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ORIGINAL ARTICLE

Predictive value of thyroid hormone assessment in septic patients in comparison with C-reactive protein

Mohamed Hosny *, **Rania Rashad, Doaa Atef, Nashwa Abed**

Critical Care Department, Faculty of Medicine, Cairo University, Egypt

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KEYWORDS

Predictive value;
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Abstract *Introduction:* Thyroid dysfunction is associated with mortality in critically ill patients. We investigated the predictive value of the thyroid hormone compared to CRP in septic patients.

Methods: 80 patients were included in a prospective, randomized study done in the critical care department.

Results: FT3, FT4, and TSH levels on the fifth day were below the normal range in 61.3%, 31.2%, and 23.8% patients respectively. There was a significant decrease in the FT3 level on admission compared to the fifth day ($p < 0.001$). By comparison of thyroid hormone levels in patients with sepsis, severe sepsis and septic shock; we found the mean level of FT3 was lower in patients with septic shock (1.3 ± 0.4 pg/ml) and severe sepsis (1.7 ± 0.2 pg/ml) as compared to patients with sepsis (2.4 ± 1.2 pg/ml). The mean FT3 level increased in survivors (2.9 ± 1.03 pg/ml) compared to non survivors (1.9 ± 0.89 pg/ml) ($p < 0.001$). Correlation of FT3 on the 5th day to CRP ($r = -0.332$, $p = 0.039$), FT3 on 5th day to IL-6 ($r = -0.339$, $p = 0.035$) in non survivors. Correlation of FT3 on the 5th day to APACHE II ($r = -0.359$, $p = 0.025$) and SOFA score ($r = -0.427$, $p = 0.007$). ROC curves indicated that FT3 on the 5th day had the greatest power for predicting ICU mortality (sensitivity 87.2% and specificity 73.2%). CRP (sensitivity 100% and specificity 92.7%) is a better tool than IL-6 (sensitivity 92.3% and specificity 80.5%) in predicting mortality in sepsis.

Conclusion: FT3 levels were negatively correlated to CRP and IL-6 levels as well as APACHE II, SOFA scores. FT3 may be used as a marker of disease severity and a predictor of mortality.

1. Introduction

Sepsis, an infection induced systemic inflammation with deleterious host response to the pathogen, may often progress to severe sepsis and finally to septic shock. Severe sepsis leads to acute organ dysfunction secondary to documented or suspected infection; the condition may progress to septic shock

* Corresponding author.

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when hypotension develops that cannot be reversed with fluid resuscitation. Therefore, severe sepsis and septic shock are recognized as major health concerns worldwide with increasing incidence. Millions of people are affected around the world each year, (killing one in four and often more) [1].

The assessment of infection response to antibiotics relies mostly on the evolution of the same criteria used for diagnosis [2]. Microbiological criteria are also of little help in the assessment of response because of the long time needed to obtain culture results. These uncertainties in the clinical decision-making process have led investigators to study the inflammatory cascade for potential objective markers of infection. These biomarkers, could be used as surrogates of infection diagnosis; C-reactive protein (CRP) is one of the most studied biomarkers in this regard [3], It has already been shown how a single CRP measurement can help in the diagnosis of infection [4]; however there are some controversies concerning prognosis. Furthermore, the serial determinations have also been found to be useful in predicting infection as well as in monitoring its response to treatment [5].

Abnormal "thyroid function test" results have often been noticed in patients suffering from various infections, because the thyroid hormone plays an important role in the adaptation of metabolic function to stress and critical illness. Such alterations in thyroid hormone levels are referred to as "nonthyroidal illness syndrome (NTIS)", characterized by low serum levels of free and total triiodothyronine (T3) and high levels of reverse T3 (rT3) accompanied by normal or low levels of thyroxin (T4) and thyroid-stimulating hormone (TSH). NTIS can be attributed to increased deiodination of thyroxine (T4) to reverse T3 (rT3), rather than T3 and increased catabolism of T3 to 3, 3-diiodothyronine (T2) [6]. With increasing severity of illness, low total and free T4 and sometimes low TSH can be observed [7]. Thyroid dysfunction has also been found to be associated with the mortality of patients admitted to the ICU [8].

