

COMPARATIVE CHARACTERISTICS OF CHANGES IN SERUM CHOLESTEROL AND CORTISOL LEVELS AFTER TRAUMA AND SURGERY

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Abstract

The study included 19 patients undergoing abdominal surgery and 30 trauma patients who were monitored for total cholesterol during hospital treatment. Cortisol, free thyroxine (fT4) and free triiodothyronine (fT3) were also studied in some patients (24 in number). The aim of the study was to compare the levels of cholesterol and hormones in the two groups. The levels of cholesterol and cortisol examined in the early postoperative period in the operated patients were compared with those of the post-traumatic patients taken immediately after their admission to ICU, and in the next few days. The results showed significantly lower serum cholesterol levels in the trauma group and higher baseline cortisol levels in the same group. High cortisol and low cholesterol levels in trauma patients immediately after ingestion indicated the severity of the trauma. The smaller deviation from normal values in the group of operated patients was the evidence of the role of anesthesia and analgesia in reducing perioperative stress and pain.

Key words: *anesthesia, trauma, stress, cholesterol, cortisol*

Introduction

The change in cholesterol levels has interested scientists for decades. This is because cholesterol is a major building block for the human body. It is indispensable in the construction of each cell (involved in the composition of the cell membrane), the myelin sheaths of nerve fibers contain cholesterol, it is a starting product for the synthesis of steroid hormones, bile acids and vitamin D. The body's cholesterol needs increase in the period of its growth, as well as in conditions of acute stress, accompanied by impaired tissue structure, when on the one hand cholesterol is needed for their recovery, and on the other for the synthesis of steroid hormones, whose levels may be significantly above normal. Such conditions are trauma, surgery, sepsis, burns. In all of them, hypocholesterolemia is observed for a shorter or longer period of time. How severe the hypocholesterolemia will be and how long it will last depend on the severity of the damaging factor, its duration of exposure, as well as the age and general condition of the individual.

Purpose. To compare the level of serum cholesterol in patients who have suffered trauma with that of patients operated on in abdominal surgery, immediately after their admission to ICU.

To compare cortisol levels in the same two groups of patients.

To find out what are the changes in the levels of thyroid hormones

Materials and methods. The study included a total of 49 patients. 19 operated on the occasion of abdominal surgery. All operated patients after the operation remained in ICU. The remaining 30 patients had an accident and after the necessary initial examinations and possibly surgical interventions were also placed in ICU.

In the group of post-traumatic patients, the first sample was taken in the first few hours after the incident (between the 2nd and 5th hour of the incident). Subsequent samples were taken in the following days, between 7:30 and 8:30 in the morning. In the operated patients, the time of blood sampling was the same, and they had one additional blood sample before the operation. After collection of the serum, the samples were frozen and stored in a chamber. Total cholesterol was tested in the laboratory of "Dr. G. Stranski" UMHAT, Pleven, the

biochemical analyzers Hitachi-model 704, the company "Hitachi" - Japan and "Integra" - Rosh Diagnostic-Germany. The results are in mmol / l. The hormones were tested in the clinical laboratory of Exacta Medica, Pleven.

In all patients operated on for abdominal surgery, the anesthesia is general balanced anesthesia. After premedication with Dormicum, Fentanyl and Atropin, rapid sequential induction of anesthesia with Propofol and Lystenon at standard dose and endotracheal intubation was performed. Relaxation was maintained with Arduan and anesthesia with inhalation anesthetic and Fentanyl, their doses adjusted according to the intensity of the surgical stimuli.

Results. It is noteworthy that the level of total serum cholesterol in traumatic patients was significantly lower than the same one in operated patients immediately after surgery. Total cholesterol in the operated patients - 4.5 ± 1.22 mmol / l, and in the other group - 2.8 ± 0.83 mmol / l. $P < 0.05$ (Figure 1)

