

THYROID HYPOFUNCTION IN SPINAL CORD INJURY PATIENTS

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Abstract. Our experience in the screening and detection of hypothyroidism in 225 spinal injury patients is described. Clinical features compatible with hypothyroidism are frequently encountered in these patients and require thyroid function testing to exclude or confirm thyroid hypofunction. Two cases of hypothyroidism, equivocal on clinical grounds alone, were first detected by a low value in screening tests for serum thyroxine levels and subsequently confirmed by a high serum TSH level. Low serum triiodothyronine level is frequently found in apparently euthyroid patients with tetraplegia and is necessarily not an indicator of clinical hypothyroidism in these patients.

Key words: Thyroid hypofunction in spinal injury patients; Triiodothyronine.

Introduction

EARLY symptoms of hypothyroidism are usually non-specific and of insidious onset, and a high index of clinical suspicion is important in detecting this disorder. The detection may be particularly difficult in patients with spinal cord injury. The clinical symptomatology, consisting of apathy, sleepiness and constipation, suggesting hypothyroidism, could pass as a mental or physical consequence of the spinal trauma. In such patients, assessment of deep tendon reflexes does not help in diagnosing thyroid hypofunction. Under the circumstances, laboratory tests of thyroid function would appear to be of special importance. Claus-Walker (1972) reported that serum thyroxine (T₄) levels in acute tetraplegic patients tend to be significantly lower than those among chronic tetraplegics. Accordingly, we have routinely obtained simple thyroid function test results in our spinal injury patients to help interpret these test results for diagnosing hypothyroid in such patients. This paper presents test findings and our experience with the diagnosis of hypothyroidism in our patients.

Methods and Materials

A total of 225 spinal injury patients, 222 males and three females, were studied. Their age ranged from 18-85 years, and averaged 40 years. The level of the spinal injury varied from C₄ to L₃ and was cervical in 107, thoracic in 95, and lumbar in 23 patients. The time interval between the spinal trauma and the laboratory testing of thyroid function was under 3 months in 55 patients and over 3 months in 170 patients.

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Serum triiodothyronine (T₃), T₄ and TSH were measured by radioimmunoassay (RIA) technique (Immuno-T₃, T₄ and TSH Kit, Pantex, Santa Monica, California). T₃ resin uptake T₃-RU test was done using Pantex 'T₃-uptake' kit. All patients were on a 2600 calorie diet containing 290 g carbohydrates. Venous blood was sampled after overnight fasting between 7 a.m. and 9 a.m. Twenty-five normal subjects and 115 of the 225 spinal injury patients had all four tests. Each of the other 110 patients was first screened by T₄ RIA and T₃-RU tests. TSH levels and other measurements were obtained only when one or both of the screening tests were abnormal.

The 115 patients on whom all four tests were performed were divided into five groups for analytical purposes.

Group I: Tetraplegics within 3 months post-injury (mean 56 days) referred to as 'acute tetraplegics' were also observing bedrest.

Group II: Tetraplegics over 3 months post-injury, when they were studied were referred as 'chronic tetraplegics', were ambulatory on wheelchair.

Group III: Paraplegics within 3 months post-injury (mean 55 days) were considered 'acute paraplegics' and were on bedrest.

Group IV: Paraplegics over 3 months post-injury considered as 'chronic paraplegics' were ambulating on wheelchair.

Group V: Ambulatory walking paretics (eight tetraparetics and seven paraparetics).

Results

Figures 1-4 show the results of all four tests obtained in each of the 25 normal subjects and 115 patients. The mean plus/minus up to three to four standard deviations of the values obtained in the 25 normal subjects were considered to be within the normal range: *i.e.* 4.1 to 11.4 µg/dl for T₄, 25 to 36 per cent for T₃-RU, and 0 to 8 µuv/ml for TSH, and 63 to 194 µg/dl for T₃. These ranges were all essentially identical to the corresponding normal ranges suggested by manufacturers of the test kits used in this study.

All the 115 patients had normal TSH levels (Fig. 1). Although the mean TSH level among the acute paraplegics and that among the acute tetraplegics was slightly higher than the normal mean, these small differences were of doubtful significance ($0.1 < p < 0.2$, Fig. 4). On this basis, all 115 patients were considered to be euthyroid even though two of them had subnormal T₄ levels (Fig. 2). The mean T₄ level of each of the five groups of patients was not significantly different from the normal mean value (Fig. 2). Similarly, all except one paraplegic (Group IV) had T₃-RU that appeared to be slightly higher than the normal mean (Fig. 3).

