



HORMONAL CHANGES DURING ANESTHESIA AND IN THE EARLY POSTOPERATIVE PERIOD IN ABDOMINAL SURGERY

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ABSTRACT

Purpose: The purpose of our research was to study the changes that occur in the levels of cortisol, thyroxine and triiodothyronine during anesthesia and during the first three days after surgery.

Materials and methods: There were traced 12 patients divided into two groups, undergoing abdominal surgery. Patients were tracked during anesthesia and during the first three days after surgery. We investigated serum levels of cortisol, free thyroxine (FT4) and free triiodothyronine (FT3). **Results:** The analysis of serum cortisol didn't reveal any statistically significant changes when comparing the different stages in each group separately - and comparing data between groups. We did not observe statistically significant changes in the level of thyroxine and triiodothyronine either.

Conclusion: The lack of significant changes in serum cortisol levels at all stages of the study shows that balanced anesthesia in combination with volatile anesthetic and opioid, has a good protective effect in terms of surgical stress. Changes in levels of FT3 and FT4 are negligible and this corresponds to their slower metabolism.

Key words: sevoflurane, halothane, surgical stress, cortisol, thyroxine, triiodothyronine.

INTRODUCTION

Hormonal changes occurring during surgery and the period afterwards are the expression of response of organism to changes in its homeostasis –it is the so-called stress response, aiming to adapt the organism to new requirements (1). They are a part of a systemic reaction to injury, which includes also metabolic and haemodynamic response (2). Hormonal response to stress in the perisurgical period and its prevention have been the subject of anesthetic interest for many years (2, 3, 4). Changes in the so-called stress hormones during and in the early postoperative period may not only provide information about the invasiveness of surgery and about possible complications during the operation, but also about the capacity of the particular type of anesthesia to protect the body from surgical stress (2). The hormones of the pituitary, adrenal, pancreas and thyroid belong to these hormones.

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PURPOSE

The aim of our study was to trace the changes that occur in the levels of cortisol, triiodothyronine and thyroxine (hormone involved in stress reaction) during anesthesia and the first three days after surgery.

MATERIALS AND METHODS

12 patients divided into two groups, undergoing abdominal surgical procedures were studied. The first group consisted of 8 patients. The main anesthetic sevoflurane was used in this group. The second group consisted of 4 patients with the main anesthetic-halothane. Medications/medicaments used for induction, analgesia and relaxation were the same for both groups. Patients were monitored during anesthesia and during the first three days after surgery. We measured serum levels of cortisol before the start of anesthesia, during surgery (the most traumatic moment), after recovering the patient from anesthesia and in the next 3 days. Serum levels of FT3 and FT4 were measured before the start of anesthesia, on the first and third day. During surgery and after recovering the patient from

anesthesia, FT3 and FT4 were not studied changes in their levels for such a short period were not expected. Blood samples on 1st, 2nd and 3rd day were taken in the morning between 7:30 am and 8:30 am, due to the 24-hour rhythm in cortisol biosynthesis (5). After centrifugation of blood and separation of serum, all sera were frozen and stored in the camera. The serum samples were tested in the "Exacta Medica" clinical laboratory Pleven.

Statistical data processing was carried out based on variance analysis (values of $p < 0,05$ statistically significant).

RESULTS AND DISCUSSION

The analysis of serum level of cortisol show that the average values at each stage of the study in the both groups were above the upper limit of normal. Reference values of cortisol - 171-536 nmol / l at 8am in the morning. Statistically significant changes were not found when comparing the different stages in each group separately, and comparing data between two groups (**Table 1, Figure 1**).

Table 1. Changes in the serum level of cortisol in the two groups

Cortisol	Baseline	The most traumatic moment	The end of anesthesia	1 st day after surgery	2 nd day after surgery	3 rd day after surgery
Sevoflurane	581,3±95,64	818,25±102,2	1201,06±316,58	834,87±88,94	705,6±44,50	665,85±91,80
Halothane	765,03±101,72	788,73±116,47	819,9±152,39	798,65±137,35	824,73±254,59	869,8±383,61
p	>0,05	>0,05	>0,05	>0,05	>0,05	>0,05

