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DOES ANAESTHESIA AFFECT THE STRESS RESPONSE AFTER TOTAL HIP ARTHROPLASTY?

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Abstract

A surgical intervention such as total hip arthroplasty, triggers a complex stress response in the body, involving metabolic, neuroendocrine and inflammatory reactions that influence postoperative recovery. This study aimed to compare the perioperative cortisol response and early postoperative pain in patients undergoing THA under general anaesthesia (GA) versus spinal anaesthesia (SA).

This study was conducted from October 2020 to June 2024 at the Clinic of Orthopedics and Traumatology in "Tsaritsa Yoanna" – ISUL University Hospital, and included two groups of patients: Group 1 ($n = 30$, GA) receiving general anaesthesia and Group 2 ($n = 30$, SA) receiving spinal anaesthesia. The examined parameters were: serum cortisol levels (reference values 4.3–22.4 ug/dl) at four time points preoperatively, 30 min after the surgical incision, 1 h after the end of surgery, and 24 h postoperatively. Pain intensity was assessed on days 1, 2, and 3 at rest using the VAS (Visual Analogue Scale).

The results show that the patients in Group 1 (GA) had higher cortisol levels 30 min after the surgical incision, 1 h postoperatively, and 24 h after surgery, compared to the SA group, with the difference being statistically significant ($p < 0.001$). At 24 h postoperatively, cortisol levels in Group 1 showed a trend toward normalization but remained higher than in Group 2. Pain scores on the day of surgery were significantly higher in the general anaesthesia (GA) group. However, on the second and third postoperative day, pain levels in both groups normalized and the differences became statistically insignificant.

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The results of our study indicate that the choice of anaesthesia significantly affects the stress response and pain in patients undergoing hip joint surgery. Cortisol measurement analysis suggests a pronounced attenuation of stress response in patients with spinal anaesthesia undergoing this kind of surgery.

Key words: total hip arthroplasty, cortisol, stress response, spinal anaesthesia, general anaesthesia, postoperative pain

Introduction. Surgical intervention triggers a complex stress response, involving metabolic, neuroendocrine and inflammatory reactions that influence postoperative recovery [1, 2]. Activation of the sympathetic nervous system leads to multiorgan manifestations such as hypertension, arrhythmias and myocardial ischemia. There are different negative pathophysiological cortisol-induced responses: metabolic alterations including protein catabolism and hyperglycemia (cortisol-induced glycogenolysis), and immune suppression with increased risk of infections. The kidneys respond with reduced excretion and retention of water and electrolytes [3, 4]. The systemic stress-response to surgical trauma is characterized by non-infectious inflammation and activation of the neuroendocrine hypothalamic-pituitary-adrenal axis (HPA axis). Dysregulation of this axis affects the response to perioperative stressors, leading to changes in cortisol physiology [5]. Cortisol secretion is regulated by the HPA axis. The paraventricular nucleus of the hypothalamus receives information from the limbic system, associated with cognitive and emotional responses, as well as from brainstem structures. Surgical trauma activates this axis through afferent stimulation caused by cytokine release, leading to hypovolemia and baroreceptor activation [6]. Corticotropin-releasing hormone (CRH) stimulates secretion that follows a circadian rhythm, with peak levels in the morning and minimal levels around midnight [7]. Under surgical stress, ACTH and cortisol levels increase significantly and remain elevated up to 24 hours postoperatively [8, 9]. The normal levels of cortisol are between 4.3 and 22.4 ug/dl. Neuraxial anaesthesia attenuates afferent nociceptive input and sympathetic outflow, and may therefore reduce the neuroendocrine stress response compared with general anaesthesia [8–11]. Total hip arthroplasty (THA) is associated with significant tissue trauma and postoperative pain; thus, optimization of anaesthetic technique is important to facilitate early recovery [12–14]. The study aimed to compare the perioperative cortisol response and early postoperative pain in patients undergoing THA under general anaesthesia (GA) versus spinal anaesthesia (SA).