As shown in Figure 4, the T₃ level of the walking paretics was not significantly different from the normal value, but the paraplegics and especially the tetraplegics tended to have a low normal or subnormal T₃ level. Mean serum T₃ level of acute paraplegics was 100.3 ng/dl and that of chronic paraplegics was 114.3 ng/dl; both of these were significantly lower than the mean serum T₃ of the normal group ($p < 0.005$ and $p < 0.02$ respectively). Similarly, chronic tetraplegics had a significantly lower T₃ level of 92.6 ng/dl ($p < 0.001$). The lowest mean T₃ levels were found among the eight acute tetraplegics. Their mean T₃ level of 67.7 ng/dl was much lower than the normal group ($p \ll 0.001$). Of the eight patients, four had low normal (64 to 84 ng/dl), and three had subnormal values (under 64 ungd/dl). Five of the 46 chronic tetraplegics had subnormal T₃. All of the

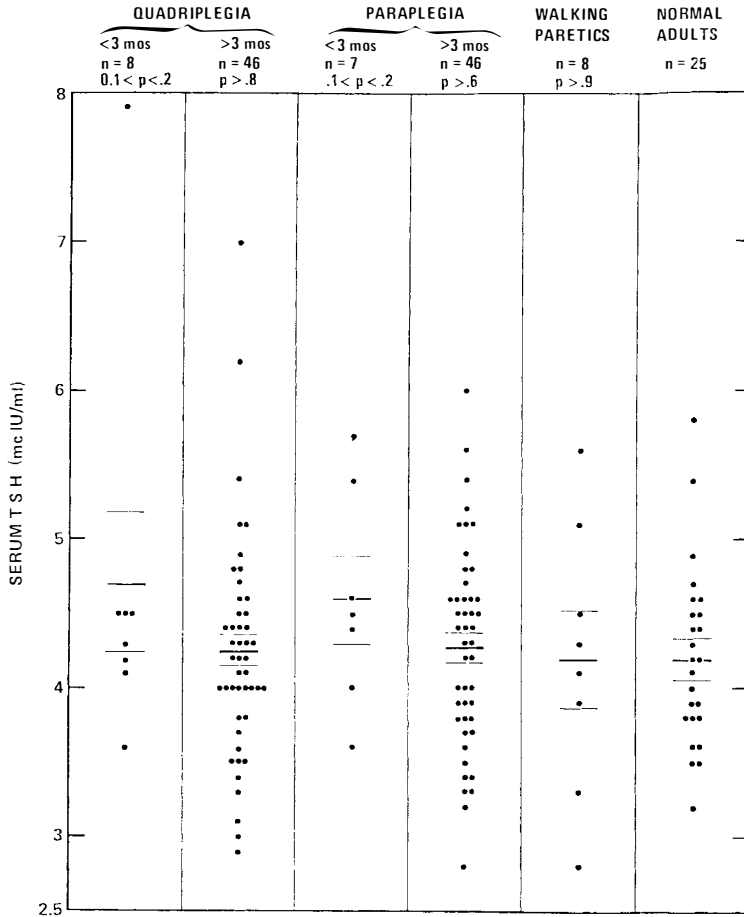


FIG. 1

Serum thyroid stimulating hormone levels in normal adults, walking paretics, paraplegics and tetraplegics. The latter two groups of patients are each further subdivided into acute and chronic cases, according to whether the interval between the injury and the study is under or over 3 months. The number of subjects or patients in each of the six groups is indicated by 'n'. The student 't' testing for the significance of differences in means between a patient group and the normal adult group is shown in terms of p values for each of the five patient groups. In the figure, each dot represents a subject, bold bar a group mean, and distance between a bold bar and an adjacent light bar the standard error of a mean.

three acute and the five chronic tetraplegics had normal T_4 , T_3 -RU, and TSH, and all were considered to be clinically euthyroid.

Of the other 110 patients screened with T_4 -RIA and T_3 -RU, none had a subnormal T_3 -RU. Only two had subnormal T_4 levels of 1.2 and 2.5 $\mu\text{g}/\text{dl}$, respectively. They also had low normal T_3 -RU (27 per cent) and grossly elevated TSH levels of 335 and 117 $\mu\text{IU}/\text{ml}$, respectively. Thus, they were considered hypothyroid. One of them had undergone radiation therapy for carcinoma of the esophagus and developed radiation myelopathy and possibly radiation thyroiditis