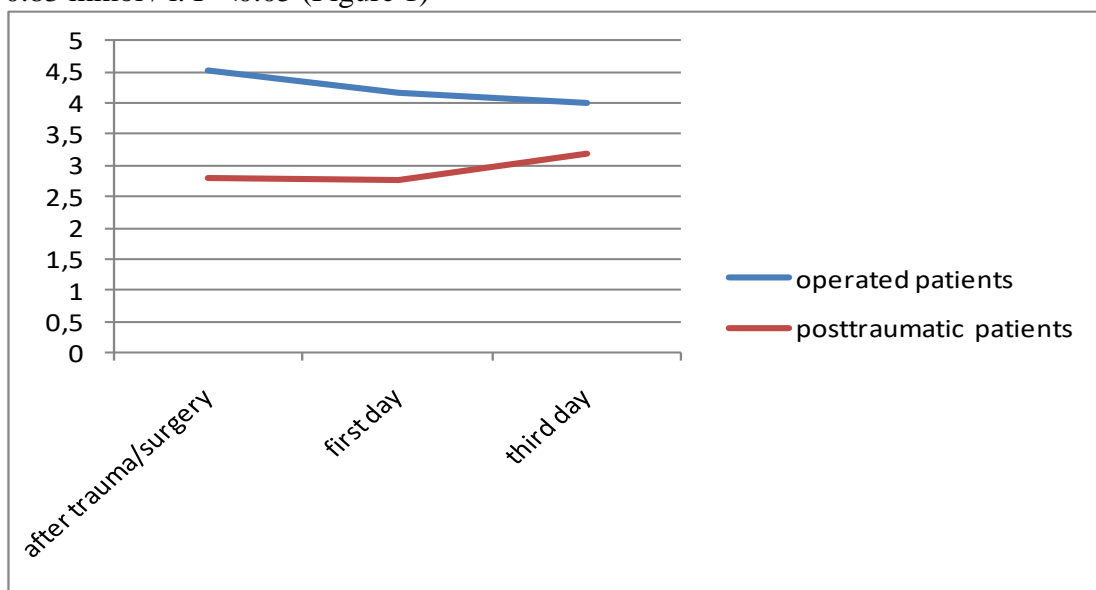


Fig. 1 Change in cholesterol level

Examination of the serum cortisol level revealed that it was 2-3 times above the reference values after the accident, with normalization observed 2-3 days after the injury. Cortisol norm - 171-536 nmol / l at 8 o'clock in the morning. In the operated patients the values postoperatively were also high (1074.0 ± 705.8 nmol / l), but lower than those in the group of post-traumatic patients (1453.8 ± 698.16 nmol / l), and suffered a gradual decrease in the following days (Figure 2).

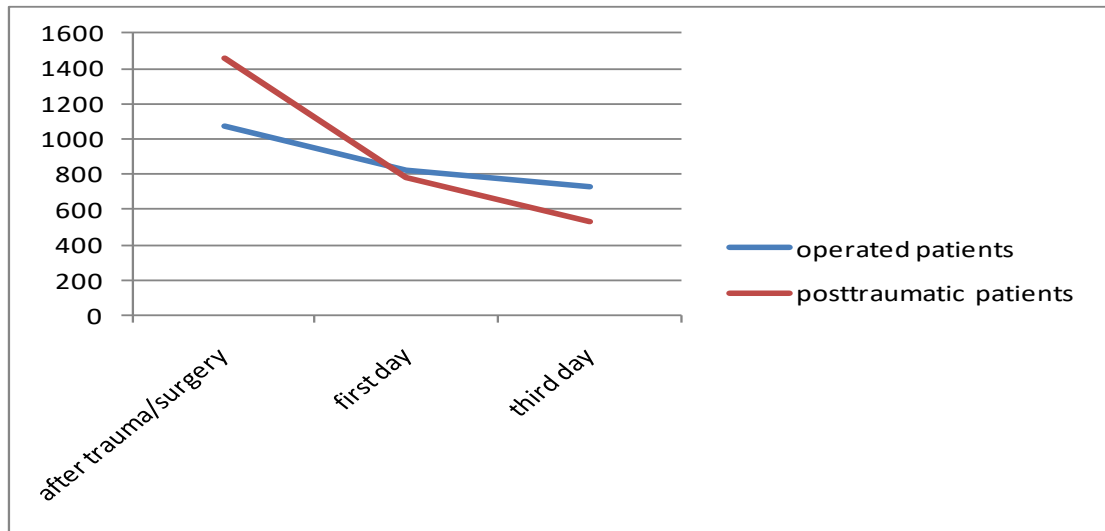


Fig.2 Change in cortisol level

In contrast to cortisol, no statistically significant changes were observed in fT3 and fT4 (fig.3 and fig.4). The values of both hormones remained within the normal range throughout the study. Reference values for FT3 - 2.8-7.1pmol / l. FT4 reference values - 12-22 pmol/l.