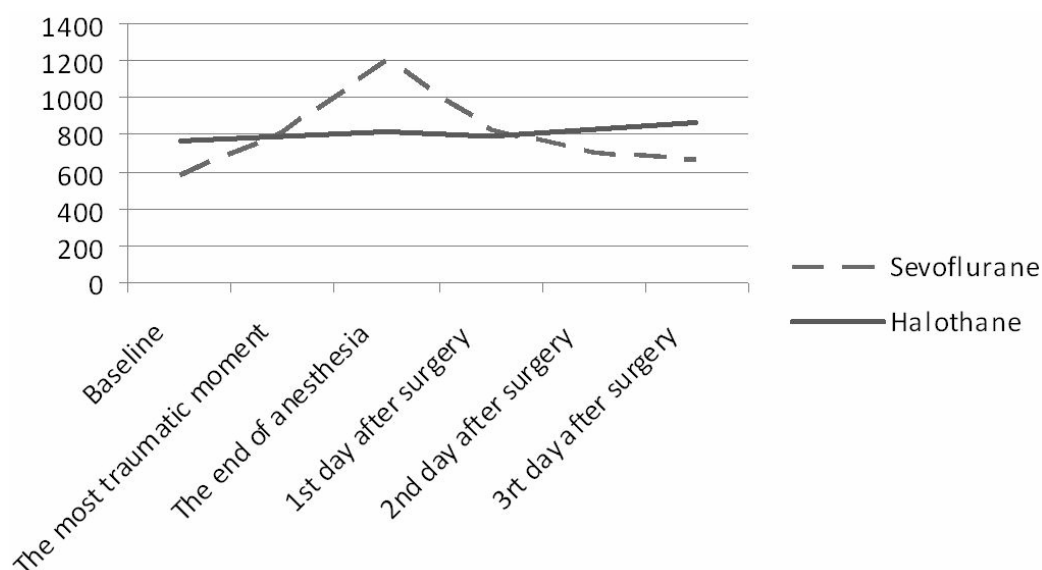


Figure 1. Changes in the serum level of cortisol in the two groups

We did not observe statistically significant changes in the level of FT3 and FT4. The values of both hormones remained within

normal limits for both groups throughout the study. (**Table 2 and Table 3**).

Table 2. Changes in the serum level of FT3 in the two groups

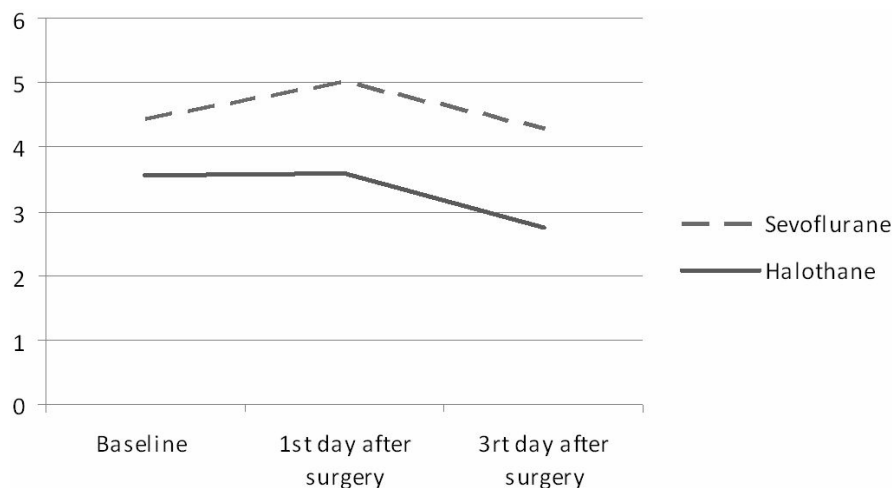
FT3	Baseline	1 st day after surgery	3 rd day after surgery
Sevoflurane	4,415±0,84	5,00±0,69	4,28±0,76
Halothane	3,575±0,57	3,588±0,33	2,73±0,51
p	>0,05	>0,05	>0,05

Table 3. Changes in the serum level of FT4 in the two groups

FT4	Baseline	1 st day after surgery	3 rd day after surgery
Sevoflurane	17,567±1,47	20,599±1,15	18,745±0,55
Halothane	20,083±0,996	18,738±1,29	19,39±0,83
p	>0,05	>0,05	>0,05

While a trend in FT4 could not be established, such a trend in FT3 was obvious (**Figure 2**).

Reference values for FT3 - 2,8-7,1pmol / l. Reference values for FT4 - 12 - 22pmol / l.