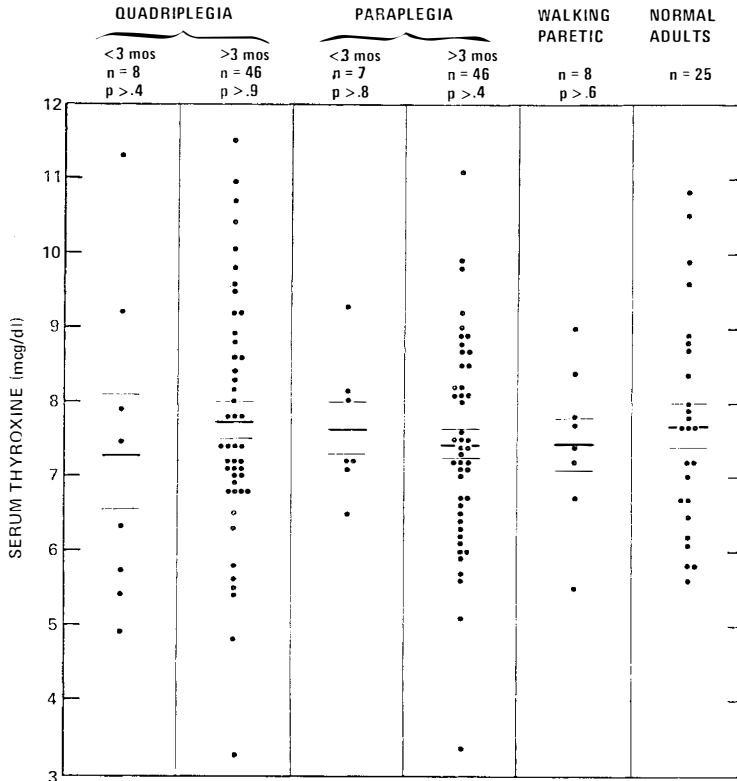


FIG. 2

Serum thyroxine levels in the six groups of subjects described in Figure 1.

leading to hypothyroidism. The case histories of the other hypothyroid patient and that of one euthyroid patient who clinically appeared to be hypothyroid are illustrated.

Case No. 1: 32-year-old C5 tetraplegic following a diving injury was admitted to Palo Alto V.A. Hospital about a year post-injury. He appeared to be apathetic and drowsy with slow speech. These symptoms were clinically thought to be due to depression. Physical examination revealed an obese tetraplegic male. There was no palpable goiter. The laboratory thyroid tests revealed a T₄ level of 1.2 μgm per cent, T₃-RU of 26.8 per cent and TSH of 335 μIU/ml. His ¹³¹I thyroid scan showed minimal patchy uptake in the gland, with a 24-hour uptake of only 2 per cent. Antimicrosomal antibodies were raised to 4500 units/ml (normal <25). Thus, he was felt to have an autoimmune thyroid disease as the cause of his hypothyroidism. His therapy was started with 50 μgm of T₃ and T₄. After a few days, the T₃ was discontinued and the T₄ dose gradually increased to 150 μgm/day with a return of serum levels of both T₄ and TSH to within normal limits. He showed a general improvement in well being.

Case No. 2: This 56-year-old man had an automobile accident and became C5 tetraplegic and was transferred to Palo Alto V.A. Hospital 6 weeks post-injury.