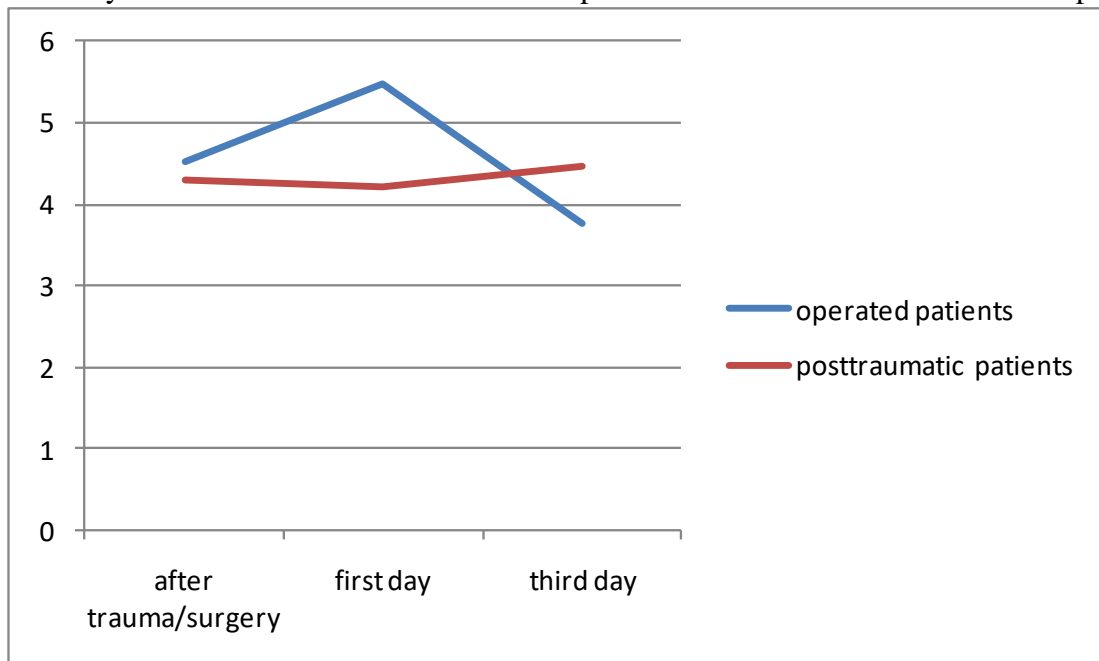


fig.3 Change in fT3

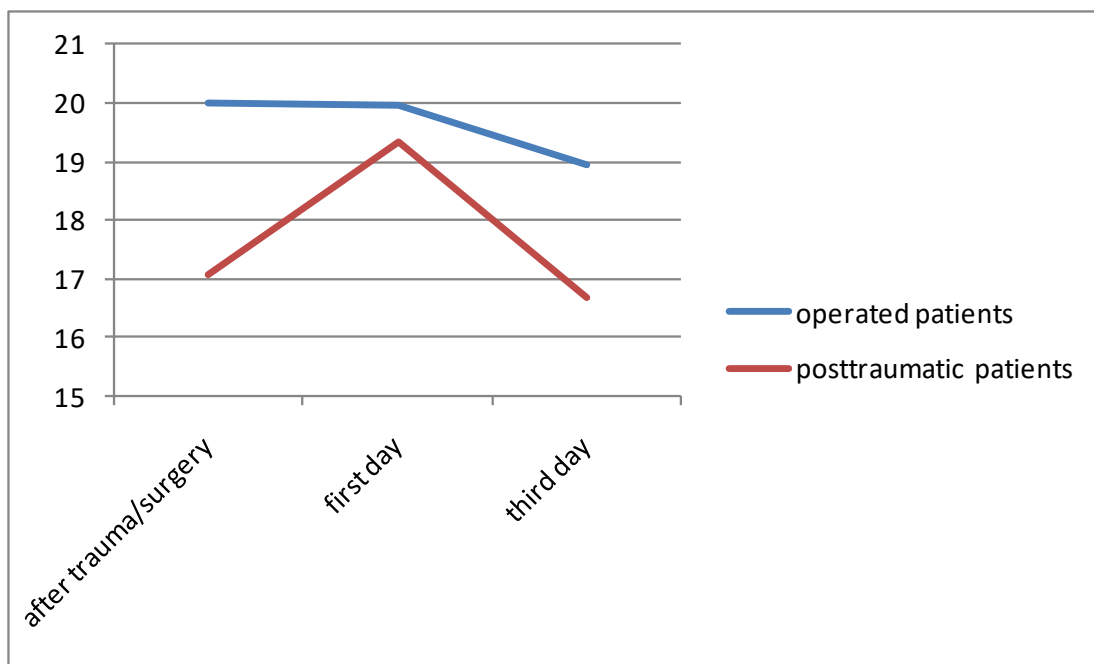


fig. 4 Change in fT4

Discussion

Cholesterol is an essential element of cell membranes and is indispensable in the processes of tissue repair after trauma, burns (1) and sepsis (2, 3). Hypocholesterolemia is an indicator of a metabolic response to stress (4). Low cholesterol is associated not only with reduced intake and hypoproteinemia. Tissue repair requires large amounts of cholesterol to synthesize new cell membranes (2). And there is also a reduced synthesis of cholesterol in the liver.