Therefore, thyroid hormone is also an important predictor in the mortality in patients with sepsis. The magnitude of the thyroid function test result abnormalities seems to depend on the severity and duration of illness, rather than the type of illness [9].

Researchers in some studies demonstrated that free triiodothyronine (FT3) levels in non survivors were significantly lower than those in survivors in acute respiratory distress syndrome and prolonged mechanical ventilation [10], whereas other researchers showed that there was no association between FT3 levels and ICU patient outcomes [11]. Conflicting results also were reported in terms of other indicators, such as FT4 and TSH [12].

Here we investigated the relation between thyroid hormone and mortality in patients with sepsis, severe sepsis and septic shock in comparison with C reactive protein.

2. Patient and methods

This prospective study was conducted in several Critical Care Units of Kasr Al-Ainy Hospital, Cairo University. A total of eighty patients, who were admitted to ICU with sepsis during the period from October 2013 to March 2014, were included.

The patients were categorized into three groups: (i) sepsis group included 36 patients with culture-proven or visually identified infection accompanied by two or more of the following abnormalities (temperature $>38.5\,^{\circ}C$ or $<36\,^{\circ}C$, heart rate >90 beats/min, respiratory rate >20 breaths/min or $PaCO_2$ <32 mmHg and TLC count $>12{,}000$ cells/mm^3, <4000 cells/mm^3, or >10 percent immature (band) forms; (ii) severe sepsis group included 23 patients with sepsis accompanied by organ failure or hypoperfusion (including oliguria and altered mental status); (iii) septic shock group included 21 patients with severe sepsis accompanied by hypotension (systolic blood pressure <90 mmHg or a fall off >40 mmHg from the baseline in the absence of other causes of hypotension).

Patients with the following criteria were excluded from our study: (i) history of any thyroid diseases such as hyperthyroidism, hypothyroidism, thyroid tumors, and thyroid nodule discovered by clinical examination on admission to the ICU; (ii) pregnancy within the previous six months; (iii) intake of drugs altering thyroid functions such as amiodarone, dopamine, and phenytoin.

3. Data collection

Medical history with a special emphasis on the history of drug intake or any thyroid disease of all patients was recorded. All patients are subjected to full clinical examination including vital signs assessment (heart rate, respiratory rate, blood pressure, and temperature). Pan Cultures (blood, sputum, urine or other suspected sites of infection) were collected on admission.

Blood samples were collected from each participant on the day of admission (D1) and fifth day after admission (D5) for free triiodothyronine (FT3), free thyroxine (FT4), thyroid-stimulating hormone (TSH), and C-reactive protein (CRP); IL-6 was also determined on the day of admission. Informed consent was obtained from the patient or his relatives. All patients were followed up until discharge or death. Finally, the patients were again divided into two groups: survivors and non survivors.

4. Measurements

Thyroid function tests (FT3, FT4 and TSH) were performed in Chemical Pathology Unit, Kasr Al-Ainy Hospital on ELISA Reader Stat Fax – 2100 using Enzyme Immunoassay Kits supplied by BioCheck (323 Vintage Park Drive Kits Foster City, CA 94404).

Following are the normal ranges of serum hormone concentrations: FT3 = 1.7–4.5 pmol/L, FT4 = 0.8–2 pmol/L, and TSH = 0.3–5.50 mIU/L. Serum creatinine and albumin levels were determined using chemistry auto analyzer (Hitachi 917) using Roche Diagnostics Kits. Serum CRP was measured using the kits supplied by Teco Diagnostics (1268 N. Lakeview Ave. Anaheim, CA 92807 USA. Serum IL-6 was measured using Human IL-6 ELISA kit supplied by Ani Biotech (Orgenium Laboratories Business Unit).

5. Scoring systems

Our study included the calculation of scoring systems: Acute Physiology and Chronic Health Evaluation (APACHE) II and sequential organ failure assessment (SOFA) scores. They allow an assessment of the severity of disease and provide an estimate of in-hospital mortality.