Euthyroid sick syndrome in head injury patients compared with Glasgow Coma and Outcome Scales

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Abstract

BACKGROUND: Evaluation of the role of euthyroid sick syndrome and pituitary gland hormonal changes and the prognosis of patient mortality after severe brain injury.

METHODS: The research was conducted on 65 patients with isolated severe brain injury. Blood samples were obtained as soon as possible after the injury and on the 1st, 2nd, 3rd, 5th and 7th day after the injury. Blood concentrations of T_3, rT_3, T_4, FT_4, TSH, and PRL were estimated. The patients' state of health was evaluated in the sixth hour after the injury, using Glasgow Coma Scale, and after 180 days, using the Glasgow Outcome Scale. Multidirectional correlation was sought between the concentrations of the estimated hormones and the score obtained in the Glasgow Coma Scale and Glasgow Outcome Scale.

RESULTS: Cluster analysis showed that concentrations of the hormones in the patients who died are grouped in different clusters from those in the patients who survived. This proves that hormonal patterns are different in these groups. Statistically significant lower T_3 concentrations were observed on the 3rd day in comparison with the 0 day. Cumulative proportion surviving was lower for the OP group in comparison with the NOP group and amounted to 0.57.

CONCLUSIONS: In all patients covered by the research euthyroid sick syndrome was diagnosed. T_3 concentration on the 3rd day after the injury together with the evaluation in Glasgow Coma Scale allows for more precise prognosis.

Key words: brain injury, euthyroid sick syndrome, thyroid hormones, thyreotropin, prolactin, risk factors

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Introduction

The increase in frequency and seriousness of body injuries is a phenomenon currently observed in all developed countries. The main reason for this is the rapid development of motorisation and industry.

A special group of patients after accidents are those with brain injuries, which cause more than 2/3 deaths after car accidents. These injuries also lead to severe and irreversible physical and mental disability (1, 2). Computer Tomography (CT) examination is the standard procedure in this state. The appearance of haematoma during CT causing the mass effect is the indication for conducting a neurosurgical operation. The evaluation of the clinical state of patients after brain injury is mainly based on neurological examination with Glasgow Coma Scale (GCS) assessment (3, 4). Knowing other prognostic factors could help in treatment and could also give the possibility of the more economic handling of expensive medical procedures.

Euthyroid sick syndrome (ESS) refers to changes in thyroid hormone metabolism and regulation in patients with nonthyroidal illnesses (NTI). It includes a decrease in serum T_3, an increase in serum rT_3 and a decrease in serum T_4 depending on the severity of NTI. It was observed that during some NTI the severity of ESS is connected with mortality (5, 6, 7, 8).

The aim of the work was an evaluation of concentrations of thyroid hormones (T_3, T_4, FT_4, rT_3) and pituitary gland hormones (PRL, TSH) with parallel grading in GCS and Glasgow Outcome Scale (GOS) (9, 10, 11).

Methods

The research was conducted on 65 patients with severe isolated brain injury (intracranial haematoma). They were hospitalised in the Neurotraumatology Clinic of the Silesian Medical Academy in Bytom in 1996–1998. The research was conducted with the approval of The Regional Committee for Scientific Research. In clinical examination the patients were qualified twice: for the first time during their stay in hospital and for the second time at the end of their hospital treatment. After the end of hospitalisation the material for research was collected and the final classification was conducted.

Patients who were taken to hospital because of isolated brain injury with intracranial haematoma were qualified for the research. Patients were excluded from the research if they:

— suffered from thyroid disorders at that time or in the past,
— had metabolic or hormonal disorders,
— had any pathology in thyroid ultrasonography,
— had to be given catheholamines during hospital treatment,
— were under alcohol intoxication.

Patients qualified for the research were divided into 4 groups. Two criteria were taken into account: the treatment (operated or non-operated) and death within 180 days. The following groups were selected:

— patients operated on — OP,
— non-operated on patients — NOP,
— patients who survived — S,
— patients who died — D.

The evaluation in GCS (Table 1) was conducted in the 6th hour after the injury.

Patients were observed during their stay in hospital and during check-ups but not longer than for 180 days from the day of injury. The evaluation in GOS (Table 2) was conducted after 180 days.

