Rev. Inst. Med. trop. S. Paulo
38(3):227-228, maio/junho, 1996

BRIEF COMMUNICATION

TRH-TSH TEST IN PATIENTS WITH SCHISTOSOMIASIS CHRONIC FORMS

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KEYWORDS: Schistosomiasis; TRH-TSH test; Thyroid-hormone; Liver disease.

Schistosomiasis in an endemic disease in the tropical and subtropical belts of the world. Accordingly to the WHO there are more than 200 million people infected and approximately 5 to 6 hundred million people exposed to the disease, as a consequence of poverty, poor housing and sanitation[10]. In Brazil there are approximately 10 million people chronically infected by the *S. mansoni*, 90-95% of them with the intestinal and hepatointestinal forms and 5-10% with the hepatosplenic form of the disease.

Many thyroid hormone serum concentration alterations have been reported in systemic non-thyroidal diseases including acute and chronic liver ones. Pathophysiologic mechanisms to explain these alterations have not yet been fully established, but in theory, they could take place in the thyroid itself, in the hypothalamic-pituitary-thyroid axis ("central") or in any of the "peripheral" sites of iodothyronines metabolism[2].

The aim of our study is to investigate the hypothalamic-pituitary axis in patients with schistosomiasis chronic forms as a way to establish if the previously reported derangements[3, 4] are "central" or "peripheral" in origin.

Seventeen male euthrophic adults, age range 20 to 60 years (mean 32 years) were selected for this study. Alcoholism, intravenous drug abuse, use of hepatotoxic medicines, presence of viral hepatitis B and C serum markers as well as chronic diseases, other than schistosomiasis, were carefully excluded. They were divided into 3 groups; group I (control) with 5 dyspeptic patients with 3 negative stools exams for *S. mansoni*, group II and III with 6 hepatointestinal and 6 compensated hepatosplenic patients respectively.

Group II and III patients had *S. mansoni* viable ova either in stools (Hoffman/Kato-Katz) or in rectal valves biopsy. Ultrasound and upper digestive endoscopy were performed to exclude or confirm the presence of portal hypertension in all patients.

All patients were submitted to two blood samples collection. The first sample, collected at time zero, was used for liver tests (ALT, AST, Alkaline Phosphatase, γ GT, Albumin), viral hepatitis B and C serum markers (ELISA technique, HBsAg – Auzyme monoclonal, Anti-HBc – Corzyme, Anti-HCV – 2nd generation, from ABBOTT Laboratories, North Chicago – USA) and T_3, T_4, free T_4 and TSH determination by radioimmunoassay. The second sample was drawn 30 minutes after intravenous administration of 200 μg of TRH (purchased from the Department of Biophysics – UNIFESP/EPM) and used for TSH determination by radioimmunoassay technique. The study was approved by the ethics committees of the Universidade Federal de São Paulo and Hospital São Paulo. All subjects gave informed consent.

The hepatic tests and thyroid hormones determination performed were normal for the three studied groups. Basal and post TRH administration TSH serum values are in table 1 as means ± standard error. Variance analysis failed to demonstrate any statistical difference ($p > 0.05$) for any of the tests performed among the studied groups.

Multiple alterations of thyroid hormones serum concentration have been reported in chronic liver diseases. Low T_3 and elevated rT_3, (low T_3 syndrome), were described in cirrhosis. These alterations result from diminished peripheral

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TABLE 1
Iodothyronines and TSH before and after (30 min) intravenous TRH (200 μg) administration in controls and schistosomiasis patients.

Group	T3	T4	Free T4	TSH (μU/ml)		
	(ng/dl)	(μg/dl)	(ng/dl)	basal	post-stimulus	increment
I	153 ± 21	7.9 ± 0.5	1.3 ± 0.1	1.7 ± 0.3	12.5 ± 1.6	10.8 ± 1.3
II	156 ± 12	9.4 ± 0.6	1.1 ± 0.1	1.6 ± 0.2	10.1 ± 1.7	8.6 ± 1.6
III	122 ± 24	7.7 ± 0.9	1.2 ± 0.1	1.8 ± 0.1	10.6 ± 1.5	8.8 ± 1.4

production of T_3 from T_4 and reduced clearance of rT_3, respectively, and are indicative of progressive loss of liver function[6]. In contrast, the elevated T_4 syndrome was the alteration reported in the compensated hepatosplenic form of schistosomiasis mansoni[3,4]. The interpretation of the latter finding is a complex matter, specially if we consider that this illness is characterized by liver function preservation, no matter the degree of portal hypertension, at least, in "pure" schistosomotic patients. The authors suggest that it maybe an early sign, a subclinical one, of hepatic function disorder, as none of their patients appeared to have hyperthyroidism[3,4].