Materials and methods. ***Study design.*** This prospective, randomized, single-centre study was conducted at the Department of Orthopedics and Traumatology, "Tsaritsa Yoanna" – ISUL University Hospital, Sofia, Bulgaria, between October 2020 and June 2024. Inclusion criteria: adults aged $\geq$ 18 years, from 28 to 88 (mean 60.1, SD 10.32) years old, males – 24, females – 36, BW 65–105 (mean 82, SD 12.23) kg and height 159–188 (mean 171, SD 8.43) cm, scheduled for elective primary total hip arthroplasty, ASA I–III class. All patients were

divided into two groups with no statistical difference by age ($p = 0.128$), weight ($p = 0.135$), height ($p = 0.148$) and ASA class ($p = 0.457$). Exclusion criteria: revision surgery; chronic systemic corticosteroid therapy or other drugs affecting HPA axis; endocrine disorders (e.g., Cushing's disease, Addison's disease, Diabetes mellitus). Randomization and blinding patients were randomized 1:1 to GA or SA using a computer-generated random sequence. Anaesthetists performing the techniques were not blinded; however, laboratory personnel measuring cortisol and the staff recording postoperative pain scores were blinded to group allocation.

Group 1: 30 patients underwent general anaesthesia induced with propofol 2 mg/kg; succinylcholine 1 mg/kg and endotracheal intubation, verification of correct intubation and ventilation with lung auscultation and capnography. Mechanical ventilation was done with anaesthesia machine Datex-Ohmeda-Aespire S/5. Respiratory parameters RR12/min, Vt 8 ml/kg, ETCO2: 35–40 mmHg. Maintnance of GA: isoflurane (MAC 1.0), gas mixture O2:Air (1:1), FFG 2 l/min. Intraoperative analgesia with fentanyl 7 mcg/kg/h, intravenously, fractionated up to the joint access. The fentanyl dose was titrated according to the intensity of intraoperative pain and the duration of the procedure. The opioid analgesic provides adequate analgesia during THA, while maintaining hemodynamic stability.

Group 2: Thirty patients underwent spinal anaesthesia (SA) by intrathecal administration of bupivacaine 0.5% (15 mg) and morphine 200 mcg, puncture at L3-L4. Spinal anaesthesia was performed without barbotage. Sensory block Th 8–10, motor block Th 10–12, sympathetic block Th 6–8. In all patients the surgery is performed in the lateral decubital position. No additional sedation was administered to patients operated under spinal anaesthesia. Intrathecal morphine provides strong neuraxial anaesthesia with prolonged effect and postoperative analgesia.

The mean duration of surgery was 45–60 min. Average blood loss 300–400 ml. There were no postoperative clinical complications in either patient group. Postoperative analgesia paracetamol 15 mg/kg, dexketoprofen 0.5 mg/kg, tramadol 1.5 mg/kg. Group 1 needed analgesia 2–4 postoperative hour, Group 2 needed analgesia 22–24 hours after intrathecal administration of morphine.

Venous blood samples were collected at four time points to measure perioperative cortisol levels:

Sixty minutes before surgery, 30 min after skin incision, 60 min after the end of surgery, 24 h after the end of surgery. The specified time intervals are approximate and are based on the anticipated psychological stress response to pain and psychological stress associated with surgical intervention. The measurement before operation provides baseline level, 30 min after the initial surgical stimulus shows early stress response to surgical trauma, one hour after the end of surgery shows the peak or immediate postoperative response, 24 h after the end of operation shows recovery and whether hormone levels are returning to normal.

Blood cortisol levels were measured using an immunochemical method with electrochemiluminescence detection (ECLM). The test was performed in the clinical laboratory of "Tsaritsa Yoanna" – ISUL University Hospital. The intensity of postoperative pain was assessed on days 1, 2, and 3 at rest using the VAS (visual analogue scale). The assessment is performed on these days because this allows for an evaluation of acute pain and the influence of the type of anesthesia on its intensity, the effectiveness of analgesic therapy, and the course of the patient's recovery.

Statistical analysis. Descriptive statistics: quantitative variables are presented using summary statistical measures: arithmetic mean (mean), standard deviation (SD). Categorical variables are presented using absolute (n) and relative (%) percentages. One-Sample Kolmogorov–Smirnov Test, Chi-square test, Independent samples t-test, and Paired samples t-test were employed. Accepted significance threshold: $\alpha = 0.05$. Statistical significance is accepted at $p < 0.05$. Data processing used statistical software SPSS (Statistical Package for the Social Sciences), version 20.0.

Legend:

- Mean – arithmetic mean
- SD – standard deviation
- Min – minimum value
- Max – maximum value
- p – level of statistical significance.