Table 1. Glasgow Coma Scale

Motor	Obeys verbal commands	6
	Localises to noxious stimuli	5
	Normal flexion to noxious stimuli	4
	Abnormal flexion to noxious stimuli (Decorticate posturing)	3
	Extension to noxious stimuli (Decerebrate posturing)	2
	No response to noxious stimuli	1
Verbal	Fully oriented and converses	5
	Disoriented and converses	4
	Voices inappropriate words	3
	Makes incomprehensible sounds	2
	No vocalisation	1
Eye opening	Opens eyes spontaneously	4
	Opens eyes to verbal command	3
	Opens eyes to noxious stimuli	2
	No eye opening	1

To obtain a GCS score add the points given from each of the three categories together (minimum score = 3, maximum score = 15). The points given in each category should reflect the best response in a given time period. Use the greater motor score in the total GCS score

Table 2. Glasgow Outcome Scale

Score	Rating	Definition
5	Good Recovery	Resumption of normal life despite minor deficits
4	Moderate Disability	Disabled but independent; can work in sheltered setting
3	Severe Disability	Conscious but disabled; dependent for daily support
2	Persistent Vegetative	Minimal responsiveness (i.e. eye state opening with sleep/wake cycles)
1	Death	No survival

Blood samples (1 ml) were obtained as soon as possible after injury and on 1st, 2nd, 3rd, 5th and 7th day after injury (between 7 and 8 a.m.). Serum concentrations of thyroid hormones (T_3, T_4, FT_4, rT_3) and pituitary gland hormones (PRL, TSH) were determined. T_3, T_4, FT_4, rT_3 concentrations were estimated using modified coated tube radioimmunoassay method, Spectria Orion Diagnostica Finland. rT_3 concentration was estimated using radioimmunoassay RIA. TSH and PRL concentrations were estimated using coated tube immunoradiometric assay. Internal and external assay control was conducted.

Statistical analysis was conducted using Shapiro-Wilk's test for normality. The cluster analysis was used to find the interdependence between the observed data, then multidirectional correlation between observed serum hormones concentrations and results in GCS and GOS was estimated.

For survival analysis Kaplan-Meier method was used. The curves were checked by Cox-Mantel test. As the criterion of significance the probability $p < 0.05$ was taken.

The data were statistically evaluated by means of Statistica 5.1 PL StatSoft.

Results

The mean age of the patients studied was 47.4 ± 2.12 (male 77, female 8). The ratio of OP to NOP was 3 : 2. In the whole group 67.7% survived. In the OP group 61% survived and in the NOP group 69%. The mean score for all the patients in GCS was 5.8 (OP group 5.9, NOP group 5.8). The patients' evaluation in S group was 6.8, and in D group 5.4. In the case of patients who obtained 8 points in GCS no deaths occurred. For subsequent days in all groups the arithmetic mean and standard deviation or median and quartile range were estimated. The following values were set as normal: (T_3 (1.3–3.0 nmol/l), rT_3 (0.09–0.35 ng/ml), T_4 (51–148 nmol/l), FT_4 (11.7–27), TSH (0.4–6.0 mj/ml), PRL (40–470 mIU/l)). For the analysis of the obtained results cluster analysis was taken. As the starting data the correlation coefficients of hormone concentrations (T_3, T_4, FT_4, rT_3, TSH, PRL) for each group on the subsequent days of the test were taken. The linkage between groups S and D was 0.255 (Figure 1). The above data prove that hormones in those groups behave differently.

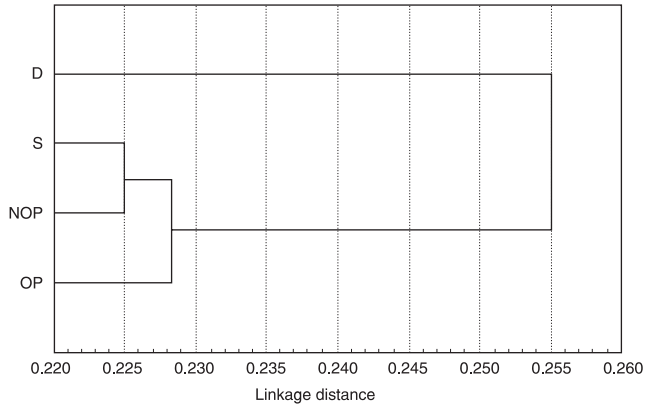

Figure 1. Cluster analysis for groups S and D.