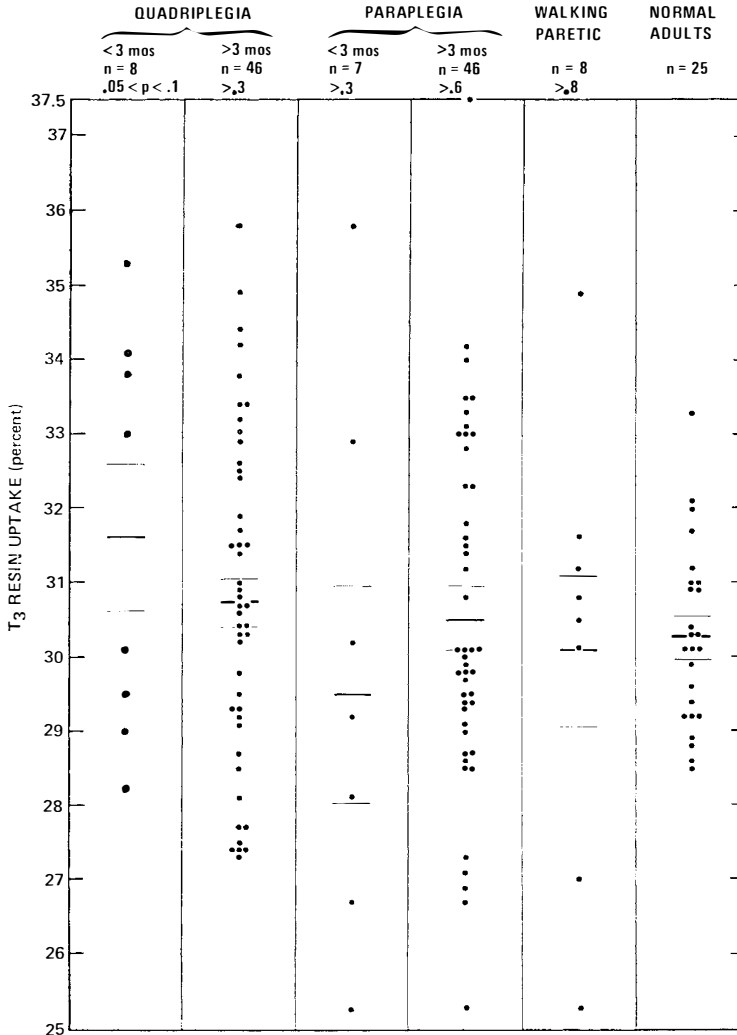


FIG. 3

T₃ resin uptake values in the six groups of subjects described in Figure 1.

He appeared to be dull and lethargic with dry and atrophic skin. He was hypothermic (96–98°F) and also had bradycardia (50–60/min). He was thought to have a clinical hypothyroidism. After drawing blood for thyroid function and other laboratory tests, he was started on 5 μg T₃ per day. The tests revealed normal haemoglobin and electrolytes, Serum T₄ 5.4 μg per cent, T₃-RU 29.5 per cent, T₃ 48 ng per cent, TSH 4.5 μIU/ml, and cholesterol 205 mg per cent. The normal TSH level clearly showed absence of primary hypothyroidism. Since he had a head injury, the possibility of a secondary (pituitary) hypothyroidism was further evaluated by measuring serum levels of follicular stimulating hormone, lutenising hormone and growth hormone—they were all normal. Thus, he was felt to be euthyroid and the T₃ therapy was discontinued.

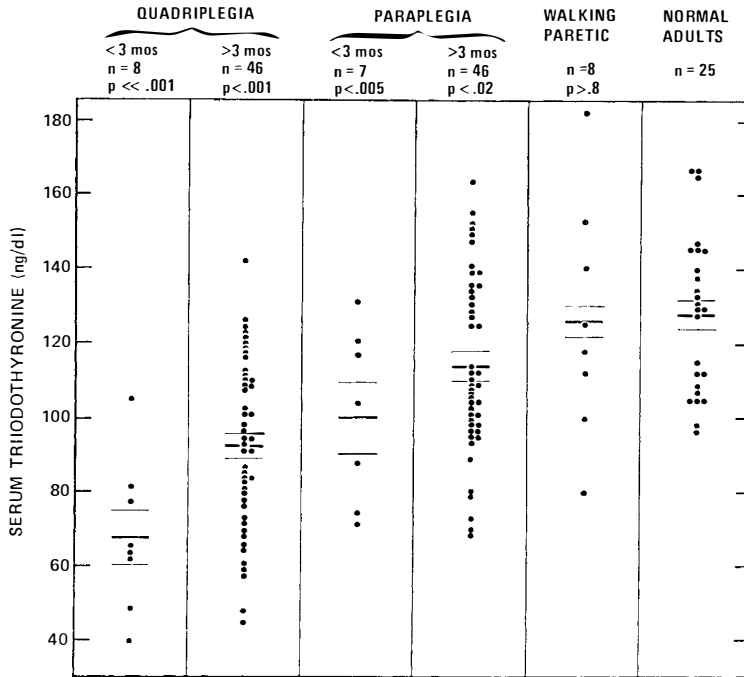


FIG. 4

Serum triiodothyronine levels in the six groups of subject described in Figure 1.

Discussion

In this study, the serum T₄ level of spinal injury patients did not differ from that of normal controls. This observation does not corroborate the earlier findings of Claus-Walker (1977) who observed a decreased serum T₄ in acute tetraplegic patients. Four of our patients had subnormal T₄ levels. Two of these four also had abnormally high TSH levels and thus were hypothyroid. Clinically, both these patients did not appear to be hypothyroid, and the diagnosis could have been missed without the laboratory assessment of their thyroid function.

The two cases of hypothyroidism represent an incidence of 0.9 per cent of our 225 patients. As a proportion to total hospital admissions, the incidence of hypothyroidism has been reported to be 0.01 to 0.08 per cent by Mean (1948), and this figure could be an underestimate since mild cases of hypothyroidism are clinically not easily detectable and laboratory diagnosis of thyroid dysfunction has much advanced since then. A recent survey by Tunbridge (1975) shows a prevalence of hypothyroidism of 0.9 per cent in Wickham, north-east England. However, our series is small, and it is difficult to compare the incidence of hypothyroidism in our spinal injury patients with that of the general population.

