

Usefulness of Thyroid Hormones Measurement in Predicting the Prognosis of Patients with Severe Multiple Injuries

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(Received April 12, 1999)

To determine the usefulness of thyroid hormones measurement in predicting the prognosis of patients with severe multiple injuries, a total of 55 patients with severe multiple injuries (34 males and 21 females, with a mean age of 50.7 years) were evaluated between September 1996 and February 1999. The patients were evaluated within 2 hours of admission, and the serum free thyroxin (FT₄), thyroxin (T₄), free triiodothyronine (FT₃), triiodothyronine (T₃), thyroxin-binding globulin (TBG), injury severity score (ISS), and the acute physiology and chronic health evaluation (APACHE II) score were determined. The same tests were repeated with the exception of the APACHE II on day 1, day 3 and day 7. A comparison was made of these variables between the survivors (37 patients) and non-survivors (18 patients). The mean ISS was 35.1 ± 15.3 and the mean APACHE II score was 17.7 ± 12.0. The best predictors of the prognosis in a descending order were T₄ (p<0.0001), T₃ (p<0.0001), FT₄ (p<0.0001), ISS (p<0.01), and APACHE II score (p<0.01). Measuring the thyroid hormones (T₄, T₃ and FT₄) within 2 hours of admission together with ISS and APACHE II score appear to be useful in predicting the prognosis of patients with severe multiple injuries.

Introduction

Decreased serum triiodothyronine (T₃) and increased serum reversed T₃ (rT₃) are frequently observed in patients with severe non-thyroidal illnesses (NTI). These findings are also often accompanied by a low thyroxin (T₄) level though the serum TSH usually remains normal¹⁾. This pattern of change in thyroid hormone metabolism is referred to as the "sick euthyroid syndrome", and it has been observed in association with major surgery²⁾, burns³⁾, critical illnesses⁴⁾, starvation⁵⁾, and drug therapy⁶⁾. The reason for this ex-

treme hypothyroxemia that can occur in severe illnesses is not clear, but a relation between the T₄ levels and both severity and outcome has been observed in patients under intensive care⁴⁾⁷⁾⁸⁾.

The objective of this study was to determine the usefulness of the thyroid hormones measurement in predicting the prognosis of patients with severe multiple injuries.

Subjects and Methods

Patients

The extent and severity of injury were evaluated using the injury severity score (ISS) in

which the degree of injury is assessed in each of five body areas and the score is calculated using the three most severely injured areas. The range of this score is from 0 to 75⁹⁾. The severity of illness was graded using the Acute Physiology and Chronic Health Evaluation (APACHE II)¹⁰⁾. We defined "severe multiple injuries" as a patient who sustained injury in two or more body areas as described above and each injury score was 3 or higher based on the Abbreviated Injury Scale (AIS). Patients with thyroid or pituitary/hypothalamic diseases and patients taking drugs known to interfere with thyroid hormones metabolism or regulation such as glucocorticoids, propranolol, estrogens and anti epileptics were excluded from this study.

A total of 55 patients (34 males and 21 females with a mean age of 50.7 years) with severe multiple injuries were taken directly in an ambulance from the scene to the department of emergency medicine of Fukui Medical University and examined prospectively following admission between September 1996 and February 1999. It should be noted that 47 (87.5%) of the 55 patients were initially in shock.

All patients gave informed consent. The study was approved by the Fukui Medical University Hospital committee on medical ethics.

Methods

The patients were evaluated on arrival and a set of variables were measured. On day 0, specifically serum free thyroxin (FT₄) and free triiodothyronine (FT₃) were measured by AMERLEX-MAB FT₄, AMERLEX-MAB FT₃ (MBC Lab, Tokyo Japan), radio immuno assay (RIA), thyroxin (T₄) and triiodothyronine (T₃) were measured by T-4 RIABEAD, T-3 RIABEAD (MBC Lab), RIA, and TSH, thyroxin-binding globulin (TBG) were measured by RIA-gnost hTSH, RIA-gnost hTBG (MBC Lab), immuno-radio metric assay (IRMA) as soon as those patients were brought