Table 3. Correlation coefficients of serum hormones concentrations v. GCS

	T_3	rT_3	T_4	FT_4	TSH	PRL
day 0	–0.23	0.15	–0.06	0.20	0.17	0.32
1st day	0.32	–0.01	0.37	0.45	–0.19	0.39
2nd day	0.30	0.14	0.32	0.05	0.42	0.42
3rd day	0.55	–0.04	0.48	0.37	–0.43	0.37
5th day	0.30	–0.04	0.16	0.19	–0.11	–0.01
7th day	0.23	–0.32	0.08	0.12	0.24	0.38

(darkened fields show probability $p < 0.05$)

Table 4. Correlation coefficients of serum hormones concentrations v. GOS

	T_3	rT_3	T_4	FT_4	TSH	PRL
day 0	0.10	–0.07	0.14	0.14	0.13	0.35
1st day	0.28	–0.15	0.31	0.35	–0.10	0.38
2nd day	0.25	–0.12	0.21	0.06	0.28	0.14
3rd day	0.52	–0.21	0.30	0.26	–0.08	0.07
5th day	0.61	–0.42	0.36	–0.22	0.21	0.07
7th day	0.45	–0.41	0.27	0.08	0.27	0.39

(darkened fields show probability $p < 0.05$)

Table 3 presents correlation coefficients between estimated hormones and the number of points obtained in GCS score. On the first day statistically significant positive correlation between T_4, FT_4, PRL concentrations and the number of points obtained in GCS was found. On the second day statistically significant positive correlation was found for TSH and PRL. On the third day statistically significant negative correlation between GCS and TSH blood serum concentrations and statistically significant positive correlation between GCS and T_3, T_4 concentrations was found. Statistically significant positive correlation between T_3 blood serum concentration and points obtained in GOS on the 3rd, 5th and 7th day (Table 4) was found. It was found that patients who had T_3 concentrations on the 3rd day higher than 1.245 nmol/l obtained after 180 days 4 or 5 points in GOS.

For OP and NOP group curves of survival were drawn (Figure 2). The result was proved by Cox-Mantel. OP and NOP curves are statistically significantly different ($p < 0.05$).

Cumulative proportion surviving after 180 days in NOP group was 0.69 and in OP group 0.57. The increased hazard rate in NOP group in the first period of observation becomes equal on the 18th day and becomes lower in NOP group (Figure 3).

Discussion

Great similarity of the studied population to populations evaluated by other authors (12, 13) shows that the studied group was representative. Observed death percentage in the studied populations does not differ from results obtained in other studies on bigger populations. Hormonal changes observed in all patients: the increase in rT_3 and decrease in T_3, suggest that in patients with brain injuries euthyroid sick syndrome appears. The syndrome is diagnosed in various disorders not necessarily connected with thyroid pathology (14). Chiolero et al. observed a decrease in T_3

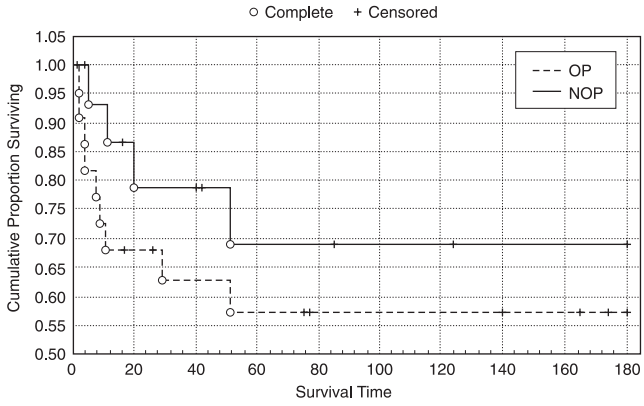

Figure 2. Kaplan-Meier curve for OP and NOP group.