**Figure 2.** Changes in the serum level of FT3 in the two groups

Cortisol is related to glucocorticoids, which are directly related to stress. They are some of the most important adaptive hormones (4). They are of vital importance in the regulation of vascular tone, endothelial integrity and capillary permeability. Their secretion is influenced by the hypothalamic-pituitary system. Cortisol is synthesized from cholesterol under control of corticotropin releasing hormone and ACTH (6).

Biosynthesis of cortisol is in an “instant” - glucocorticoids appear about 2 minutes after stimulation of the adrenal gland by Adrenocorticotrophic hormone (ACTH) in the peripheral circulation. The daily level secreted in normal condition (no stress) is $\approx 1\text{mg/kg/d}$ for almost all species. In man secretory levels from 25 to 35 mg / kg / d are described .

Thyroid hormones are also part of the response of the patient's body to change in its homeostasis. Thyroid hormones - thyroxine (T4) and triiodothyronine (T3) are secreted into circulation by the thyroid gland under the influence of thyroid-stimulating hormone (TSH) (5, 6). In tissues T4 (prohormon) converse into T3 (7), which is 3 to 5 times

more active than T4. In fact metabolically active are very small amounts of thyroid hormones that are associated with proteins called free T3 and T4 (FT3, FT4). FT3 and FT4 are in equilibrium with associated with proteins thyroid hormone (3).

The concentration of total and free T3 decreases under the influence of stress resulting from a traumatic accident or surgery. The exact causes of these changes are not fully understood but it is believed this is due to the close relationship between thyroid hormones, catecholamines and cortisol. Large amounts of cortisol suppress the production of thyroid hormones, and enzymes that process less active T4 to T3.

Hormonal response to stress in the perioperative period and its prevention has been the subject of anesthetic interest for years. This is because in response to the surgery the patient's body reacts with complex protective reactions involving metabolic, hormonal and hemodynamic changes (4). As a result activation of the central nervous system (CNS) and endocrine system is observed . Primary hypersecretion of releasing factors from the

nerve centers of the hypothalamus lead to a sharp increase in the release of ACTH, adrenal hormones and neurotransmitters. Increased secretion of pituitary hormones leads to a corresponding effect on the secretion of hormone target organs (3). As a result, these patients have elevated levels of counter-

STAVROVA-HRISTOVA R., *et al.* regulatory or anti-insulin hormones: cortisol, glucagon, catecholamines. Usually, insulin levels are also increased but not enough to prevent hyperglycemia that is normally observed. The growth hormone, aldosterone and vasopressin are also increased (**Table 4**).

Table 4. Principal hormonal responses to surgery*

Endocrine gland	Hormones	Change in secretion
Anterior pituitary	ACTH	Increases
	Growth hormone	Increases
	TSH	May increase or decrease
	FSH and LH	May increase or decrease
Posterior pituitary	AVP	Increases
Adrenal cortex	Cortisol	Increases
	Aldosterone	Increases
Pancreas	Insulin	Often decreases
	Glucagon	Usually small increases
Thyroid	Thyroxine, Tri-iodothyroxine	Decrease

*Based on Desborough and Hall, 1993

It is possible under certain conditions that the protective reaction passed into its opposite and give rise to functional, biochemical and morphological disorders. The reactions of the organism of surgery are often very pronounced. They lose their compensatory character and develop one or another complication. Adequate protection of the patient from operative stress can be achieved with the help of well-chosen combination of anesthetic agents and techniques, according to the type and complexity of surgery. Even in deep anesthesia, a certain amount of nociceptive impulses from the surgical wound can reach the CNS and activate the autonomic system. Changes in serum levels of stress hormones is proportional to the amount of operative stress.

CONCLUSIONS

Data from this survey suggest that serum level of cortisol is even in the preoperative period above the upper limit of normal, which requires better preoperative patient preparation and appropriate early premedication. The lack of significant changes in serum cortisol levels at all stages of the study shows that balanced anesthesia in combination of volatile anesthetic and opioid, has a good protective effect in terms of surgical stress. The higher value of cortisol in stage end of anesthesia in the

sevoflurane group corresponds to a rapid recovery of patients from anesthesia and early recovery of senses and reflexes. Changes in levels of FT3 and FT4 are negligible and this corresponds to their slow metabolism.

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