Hypocholesterolemia is common in patients with various acute diseases (5), as well as after surgery (6, 7). Change in lipid metabolism is observed after trauma, surgery, burns, sepsis (5, 8). Anabolic and catabolic processes are accelerated after tissue damage due to trauma, with catabolic dominance. Accelerated synthesis and degradation after trauma are also observed in cholesterol (9). In trauma patients, high adenocorticotrophic hormone (ACTH) production may lead to lower plasma cholesterol levels due to stimulation of high cortisol secretion (10).

Low serum cholesterol, during surgery and after, trauma, sepsis and others, according to most authors, is the result of three main causes: blood loss and its replacement with saline and colloidal solutions, increased body needs for cholesterol or decreased synthesis (11). Bakalar and co-authors (10) set themselves the task of testing their hypothesis that reduced cholesterol synthesis in trauma patients is a major cause of hypocholesterolemia. They conclude that the reduced production of cholesterol precursors is the cause of hypocholesterolemia.

The liver is a very important organ responsible for many functions, including fat and cholesterol metabolism (12). When there is liver dysfunction, it affects the metabolism of carbohydrates, cholesterol, bile salts and more (12). Inhaled anesthetics to a greater or lesser extent affect the hepatic blood supply and from there may affect function of liver, including cholesterol metabolism (13). We observed in one of the traumatic patients, who also had a

liver injury, very low cholesterol levels, which remained so for more than 20 days. Cholesterol on day 21 - 2.71mmol / l and this is twice its level in the first days.

Plasma cholesterol tends to decrease in stressful conditions, such as surgical trauma and in the event of complications – sepsis (7), liver failure, hemorrhage. The end effect is cumulative and the severity of hypocholesterolemia reflects the importance of the adverse factors that determine the severity of the disease (11, 14, 15). Monitoring of total cholesterol in patients with severe trauma is desirable (7).

The need for cholesterol is increased with increased synthesis of stress hormones and for the production and function of new cells in tissue repair (16). Cholesterol is indispensable in the recovery period after a severe injury.

In the first 12-24 hours after trauma, a sharp activation of the central nervous system (CNS) and endocrine system is observed (17, 18). The stress response is characterized by increased secretion of pituitary hormones and activation of the sympathetic nervous system (19, 20). Changes in pituitary secretion lead to a corresponding effect on the hormonal secretion of the target organs. As a result, these patients have elevated levels of counter-regulatory or anti-insulin hormones: cortisol, glucagon, catecholamines (18). (Table 1)(19).

Table 1 Hormonal response to stress (19)

Endocrine gland	Hormones	Change in secretion
Anterior pituitary	ACTH	Increases
	Growth hormone	Increases
	TSH (thyroid-stimulating hormone)	Increases or decreases
	FSH and LH	Increases or decreases
Posterior pituitary	AVP(arginine vasopressin)	Increases
Adrenal medulla	Cortisol	Increases
	Aldosterone	Increases
Pancreatic	Insulin	More often decreased
	Glucagon	Usually slightly elevated
Thyroid	Thyroxine	Decreased
	Triiodothyronine	Decreased

Glucocorticoids are directly related to stress. They are one of the most important adaptive hormones (16). Their secretion is influenced by the hypothalamic-pituitary system.

The most important glucocorticoid in humans is cortisol. It is synthesized from cholesterol under the control of corticotropin releasing hormone and ACTH (19).

The biosynthesis of cortisol is extremely fast – a few minutes after the activation of the adrenal gland by ACTH in the peripheral circulation appear glucocorticoids (19, 20, 21). The daily secreted level in normal condition (without stress) is $\approx 1\text{mg} / \text{kg} / \text{d}$ for almost all species. In humans, secretory levels ranging from 25 to 35 $\text{mg} / \text{kg} / \text{d}$ have been reported (20). Cortisol has a complex metabolic effect on carbohydrates, fats and proteins (17, 19).

Large amounts of cortisol suppress the production of thyroid hormones, as well as the enzyme that converts less active thyroxine (T4) into triiodothyronine (T3) (1, 19).

Under the influence of thyroid-stimulating hormone (TSH), the thyroid gland secretes T4 and T3, which enter the bloodstream (19). Then In the tissues, T4 becomes T3 (1). T3 is several times more active than its prohormone (T4). Most thyroid hormones are protein bound and inactive. A small part of them are free, the so-called free T3 and T4 (fT3 and fT4). fT3 and fT4 are metabolically active and they are in balance with protein-related thyroid hormones (19). The concentration of total and free T3 decreases under the influence of stress (17), as a result of a traumatic accident or surgery. The exact cause of these changes is not fully understood, but it is thought that this is due to the close relationship between thyroid hormones, catecholamines and cortisol (19).