A striking finding in our study is a low T₃ level in many of our spinal injury patients who are euthyroid clinically and by other thyroid function tests. The depressed T₃ level does not appear to indicate a thyroid hypofunction. This impression is further supported by others, where low T₃ levels have been recorded in a variety of other non-thyroidal conditions. These conditions include fasting

(Spaulding, 1976); disseminated malignancy (Carter, 1977); and many other acute and chronic illnesses (Burger, 1976).

Most endogenous T₃ is produced by an extrathyroidal conversion of T₄ to T₃ (Cavalieri, 1977). The low serum T₃ level in spinal injury patients probably represents a diminished peripheral conversion of T₄ to T₃. Little is known about the control of T₄ to T₃ conversion. Our data suggest an association between serum T₃ depression and physical inactivity; the T₃ level is generally lower in tetraplegics than in paraplegics, the depression being greater in acute cases than in chronic cases, and the walking paretics have normal T₃ levels. It is tempting to speculate that physical inactivity may bring about a diminished T₄ to T₃ conversion peripherally. Caloric restriction readily induces low serum T₃ levels in normal individuals (Merrimec, 1976). Although all of our patients were on regular diet, decreased intake of calories in acutely ill patients may be contributing to low T₃ levels.

T₄-RIA and T₃-RU tests are simple and require few hours to complete and appear to be suitable as primary screening tests in spinal cord injury patients with suspected hypothyroidism. If these tests are consistent with the diagnosis of hypothyroidism, the suspicion may then further be confirmed by TSH RIA, which is generally 1-day procedure. Since almost all spinal cord injury patients with abnormally low T₃ RIA were felt to be euthyroid, serum T₃ estimation does not seem to be as useful as the above-mentioned tests.

Summary

Thyroid function tests were performed in 225 spinal cord injury patients. Serum T₄ level and T₃ resin uptake, but not serum T₃ level, were found to be useful as screening tests, for thyroid hypofunction. Suspicion of hypothyroidism based on T₄ and T₃ resin uptake test was confirmed by serum TSH level. Clinically unsuspected hypothyroidism was detected in two patients (0.9 per cent). Among the paraplegics and the tetraplegics tested, the serum T₃ level tended to be in the low normal or subnormal range, even though they were clinically euthyroid and the other thyroid functions were normal. Subnormal serum T₃ levels (under 64 µg/dl) were found in three out of eight euthyroid acute tetraplegics tested.

RÉSUMÉ

La fonction thyroïdienne a été testée chez 225 malades atteints de lésions médullaires. Le taux sérique de T₄ et le taux d'absorption sur résine de T₃ permettent de détecter l'hypofonctionnement thyroïdien. Par contre le taux sérique de T₃ s'est avéré inutile. Le diagnostic d'hypofonctionnement thyroïdien fut confirmé par le niveau plasmatique de T.S.H. Un hypothyroïdisme insoupçonné fut trouvé chez 2 malades (0.9%). Chez les paraplégiques et les tétraplégiques examinés, le niveau plasmatique de T₃ était à la limite inférieure du taux normal, ou un peu au-dessous, même s'ils étaient euthyroïdiens cliniquement, et les autres tests thyroïdiens étaient normaux. Nous avons trouvés des niveaux plasmatiques de T₃ subnormaux (inférieur à 64 µg/dl) chez 3 des 8 tétraplégiques aigus euthyroïdiens examinés.

ZUSAMMENFASSUNG

Schilddrüsen Funktionsteste wurden an 225 Patienten mit Rückenmarkverletzungen durchgeführt. Serum T₄ und T₃ 'resin' stand aufwärts jedoch kein Serum T₃ stand, erwies sich von Nutzen beim 'Screening Test' für Schilddrüsen 'Hypofunktion'. Verdacht von 'Hypothyroidism' begründet auf 'T₄ und T₃ Resin uptake' hat sich durch 'Serum TSH Level' bestätigt. Klinisch unverdächtiger 'Hypothyroidism' wurde in 2 patienten

entdeckt (0.9%). Unter den Paraplegics und Tetraplegics untersucht, hatte das 'Serum T₃ Level' die Tendenz sich in der niederen—Normalen oder unter-Normalen Region zu halten, trotzdem sie klinisch 'Euthyroid' waren und die anderen Schilddrüsen Funktionen normal waren. Unter normale 'Serum T₃ Level' (unter 64 ug/dl) wurden in 3 von 8 Euthyroid acuten Tetraplegics Patienten, welche getestet wurden, gefunden.

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