Original Research Article

Relationship between thyroid function and ICU mortality (sick euthyroid syndrome)

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ABSTRACT

Background: Sick euthyroid syndrome refers to alterations that occur in thyroid hormone levels in response to any critical illness like sepsis, ARDS, patients on mechanical ventilation and also any ICU patients. This study aimed at the relationship between thyroid hormone level changes and critical illness in ICU patients and predict the mortality based on thyroid hormone levels.

Methods: A prospective study was designed to carry out in intensive care unit (ICU), Institute of internal medicine, Rajiv Gandhi government general hospital, Chennai for six months from May to August 2015. A total of 40 patients were selected who fulfilled the selection criteria.

Results: APACHE II scores were calculated for all the 40 patients to assess whether thyroid function tests could independently predict the outcome of the patients. Again, the thyroid profile was compared with APACHE II scores in predicting the outcome. Values showed statistically significance.

Conclusions: Thyroid profile can be used as an independent factor in predicting the outcome of the patients. Thyroid profile can also increase the sensitivity of APACHE II score in predicting the outcome.

Keywords: APACHE II, ICU patients, Sick euthyroid syndrome, TFT

INTRODUCTION

Nonthyroid illness syndrome or sick euthyroid syndrome refers to alterations that occur in thyroid hormone levels in response to any critical illness like sepsis, ARDS, patients on mechanical ventilation and also any ICU patients.[1] The metabolic response to any critical illness involves every organ but the underlying pathology is not completely understood. Despite the primary diagnosis, as a stress induced response in critical illness, a state of hyper metabolism prevails leading to increased energy expenditure, hyperglycemia and muscle loss.

Thyroid hormone alterations commonly occur in critical illness in patients with no previous known intrinsic thyroid disease.[2] The changes in thyroid hormone levels is not an isolated phenomenon as it is also associated with changes in other endocrine axis as a response to stress.

Various theories have been proposed for alterations in thyroid function. In early course of the illness, the peripheral conversion of T4 to T3 is reduced leading to decreased free T3 with normal or reduced T4 associated with an increase in reverseT3 (rT3) and no alterations in TSH.[3] In prolonged illness, central hypothyroidism occurs leading to reduced TSH and T4 along with T3. In this study, thyroid profile was taken from patients admitted in ICU on day 1 and day 7 and to correlate the levels the thyroid hormones and the outcome of the patients and also to know the outcome of the disease can

be prognosticated with thyroid function tests in patients admitted in ICU.

The objective of this study was to study the relation between thyroid hormone level changes and critical illness in ICU patients. And to predict the mortality based on thyroid hormone levels in ICU patients.

METHODS

A prospective study was designed to carry out in intensive care unit (ICU), Institute of internal medicine, Rajiv Gandhi government general hospital, Chennai for six months from May to August 2015. A total of 40 patients were selected who fulfilled the selection criteria.

Inclusion criteria

- Patients admitted in ICU irrespective of the diagnosis
- Patients with ICU stay more than 7 days.

Exclusion criteria

- Patients with previous intrinsic thyroid, hypothalamic: pituitary axis disease
- Usage of iodine contrast agents in the past 8 weeks
- Usage of drugs causing hypothyroidism.

Data collection

Patients eligible for the study were subjected to clinical examinations and investigations.

Methodology

Patients admitted in ICU irrespective of their primary diagnosis were selected for this clinical study as per inclusion/exclusion criteria and were subjected to history taking and clinical examination after obtaining informed consent.

After clinical examination patients were subjected for routine investigations like complete hemogram, renal function tests, liver function tests, arterial blood gas analysis, blood and urine culture and sensitivity (if required). Patients were also subjected to thyroid function test on day 1 of their ICU stay.

All the patients in the study were followed up in ICU as they are getting treated and their status is monitored over a week. After 1-week time patients were again subjected to thyroid function tests (TFT) on day 7 of their ICU stay. Clinical progression over days was observed in terms of recovery from the illness or death of the patient. Finally, TFTs were analyzed whether they can predict the outcome of the patient by serial monitoring over 7 days. The APACHE II score (Acute Physiology and Chronic Health Evaluation) was calculated, a system for classifying patients in ICU. Physiologic scores of the patients correlate with severity of illness. The clinical

status of the patients in ICU was usually revealed by this scoring system.[4]

Statistical analysis

Data were expressed as number and percentage of total. Demographic and clinical characteristics were analyzed by using Chi square test. The level of significance was estimated with 95% confidence intervals and P value <0.05. Software used was SSPS 2.0.