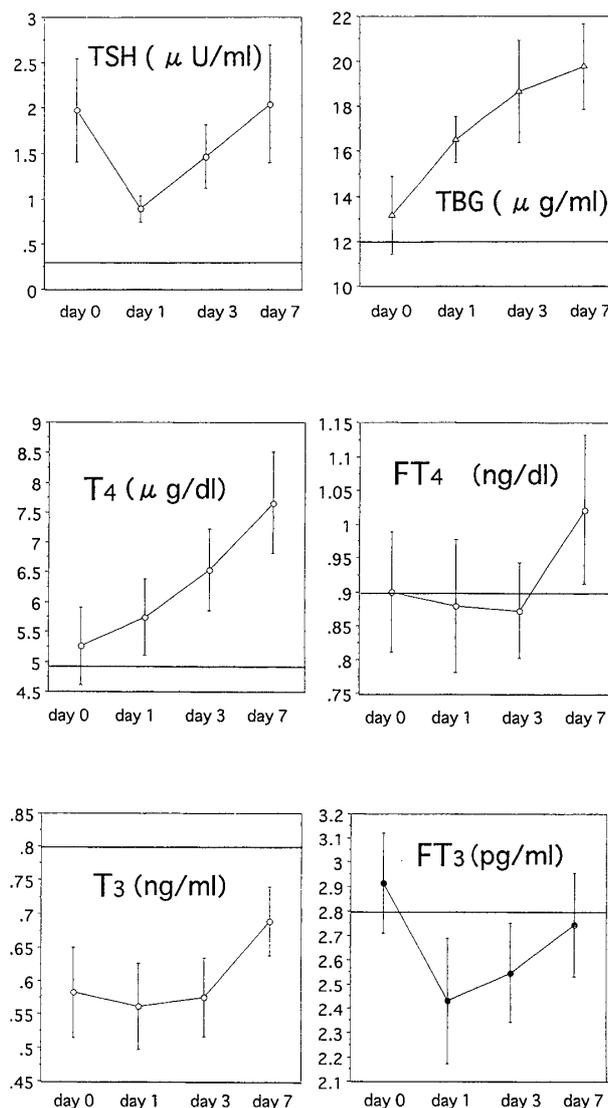


Fig. 1 Serum TSH, TBG, T₃ and FT₄, FT₃ levels in severe multiple trauma during the first 7 days following injury

Values are mean ± SEM.

— : indicates the normal lower limit of each hormone.

to the emergency room. No patient had received dopamine or any other drugs before taking the first blood samples. The ISS and APACHE II scores were also calculated. The same tests were repeated with the exception of the APACHE II on day 1, day 3, and day 7.

The patients were divided into the two groups; namely survivors and non-survivors. The total number of survivors was 37 and the total number