TNF[7], TRIAC[1], TETRAC[1], selenium[8] concentrations, T_3 receptor expression alterations and binding of T_4 to inhibiting serum binding proteins[2] have been proposed as possible participating factors in the genesis of the multiple alterations in the serum concentrations of iodothyronines verified in systemic non-thyroidal illnesses.

We now report, for the first time, that the hypothalamic-pituitary axis is normal[5] in schistosomiasis patients. Considering that the TRH-TSH test is reliable to study the referred axis, we can exclude a "central" disorder as a possible explanation for the elevated T_4 syndrome described in schistosomiasis compensated hepatosplenic form, and suggest that it is probably "peripheral" in origin.

RESUMO

Prova do TRH-TSH em pacientes portadores de formas crônicas da esquistossomose mansônica

Diversas alterações na concentração sérica dos hormônios tiroidianos têm sido descritas em associação a doenças crônicas não-tiroidianas. Com relação às doenças hepáticas crônicas, a síndrome do T_3 baixo foi descrita em pacientes cirróticos, enquanto a síndrome do T_4 elevado foi encontrada em esquistossomóticos com a forma hepatoesplênica compensada. Com o intuito de verificar se as alterações relatadas na esquistossomose mansônica eram de origem "periférica" ou "central", realizamos a prova do TRH-TSH em 12 pacientes esquistossomóticos "puros" (6 hepatointestinais e 6 hepatoesplênicos compensados) e em 5 indivíduos controle. Os resultados obtidos demonstram que o eixo hipotálamo-hipofisário é normal nas formas crônicas da esquistossomose e que provavelmente as alterações previamente relatadas devem ser "periféricas" e não "centrais".

REFERENCES

1. CARLIN, K. & CARLIN, S. – Possible etiology for euthyroid sick syndrome. **Med. Hypotheses, 40**:38-43, 1993.
2. DOCTER, R.; KRENNING, E.P.; DE JONG, M. & HENNEMANN, G. – The sick euthyroid syndrome: changes in thyroid hormone serum parameters and hormone metabolism. **Clin. Endocr., 39**:449-518, 1993.
3. GAMMAL, S.H.; BORGES, D.R.; MACIEL, R.M.B.; MANOUKIAN, N. & RUSSO, E.M.S. – High T_4 syndrome in schistosomiasis. **Dig. Dis. Sci., 31**:269S, 1986.
4. GAMMAL, S.H.; MANOUKIAN, N.; RUSSO, E.M.S.; MACIEL, R.M.B. & BORGES, D.R. – Avaliação da função microssomal hepatocítica pela determinação da razão triiodotironina/tiroxina (T_3/T_4), na esquistossomose hepatoesplênica. **GED, 6**:95-98, 1987.
5. JACKSON, I.M.D. – Thyrotropin-releasing hormone. **New Engl. J. Med., 306**:145-155, 1982.
6. KABADI, U.M. & PREMACHANDRA, B.N. – Serum T_3 and reverse T_3 levels in hepatic cirrhosis. Relation to hepatocellular damage and normalization on improvement in liver disfunction. **Amer. J. Gastroent., 78**:750-755, 1983.
7. VAN DER POLL, T.; ROMIJN, J.A.; WIERSINGA, W.M. & SAUERWEIN, H.P. – Tumor necrosis factor: a putative mediator of the sick euthyroid syndrome in man. **J. clin. Endocr., 71**:1567-1572, 1990.
8. VAN LENTE, F. & DAHER, R. – Plasma selenium concentrations in patients with euthyroid sick syndrome. **Clin. Chem., 38**:1885-1888, 1992.
9. WILLIAMS, G.R.; FRANKLYN, J.A.; NEUBERGER, J.M. & SHEPPARD, M.C. – Thyroid hormone receptor expression in the sick euthyroid syndrome. **Lancet, 2**:1477-1481, 1989.
10. WORLD HEALTH ORGANIZATION – Major parasitic infections: a global review. **Wld. Hlth. statist. Quart., 39**:45-60, 1986.

Recebido para publicação em 18/04/1996
Aceito para publicação em 21/06/1996