RESULTS

40 patients who fulfilled the selection criteria were subjected to history taking and clinical examination. Patients were followed up in ICU over day 1 and 7. Progress was observed in terms of recovery from illness. In this study, 14 out of 40 patients were in the age group between 41 - 50 years. But this is not statistically significant. Among 40 patients, 23 were found to be males and 17 were found to be females. Out of 40 patients 20 of them were on ventilator, 22 were having diabetes mellitus and 20 were having hypertension.

Table 1: Demographic and clinical characteristics of the study participants.

Characteristics	Frequency	Percentage (%)
Age in years		
Below 30	9	22.5
31-40	10	25.0
41-50	14	35.0
Above 50	7	17.5
Sex		
Male	23	57.5
Female	17	42.5
Ventilator requirement		
Yes	20	50.0
No	20	50.0
Diabetes mellitus		
Yes	22	55.0
No	18	45.0
Patients having hypertension		
Yes	20	50.0
No	20	50.0

60% of patients out of 40 were alive at the end point and were discharged. 40% patients were expired. Even though 14 out of 40 patients were in the age group between 41- 50, this is not statistically significant. The male and female ratio was not shown any statistical significance. The p value is 0.601 which is not significant. The Acute Physiology and Chronic Health Evaluation (APACHE) II score levels correlated with mortality. The p value for this correlation is <0.001.

Thyroid function tests were done on day 1 of ICU stay. The p value for T3 levels on day 1 is 0.087 and for day 7 is <0.001. The p value for T4 levels on day 1 is 0.980 and

for day 7 is <0.001. The p value for TSH levels on day 1 is 0.085 and for day 7 is <0.001. Based upon the results, the serial measurement of T3, T4 and TSH levels will help in predicting the outcome of the patients as an independent factor or in association with APACHE II scores. The significance increases depending on duration of illness.

Table 2: Comparison of demographic and clinical characteristics with outcome.

	Frequency	Outcome		Total	P value
		Alive	Died		
Age in years					
Below 30	Count	5	4	9	
	% Within age in years	55.6%	44.4%	100.0%	
	% Within outcome	20.8%	25.0%	22.5%	
31-40	Count	9	1	10	
	% Within age in years	90.0%	10.0%	100.0%	
	% Within outcome	37.5%	6.3%	25.0%	
41-50	Count	8	6	14	0.080
	% Within age in years	57.1%	42.9%	100.0%	
	% Within outcome	33.3%	37.5%	35.0%	
Above 50	Count	2	5	7	
	% Within age in years	28.6%	71.4%	100.0%	
	% Within outcome	8.3%	31.3%	17.5%	
Total	Count	24	16	40	
	% Within age in years	60.0%	40.0%	100.0%	
	% Within outcome	100.0%	100.0%	100.0%	
Sex					
Male	Count	13	10	23	
	% Within sex	56.5%	43.5%	100.0%	
	% Within outcome	54.2%	62.5%	57.5%	
Female	Count	11	6	17	
	% Within sex	64.7%	35.3%	100.0%	0.601
	% Within outcome	45.8%	37.5%	42.5%	
Total	Count	24	16	40	
	% Within sex	60.0%	40.0%	100.0%	
	% Within outcome	100.0%	100.0%	100.0%	
Ventilator					
Yes	Count	8	12	20	
	% Within outcome	33.3%	75%	50%	
No	Count	16	4	20	0.010
	% Within outcome	66.7%	25%	50%	
Total		100%	100%	100%	
Diabetes mellitus					
Yes	Count	14	8	22	
	% Within outcome	58.3	50	55	
No	Count	10	8	18	0.604
	% Within outcome	41.7	50	45	
Total		100	100	100	
Hypertension					
Yes	Count	11	9	20	
	% Within outcome	45.8	56.3	50	
No	Count	13	7	20	0.519
	% Within outcome	54.2	43.8	50	
Total		100	100	100	

Table 3: Comparison between APACHE II and outcome.