Serious bodily injury, whether an accident or surgery, elicits a metabolic, hormonal and hemodynamic response (19). The magnitude of these changes is proportional to the amount of trauma and the serum levels of stress hormones.

Conclusions

High cortisol and low cholesterol levels in trauma patients immediately after ingestion indicate the severity of the trauma. The smaller deviation from normal values in the group of operated patients is evidence of the role of anesthesia and analgesia in reducing perioperative stress and pain.

References

1. Batstone GF. metabolic and biochemical changes following thermal injury. 1982;75(I):12–9.
2. Ali S, Mousavi J, Adeli SH, Zahedi L. Determination of Association between the Decrease in Cholesterol Concentration and Sepsis in Patients Admitted in the ICU. 2003;2:11–6.
3. Chernow B. Variables Affecting Outcome in Critically Ill Patients *. CHESTLEG [Internet]. 1999;115(5):71S-76S. Available from: http://dx.doi.org/10.1378/chest.115.suppl_2.71S
4. Угрюмов В. М. Тяжелая закрытая травма черепа и головного мозга: Издательство „Медицина“ 1974
5. Hrabovsky V, Zadak Z, Blaha V, Hyspler R, Ticha A, Karlik T. LIPID METABOLISM IN ACTIVE CROHN ' S DISEASE : PRE-RESULTS. 2006;150(2):363–6.
6. Stachon A, Bo A, Weissner H, Laczkovics A, Skipka G, Krieg M. Prognostic Significance of Low Serum Cholesterol after Cardiothoracic Surgery. 2000;1120:1114–20.
7. Dunham C Michael, Fealk Michael H, Sever Wilbur E. Following severe injury, hypocholesterolemia improves with convalescence but persist with organ failure or onset of infection: Critical Care December 2003 Vol 7 No 6 :145-153
8. Lee SH, Lee JY, Hong TH, Kim BO, Lee YJ, Lee JG. Severe persistent hypocholesterolemia after emergency gastrointestinal surgery predicts in-hospital mortality in critically ill patients with diffuse peritonitis. PLoS One. 2018;13(7):1–15.

9. With S, Liver RAT, By S, Groffman H. METABOLIC CHANGES INDUCED BY TISSUE INJURY : IN VITRO. 1971;108–12.
10. Bakalar B, Hyspler R, Pachl J, Zadak Z. Changes in cholesterol and its precursors during the first days after major trauma. Wien Klin Wochenschr. 2003;115(21–22):775–9.
11. Nuzzo G, Giovannini I. Plasma cholesterol level after hepatopancreatobiliary surgery provides information on the postoperative clinical course. 2010;131–3.
12. Soleimanpour H, Safari S, Rahmani F, Ameli H, Alavian SM. The Role of Inhalational Anesthetic Drugs in Patients with Hepatic Dysfunction: A Review Article. Anesthesiol Pain Med. 2015;5(1):1–5.
13. Морган Дж.Е., Михаил М.С. Клиническая анестезиология, Том1, ЗАО „Издательство Бином“, 2004
14. Moutzouri E, Elisaf M, Liberopoulos EN. Hypocholesterolemia. 2011;200–12.
15. Giovanini I, Chiara C, Greco F, Boldrini G, Nuzzo G. Characterization of Biochemical and Clinical Correlates of Hypocholesterolemia after Hepatectomy: Clinical Chemistry 49,No.2, 2003
16. Chiarla C, Giovannini I, Giuliente F, Zadak Z, Vellone M, Ardito F, et al. Severe hypocholesterolemia in surgical patients, sepsis, and critical illness. J Crit Care. 2010; 25: 361 e367–361 e312.
17. Царева М., Христова А., Тодорова С., Янева З., Сидерова Р. Особенности на адаптивни те Ендокринни промени при пациенти в шокови състояния от различен произход : Спешна медицина, 2000, бр 4
18. Литвицки. Патофизиология, глава19, Геотар-Мед, Москва, 2003
19. Desborough JP. The stress response to trauma and surgery. 2000;85(1):109–17.
20. Ганонг У. Медицинска физиология, 17-то издание, 1996
21. Donald S. Gann, Richard H. Egdahl. Responses of Adrenal corticosteroid secretion to hypotension and hypovolemia: Journal of Clinical investigation, Vol. 44, No. 1, 1965