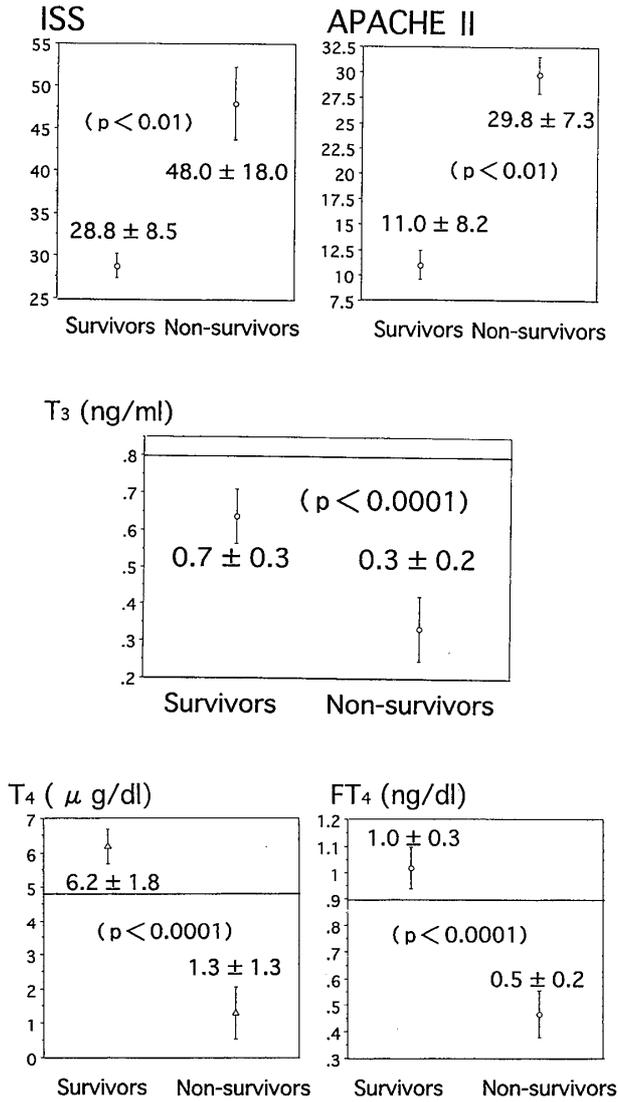


Fig. 2 Individual score for ISS, APACHE II and individual levels for serum T₃, T₄, FT₄ on day 0 in survivors and non-survivors after severe multiple injuries
 — : indicates the normal lower limit of each hormone.

of non-survivors was 18. All patients received dopamine via continuous infusion for hemodynamic support after admission. No steroids, beta-blockers or amiodarone were administered during the study.

The values obtained for each variable were compared between the survivor and non-survivor groups using the unpaired t-tests, and a p value of <0.05 was considered significant. The normal range of the measured variables are 0.9 to

1.9 ng/dl for FT₄, 4.9 to 12.4 μg/dl for T₄, 2.8 to 5.0 pg/ml for FT₃, 0.8 to 1.8 ng/ml for T₃, 12 to 30 μg/ml for TBG, and 0.3 to 5.0 μU/ml for TSH.

Results

The mean age of the patients in this study was 50.7 ± 22.7 years, the mean ISS was 35.1 ± 15.3, and the mean APACHE II score was 17.7 ± 12.0. A comparison of the thyroid hormones levels with reference intervals are shown in Fig. 1. The serum TSH levels decreased on day 1, but remained normal throughout the study period. Both T₃ and FT₃ levels decreased significantly on day 1, and all mean T₃ levels and the mean FT₃ levels on days 1, 3 and 7 fell below the normal range. Both T₄ and TBG levels decreased on day 0, and then increased but remained normal throughout the study period. The FT₄ levels decreased mostly on day 3, and the mean FT₄ levels on days 0, 1 and 3 fell below the normal range. Low T₃ syndrome (T₃ decreased, TSH normal) was observed in all of the 55 patients and low T₄ syndrome (T₃ decreased, T₄ decreased, TSH normal) was observed in 34 of the 55 patients.

A marked increase in the mean ISS and APACHE II score on day 0 in the non-survivors (n=18) compared to the survivors (n=37) was observed (p<0.01). However, a marked decrease in the mean T₃, T₄, and FT₄ levels in the non-survivors on the same day compared to the survivors was observed (p<0.0001) (Fig. 2). It should be specifically noted that the mortality rate was 100% for those patients exhibiting low T₄ syndrome with a serum T₄ level of less than 3.0 μg/dl on day 0.

Discussion

Our prospective data indicate that all patients with severe multiple injuries had decreased T₃ levels and normal TSH levels. Furthermore, 62.5 % of these patients had decreased T₄ levels, and low T₄ syndrome was found to be highly associated with mortality. Kaptein et al¹¹⁾ showed that

the mortality is even greater if nadir values of the free thyroxin index¹²⁾ are correlated, and McLarty et al⁷⁾ have found sequentially decreasing T₄ levels in moribund patients who subsequently died. The early recognition of patients with a poor outcome is potentially valuable because their identification may allow for closer observation and earlier therapeutic intervention. The typical sick euthyroid syndrome such as low T₃ or T₄ syndrome was observed in those patients with severe multiple injuries in our present study. However, few studies have been published on the sick euthyroid syndrome following severe trauma¹³⁾.

Becker et al¹⁴⁾ reported that the degree of thyroid dysfunction was generally related to the severity of injury. Chopra et al¹⁵⁾ and Oppenheimer et al¹⁶⁾ reported that the decrease in T₄ serum levels in patients with non-thyroidal illnesses can be attributed to reduction in thyroid hormone secretion as well as to presence of inhibitors of thyroid hormone binding. In addition, it has been shown that reduction in 5'-deiodinase activity also occurs in non-thyroidal illnesses which is responsible for the low T₃ levels and explains the opposite changes in the rT₃ levels⁶⁾¹⁷⁾. Low T₄ and T₃ levels with normal serum TSH levels have been reported in patients with severe non-thyroidal illnesses¹⁸⁾¹⁹⁾. Many hormones such as dopamine, glucocorticoids, endorphins, and prostaglandins are capable of reducing TSH secretion, and these hormones increase after trauma²⁰⁾. Kaptein et al¹⁸⁾ reported low TSH levels in critically ill patients receiving dopamine therapy. In our study, 85.5% of the patients were treated with dopamine therapy. Dopamine has also been shown to lower TSH and thyroidal iodine release in normal subjects¹⁸⁾, and it may also operate in the same manner in non-thyroidal illnesses. However, the serum TSH levels were normal in our patients in spite of depression of the serum T₃ levels throughout the study. It is thus doubtful that