APACHE II	Outcome	N	Mean	P value
	Alive	24	34.54	
	Died	16	43.81	<0.001**
	Total	40		

APACHE II score which is calculated within 24 hours of ICU admission is compared with thyroid function tests which is taken on day 1. The results obtained with this comparison is that on day 1 levels of T3 significantly correlated with APACHE II scores whereas T4 and TSH levels are not statistically significant.

Table 4: Significance of TFT on predicting outcome.

Parameters	Day	Outcome	N	Mean	P value
T3	1	Alive	24	48.13	0.087
		Died	16	42.44	
	7	Alive	24	67.33	0.001**
		Died	16	33.88	
T4	1	Alive	24	3.9958	0.980
		Died	16	4.0000	
	7	Alive	24	4.9667	0.001**
		Died	16	3.7000	
TSH	1	Alive	24	0.7754	0.085
		Died	16	0.4831	
	7	Alive	24	1.2988	0.001**
		Died	16	0.3462	

Table 5: Correlation between APACHE II and TFT.

Parameters	Day		Apache II
T3	1	P value	0.002
		N	40
T4	1	P value	0.551
		N	40
TSH	1	P value	0.216
		N	40
T3	7	P value	0.001**
		N	40
T4	7	P value	0.010
		N	40
TSH	7	P value	0.013
		N	40

DISCUSSION

This study was conducted in the patients admitted in ICU irrespective of the diagnosis. The study group size was 40. Patients included in the study were closely monitored and thyroid function tests were taken on day 1 and day 7 as explained in methodology. All the patients are followed till the outcome which was either recovery and discharge or death of the patient. Outcome analysis was done in comparison with whether thyroid function tests were able to predict the outcome of the patients independently. The significance is also assessed by comparison of thyroid hormone levels with APACHE II scores. Following were the main observations of the study.

Out of 40 patients, maximum number of patients was observed in the age group of 41 - 50 years with the percentage of 35% as observed in the frequency distribution table. Aging process influences various tissues to thyroid hormone.[5] Out of 40 patients, 23 (57.5%) patients were male and 17 (42.5%) patients were female. There were no significant differences found in sexes which indicates both sexes are affected.[3]

Out of 40 patients, 22 patients were having diabetes mellitus and 18 were not having diabetes mellitus. 20 patients were having hypertension and 20 patients were without hypertension. In the study group population, 20 patients required ventilator support. Out of the 20 patients, 12 patients expired and 8 of them survived. Out of 20 patients not requiring ventilator support 16 of them survived and 4 patients expired.

APACHE II scores were calculated for all the 40 patients to assess whether thyroid function tests could independently predict the outcome of the patients. The observed p value for APACHE II score predicting the mortality separately was <0.001. As documented in previous studies, in this study also APACHE II score affects the outcome of the patients.[4,6]

Thyroid profile was taken from all subjects on day 1 and day 7 as per inclusion and exclusion criteria. T3, T4 and TSH values are separately subjected to statistical analysis and also, they are compared with APACHE II score in predicting the outcome. As for day 1, the observed p values for T3 in predicting the outcome was 0.087, for T4

was 0.980 and for TSH was 0.085. These values are not statistically significant. The p values, seen on day 7 for T3 in predicting the outcome was 0.001, T4 was 0.001 and for TSH was 0.001.

Again, the thyroid profile was compared with APACHE II scores in predicting the outcome. On day 1, the observed p values for the correlation for T3 were 0.002, T4 was 0.551 and for TSH was 0.216. T3 values on day 1 correlated with APACHE II scores in predicting the outcome based on statistical analysis. Wang et al in 2012 done a study on relation between thyroid function and ICU mortality also showed that low T3 can predict the mortality of the patients.[6]

Thyroid function tests obtained on day 7 were again compared with APACHE II scores in predicting the outcome. Based upon statistical analysis the observed p values were 0.001 for T3, 0.010 for T4 and 0.013 for TSH. All these values are statistically significant. Some reports are also given that addition of thyroid hormones to the APACHE II score improves the prediction of mortality for ICU patients.[7,8]

CONCLUSION

Thyroid profile can be used in predicting the morality in ICU patients. Serial monitoring of thyroid profile will increase the sensitivity in predicting the outcome. Outcomes assessed by thyroid profile are comparable with that of APACHE II scores. Thyroid profile can be used as an independent factor in predicting the outcome of the patients. Thyroid profile can also increase the sensitivity of APACHE II score in predicting the outcome.

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