Results and discussion. The main findings in our study are that hip joint arthroplasty is recognized as a significant source of pain and stress, which is consistent with observations in contemporary medical literature. Several studies indicate that hip arthroplasty leads to a strong stress response and pain reactions, which hinders the patient's rapid recovery. The anaesthetic approach is crucial for mitigating pain and stress at the time of surgery and thereafter, as many trials reveal [1, 2]. According to certain studies [5], cortisol levels rise within minutes after the start of the surgery, with the second measurement taken 20 min after surgery. Gradual decrease occurs after completion of surgery (fixed third stage, one hour after surgery). Approximately 24 h after surgery, cortisol levels normalize (fourth measurement). Our results of anaesthesia-induced stress response, indicate that spinal anaesthesia has a greater effect on stress response attenuation than general anaesthesia [10, 11], confirmed by many authors. Multiple trials support the hypothesis that spinal anaesthesia is associated with lower stress response, reduced cortisol levels and faster patient recovery following surgery [3, 4]. Observations of higher cortisol levels in patients receiving general anaesthesia,

particularly 30 min after the start of surgery and one hour postoperatively, concur with studies demonstrating elevated cortisol levels under General anaesthesia (GA) [8, 9]. It is known that General anaesthesia (GA) may activate the sympathetic nervous system to a greater extend, leading to increased stress and higher cortisol levels than spinal anaesthesia. Recommendations in the literature on pain and recovery after hip arthroplasty also corroborate our study's results. Our observation that pain intensity was significantly higher in the general anaesthesia group (Group 1) on the day of surgery and the first postoperative day represents analytic coincidence of more pronounced pain in patients receiving general anaesthesia [12, 13]. In Group 2 pain intensity is the lowest, because intrathecal morphine provides a longer pain-free period, cardiovascular stability, no postoperative depression, and enhances recovery. By the second postoperative day, pain intensity was approximately equal in both groups, highlighting the important role of postoperative analgesia in the recovery process [14]. Based on postoperative pain intensity, we administered rescue analgesia. On the first day in Group 1, and the second and third days in both groups, according to the recorded values on the VAS [5]. For the rescue analgesia we used tramadol 1.5 mg/kg, dexketoprofen 0.5 mg/kg, paracetamol 15 mg/kg. The association between cortisol levels and pain is both significant and supported by multiple studies. We found that the normalization of cortisol levels 24 h after surgery coincides with a reduction in pain intensity, a finding highlighted in a number of studies and suggesting that lower levels of the stress hormone after surgery can lead to more effective pain relief and faster patient recovery [15].

Conclusions. The results of our study indicate that the choice of anaesthesia significantly affects the stress response and pain in patients undergoing hip joint surgery. Cortisol measurement analysis suggests a pronounced attenuation of stress response in patients with spinal anaesthesia undergoing this kind of surgery (Table 1).

T a b l e 1

Results from analysis of cortisol levels in two groups

Index	Type of anesthesia	N	Mean	SD	Min	Max	p
Presurgical cortisol	Group 1	30	11.72	20.13	0.67	111.64	0.913
	Group 2	30	11.28	8.72	0.50	28.48	
Cortisol 30'	Group 1	30	27.89	10.72	9.15	53.87	< 0.001
	Group 2	30	17.15	8.54	3.07	46.99	
Cortisol 1 h after surgery	Group 1	30	27.29	14.62	2.50	66.65	0.006
	Group 2	30	17.84	10.59	4.66	51.89	
Cortisol 24 h after surgery	Group 1	30	22.63	8.63	9.87	52.00	< 0.001
	Group 2	30	13.38	7.52	0.62	33.80	