dopamine was the main cause of the sick euthyroid syndrome. Many drugs are known to influence the thyroid function, but they were not given to the patients in the present study.

It has been reported that the decrease in thyroid hormones levels is related to the severity of illness and outcome⁴⁾⁷⁾⁸⁾. Kaptein et al⁴⁾ reported that high mortality rates have been observed in critically ill patients with markedly decreased T₄ levels (<39 nmol/l). A mortality rate of 84% was observed in 86 ICU patients with T₄ levels below 39 nmol/l, while a decrease in the mortality rate associated with increasing T₄ levels was observed by Slag et al⁸⁾. Chioloro et al²¹⁾ however reported that the TSH and T₄ levels correlated with the outcome. Increased ISS and APACHE II scores together with decreased serum T₄, T₃ and FT₄ levels were observed in the non-survivors, and the serum T₄, T₃ and FT₄ levels were significantly lower than those in survivors on day 0. It is of particular note that the mortality was 100% for those patients with low T₄ syndrome whose serum T₄ level was less than 3.0 µg/dl on day 0. Regarding the blood samples of day 0, it is not necessary to consider blood, colloid, or crystalloid solution because we got those samples before starting the medical treatment. The reason why both T₄ and TBG levels in our patients gradually increased throughout the study period seemed probably due to infusion of blood, fresh frozen plasma, and parenteral nutrition.

These results demonstrate that measuring the thyroid hormones (T₄, T₃ and FT₄) within 2 hours of admission is useful in predicting the prognosis of patients with severe multiple injuries. Our search in the Japanese and international literature showed only one report about the usefulness of thyroid hormones measurement in patients with severe multiple injuries²¹⁾.

Conclusion

Measuring the thyroid hormones (T₄, T₃ and

FT₄) within 2 hours of admission together with ISS and APACHE II score appear to be useful in predicting the prognosis of patients with severe multiple injuries.

This study was supported by a Grant from the Marine and Fire Insurance Association of Japan, INC.

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多発外傷患者の予後判定における甲状腺 ホルモン測定の有用性について

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T₃, T₄ (甲状腺ホルモン)の低下する,いわゆる euthyroid sick syndrome は慢性疾患や心筋梗塞などで見られ,その値が予後をよく反映したと報告されている.その一方,多発外傷は強い外力により生じることが多く,単独外傷に比べて著しく死亡率が高いのが特徴であり,多発外傷の予後には診断,治療を含めて複雑な因子が多いが甲状腺ホルモン値と予後に関する報告はほとんどない.今回我々はそれらにつき検討した.1996年9月より1999年2月まで福井医科大学病院救急部に入院した,多発外傷症例55例(男性34名,女性21名,平均年齢50.7歳)を survivors (生存群, S群), non-survivors (死亡群, N群)の2群に分け,それぞれの群で平均年齢,平均ISS (injury severity score),平均APACHE II (acute physiology and chronic health evaluation system II),と死亡率につき検討し, S群37例, N群18例において第0, 1, 3, 7病日にTSH値, TBG, T₃, T₄, FT₃, FT₄値を測定した.2群間の有意差検定は第0病日のみの値で, paired-t 検定で行った. S群37例とN群18例の間で, ISS, APACHE IIはそれぞれ危険率1%以下で有意差を認めた.2群間の第0病日のホルモン値の比較では,平均血清TSH値では有意差が見られず,平均血清T₃値は低下し,特にN群で著明に低下し,2群間では危険率0.01%以下で有意差を認め,平均血清FT₃値では有意差は見られなかった.平均血清T₄, FT₄値は0.01%以下の危険率で有意差を認めた.以上の結果より,多発外傷の予後の予測に関して,受傷後早期の甲状腺ホルモン,特に, T₃, T₄, FT₄値の測定は有用であると考えられた.