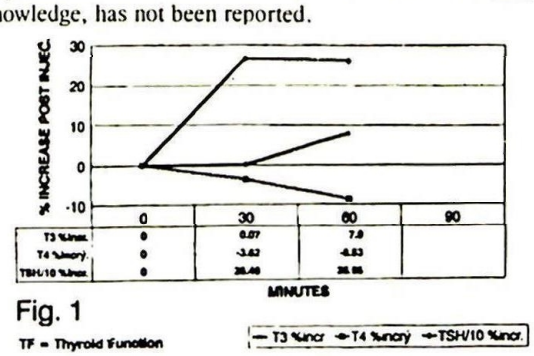

Fig. 1

Fig. 1: TF in RDT patients of Gassim, KSA. Effect of I.V. TRH on T3, T4 and TSH

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Table 2 shows corresponding effects of TRH stimulation on GH, LH, and FSH in the 12 patients studied. It can be seen that mean GH rose promptly (from 4.1 ± 1.47 to 15.10 ± 4.25 mic.IU/ml) within 30 minutes, though declining slightly to 11.97 ± 3.22 mic.IU/l at 60 minutes. This is much the same pattern seen with TSH. Unlike our observation with T3 and T4, the effect of TRH on LH and FSH did not show any discernible pattern (Fig. 2) like the reciprocal movement observed for T3 and T4.

Table 2: Effect of I.V. TRH on GH, LH and FSH

	GH μIU/ml	LH milli-IU/ml	FSH milli-IU/ml
n	12	12	12
Predial mean	4 1	23.56	22.34
± S D.	5.08	28.95	29.93
± S E.	1.47	8.36	8.47
30-minute mean	15.10	23.53	22.18
± S.D	14.71	28.71	31.32
± S E	4 24	8.29	9.04
P	< 0.001	NS	NS
60-min mean	11.97	23.74	24.53
± S D	11.17	30.22	35.38
± S.E.	3 22	8.72	10.21
P	< 0.006	NS	NS

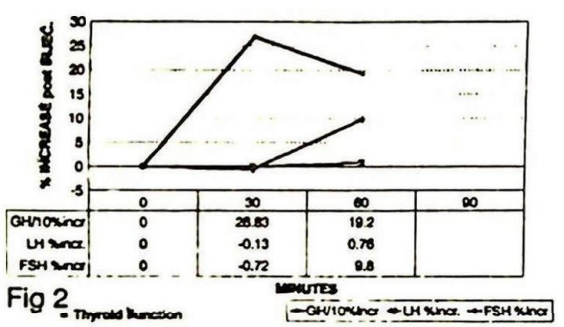

Fig 2 - Thyroid function

Fig. 2: TF in RDT patients of Gassim, KSA. Effect of i.v. TRH on GH, LH, and FSH.

Discussion

TRH stimulation clearly demonstrates some abnormality in the axis from the hypothalamus to the pituitary. The rise in TSH is prompt and exaggerated but the resulting effect on the thyroid gland is severely blunted as has been reported [1]. However, when we plotted the percentage increment over 60 minutes, an impressive pattern seemed to emerge showing that T3 increased, though only slightly, with an equally small but reciprocal decrease in T4. We have not been able to find a similar observation in literature. There was a similar reaction by GH to TRH stimulation in keeping with previous observations [1]. It is of interest that this pattern of response is not seen in non-uraemic experimental animals and human beings, thus supporting the idea of an abnormality in the hypophyseal-pituitary axis in end stage renal failure [3]. The explanation of the increase in T3 with reciprocal decrease in T4 induced by TRH stimulation is not clear. It is likely that a complex interplay between the various hormones is at work although it remains possible that TRH, the exogenously introduced substance by itself could be directly responsible for this phenomenon. However, since its administration results in a prompt and phenomenal rise of TSH and GH, it will be difficult to dissociate the effect of these on the process of converting T4 to T3. Whether this is due to enhancement of enzyme action or a direct chemical effect can only be speculative. We believe that further work on this phenomenon may assist us in the further understanding of the pathogenesis of thyroid dysfunction at the glandular and tissue level in end stage renal failure.

In a similar way, to explain the unique effect of TRH on GH in the uraemic milieu as opposed to the normal, would suggest that effective stimulation of the pituitary by the endogenous TRH is blocked by a substance in the uraemic blood. That exogenous TRH produces this marked rise does suggest that its injection either unblocks such a substance which has previously accumulated in the uraemic blood or that in combination with the blocking substance, it hyperstimulates the pituitary gland, which by itself could have been affected somewhat by the uraemic process. The possible role of prolactin must of course be kept in mind. Clearly, further work remains to be done which may elucidate the pathogenesis of renal dwarfism and suggest treatment possibilities. In particular, this peculiar and great increase in GH by uraemic patients in response to TRH stimulation opens some theoretical therapeutic implications. Can renal dwarfism be treated by endogenous production of patient's growth hormone? It is noteworthy, in this respect, that oral administration of TRH has been shown to be effective in stimulating the hypophysis [4].

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