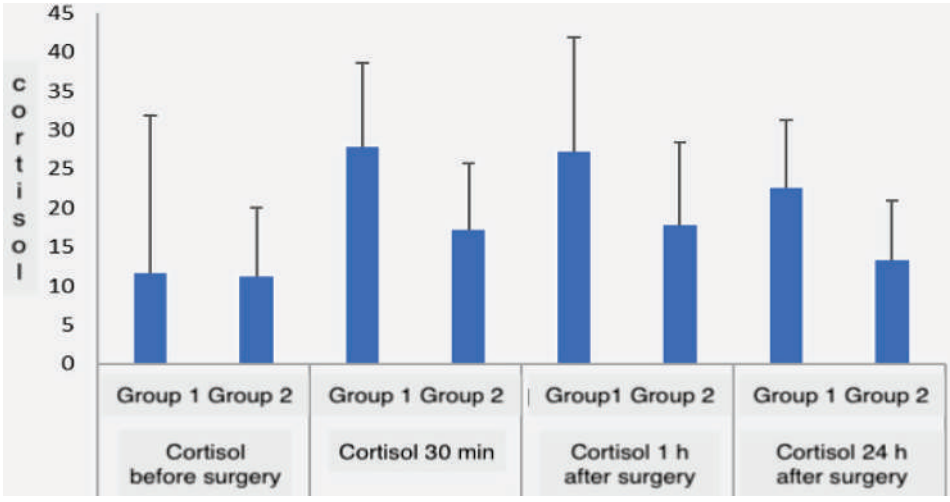


Fig. 1. Study of perioperative cortisol levels presents Mean, SD of two groups

Preoperative cortisol concentrations. Group 1: 11.72 ± 20.13; Group 2: 11.28 ± 8.72; Values are statistically insignificant ($p = 0.913$).

Values of cortisol 30 min after operative incision. Group 1: 27.89 ± 10.72; Group 2: 17.15 ± 8.54. Values of cortisol in this period in two groups are statistically significant ($p < 0.001$).

Values of cortisol one hour postoperatively. Group 1: 27.29 ± 14.62; Group 2: 17.84 ± 10.59. Values of cortisol show statistical differences in the two groups ($p = 0.006$).

Values of cortisol by 24 hours after surgery. Group 1: 22.63 ± 8.63; Group 2: 13.38 ± 7.52. Values of cortisol in the two groups are statistically significant ($p < 0.001$).

Table 2

Postoperative pain scores and analgesic consumption VAS scores at rest on postoperative days 1–3

Index	Type of anesthesia	*N*	VAS Mean	SD	Min	Max	*p*
Pain 1st day	Group 1	30	3.33	2.15	1.00	10.00	< 0.001
	Group 2	30	0.37	0.77	0.00	3.00	
Pain 2nd day	Group 1	30	4.77	1.72	2.00	9.00	0.323
	Group 2	30	4.37	1.38	2.00	7.00	
Pain 3rd day	Group 1	30	4.07	1.31	2.00	7.00	0.128
	Group 2	30	3.57	1.19	2.00	6.00	

Results of pain were assessed using VAS (visual analogue scale 0–10 cm: 0–3 cm mild pain; 3–6 cm moderate; 6–10 cm severe).

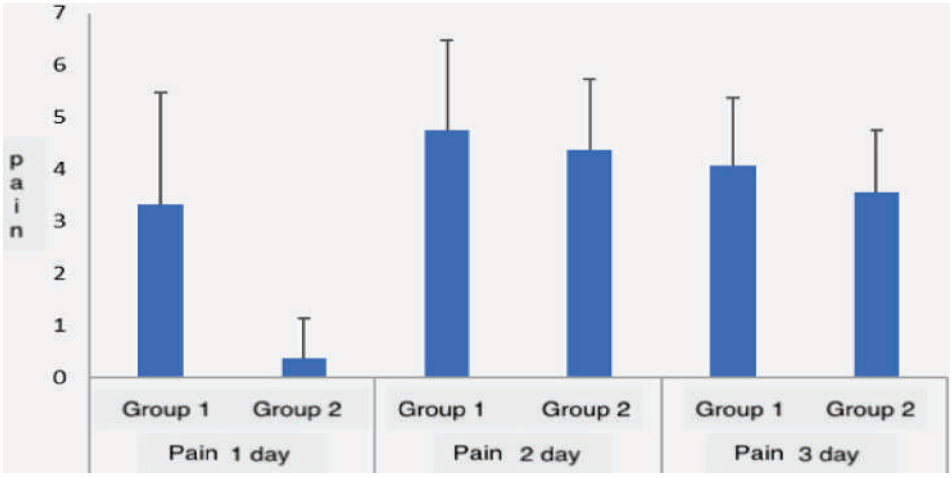


Fig. 2. Study of postoperative pain

First day in Group 1: 3.33 ± 2.15; Group 2: 0.37 ± 0.77. The results of the first day are statistically significant ($p < 0.001$).

Second day in Group 1: 4.77 ± 1.72; Group 2: 4.37 ± 1.38. Values are statistically insignificant ($p = 0.323$). Third day in Group 1: 4.07 ± 1.31; Group 2: 3.57 ± 1.19. Values are statistically insignificant ($p = 0.128$).

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