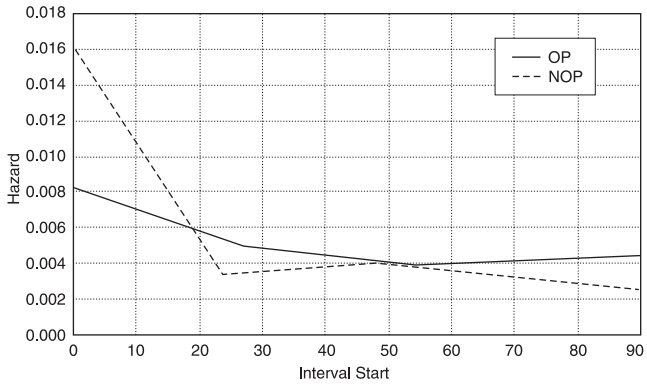

Figure 3. Hazard rate curve for OP and NOP group.

blood concentration below physiological values and a statistically significant increase in rT_3 concentration on the 4th day of treatment of patients with brain injuries (15). Cluster analysis showed the existence of interdependence between hormonal changes and mortality. T_3 estimation on the 3rd day after the injury, together with GCS, allows for a more precise evaluation of clinical prognosis, which is the number of points achieved in GOS 180 days after the injury.

Analysing the validity of obtained results for clinical prognosis of patients with brain injuries it seems that T_4 concentration on the 1st day, when it is statistically significantly lower and additionally it is in positive correlation with GCS, should be estimated. In the study, determination of rT_3 concentration was not found useful for mortality prognosis.

Comparing survival time of NOP and OP groups it can be said that group OP had lower cumulative proportion surviving in comparison with NOP. This is probably caused by the fact that NOP group patients were primarily in better clinical state although both NOP and OP groups had comparable results in GCS. Hazard rate shows that in comparison with group NOP probability of death in group OP is higher during the first days after the injury.

Conclusions

In all studied patients with brain injuries euthyroid sick syndrome was diagnosed taking into account thyroid hormonal changes.

In the case of patients with brain injury evaluation of T_3 concentrations on the 3rd day in comparison with GCS allows for more precise prognosis.

References

1. Jannet B, McMillian R. Epidemiology of head injury. Brit Med (Clin Res) 1981; 119: 101–104.
2. Kraus JF, Black MA, Hessol N, et al. The incidence of acute brain injury and serious impairment in a defined population. Amer J Epidem 1984; 119 (2): 186–201.
3. Teasdale G, Jennett B. Assessment of coma and impaired consciousness. A practical scale. Lancet 1974; 2: 81–84.
4. Teasdale G, Jennett B. Assessment and prognosis of coma after head injury. Acta Neurochir 1976; 34: 45–55.
5. Chow CC, Mak TW, Chan CH, Cockram CS. Euthyroid sick syndrome in pulmonary tuberculosis before and after treatment. Ann Clin Biochem 1995; 32: 385–391.
6. Kaptein EM, Weiner JM, Robinson WS, Wheeler WS, Nicoloff JT. Relationship of altered thyroid hormone indices to survival in nonthyroidal illnesses. Clin Endocrinol (Oxf.) 1982; 16: 565–574.
7. Pallazzo MG, Suter PM. Delivery dependent oxygen consumption in patients with septic shock: daily variations, relationship with outcome and the sick-euthyroid syndrome. Intensive Care Med 1991; 17: 325–332.
8. Vexiau P, Perez-Castiglioni P, Socie G, et al. The euthyroid sick syndrome: incidence, risk factors and prognostic value soon after allogenic bone marrow transplantation. Br J Haematol 1993; 101: 542–549.
9. Yates DW. ABC of major trauma. Scoring systems for trauma. Brit Med J 1990; 301: 1090–1904.
10. Phuenpathom N, Choomuang M, Ratanalert S. Outcome and outcome prediction in acute subdural hematoma. Surg Neurol 1993; 40: 22–25.
11. Levin HS. Neurobehavioral outcome of closed head injury: implications for clinical trials. J Neurotrauma 1995; 12: 601–610.
12. Ring IT, Berry G, Dan NG, et al. Epidemiology and clinical outcomes of neurotrauma in New South Wales. Aust-N-Z-J-Surg 1986; 56: 557–556.
13. Vincent JL. Year book of intensive care and emergency medicine 1993. Berlin Springer-Verlag, 1993.
14. Docter R, Krnning EP, de Jong M, Hennemann G. The sick euthyroid syndrome: changes in thyroid hormone serum parameters and hormone metabolism. Clin Endocrinol 1993; 39: 449–518.
15. Chiolero RL, Lemarchand-Beraud T, Shutz Y, de Tribolet N, Bayer-Berger M., Freeman J. Thyroid function in severely traumatized patients with or without head injury. Acta Endocrinol (Copenh) 1988; 117: 80–86.