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UTICAJ INTRAOPERATIVNE HIPOTERMije NA HORMONSKI ODGOVOR NA STRES KOD HIRURŠKIH BOLESNIKA

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Abstract

**Background/Aim.** Surgical stress itself, as well as hypothermia induced by general anaesthesia, and low ambient temperature activate stress hormone response with changes in catecholamines and counter regulatory hormones. The aim of this study is to investigate the acute hormone stress response in patients who underwent major surgical procedures and the efficiency of external and internal warming methods in alleviation of these changes.

**Methods.** 60 patients who underwent major open abdominal surgical procedures were randomly divided in 4 groups: control non-warmed (C), externally warmed using forced-air warming mattress (W), internally warmed using intravenous amino acids (A), and warmed with combination of external and internal method (A+W). Oesophageal temperature was used as measure of core temperature. Blood samples for hormone measurement were obtained in 2 time points for catecholamines: 90 minutes before and 120 minutes after finishing the surgery; and in additional 2 time points for cortisol, prolactin and testosterone: (24 and 48 hours after surgery). **Results.** In W and A+W group the temperatures did not significantly differ between time points, but in C and A groups decreased constantly, with statistically significant difference between the anesthesia induction and 120\textsuperscript{th} minute (35.61±0.42 vs 33.86±0.71 °C; \( p<0.000 \) and 35.81±0.54 vs 34.45±0.41 °C; \( p<0.000 \), respectively). Catecholamine concentrations in all groups showed significant increase during surgery, with highest values recorded in non-warmed group (777.07±800.08 after vs 106.13±89.63 pg/mL before surgery for epinephrine and 1349.67±984.16 vs 580.53±465.38 for norepinephrine, \( p<0.000 \)). Concentrations of cortisol and prolactine also showed significant increase at the same time point, with tendency to normalization after 48 hours. Contrary, testosterone concentrations showed decrease after 120 minutes without normalization throughout the entire period of observation. Except for testosterone, changes in all stress hormones were attenuated in warmed groups compared to controls.

**Conclusions.** Regarding both features of surgical stress investigated in this study (hypothermia and stress hormone response), combination of endogenous amino acid-induced thermogenesis and external air warming mattress is most effective.

**Key words:**

anaesthesia, general; hormonal response; hypothermia; intraoperative period; warming.
Apstrakt

Uvod/Cilj. Hirurški stress sam po sebi, kao i u kombinaciji sa hipotermijom izazivanom dejstvom opšte anestezije pokrće stresni hormonski odgovor. Cilj ovog istraživanja je da se utvrdi akutni hormonski odgovor na stress kod pacijenata podvrgnutih dugotrajnim hirurškim intervencijama, kao i da se ispita efikasnost spoljašnjeg i unutrašnjeg zagrevanja u ublažavanju ovih promena. **Metode.** 60 pacijenata podvrgnutih velikim hirurškim intervencijama na otvorenom abdomenu randomno je podeljeno u 4 grupe: kontrolnu koja nije dodatno zagrevana (C), grupu koja je zagrevana madracem sa toplim vazduhom (W), grupu koja je zagrevana infuzijom aminokiselina (A) i grupu koja je zagrevana kombinacijom ove dve metode (A+W). Unutrašnja temperatura merena je ezofagealnom sondom. Ispitivana je koncentracija adrenalina, noradreanlina, kortizola, prolaktina i testosterona. Uzorci krvi uzmene su 90 minuta pre i 120 minuta nakon završetka hirurške procedure (za kateholamine), i u dodatna dva termina za ostale hormone (24 i 48 sati nakon završetka operacije). **Rezultati.** U W i A+W grupi temperatura se nije razlikovala tokom perioda praćenja, dok se u C i A grupi konstantno snižavala, sa statistički značajnom razlikom između momenta uvođenja u anesteziju i nakon 120 minuta operacije (35,61±0,42 vs 33,86±0,71 °C; *p*<0,000, odnosno 5,81±0,54 vs 34,45±0,41 °C; *p*<0,000). Koncentracija kateholamina je u svim grupama značajno porasla tokom operacije, a najveće vrednosti izmerene su u nezagrevanoj grupi (777,07±800,08 vs 106,13±89,63 pg/mL za adrenalin and 1349,67±984,16 vs 580,53±465,38 za noradrenalin, *p*<0,000). Koncentracije kortizola i prolaktina takođe pokazuju porast u istim intervalima, sa tendencijom normalizacije nakon 48 sati. Naprotiv, koncentracije testosterona značajno padaju posle 120 minuta i niske vrednosti se održavaju kroz ceo period praćenja (48 sati). Osim u slučaju testosterona, promene svih ostalih hormona ublažene su kod zagrevanih pacijenata u poređenju sa kontrolnom grupom. **Zaključak.** Posmatrajući obe ispitivane karakteristike hirurškog stresa (hipotermiju i stresni hormonski odgovor), pokazalo se da je u prevenciji najefikasnija kombinacija endogenog zagrevanja aminokiselinama i spoljašnjeg zagrevanja madracem sa toplim vazduhom.

Ključne reči: anestezija, opšta; hormonski odgovor; hipotermija; intraoperativni period; zagrevanje.
Introduction
Low ambient temperature in operation theatre and prolonged effects of general anaesthesia may lead to intra- and postoperative hypothermia in surgical patients. Complications of hypothermia in these patients are recognized as cardiovascular and respiratory dysfunction, impairment of coagulation system and coagulopathy (1). Hypothermia during major surgical interventions may be prevented using several external warming methods, as well as internal administration of warm fluids with various composition. The result of such interventions in literature are rather controversial, which may be contributed to type of anaesthesia, type of surgery, patients age and comorbidity. In our previous studies, efficacy of two methods for preventing intraoperative hypothermia was investigated (2, 3) and the results indicated that both external warming (using air-forced warming mattress) and internal warming (administration of amino acid solution) attenuate perioperative hypothermia.

Response to surgical stress is related to cellular and tissue injuries and nociceptive stimulation which influence hormonal and metabolic processes by activation of hypothalamic-pituitary-adrenal axe and secretion of stress hormones. In addition to surgical stress, the secretion of catecholamines is also induced by hypothermia in order to increase metabolic thermogenesis (4). High concentrations of cortisol and prolactin are common immediately after and up to 4-6 days following surgical procedures. On the other hand, concentrations of testosterone in decreased after surgery and low levels may be sustained for several days, which may delay anabolic processes (5).

Considering the importance of stress hormonal response in surgical patients, as well as the impairment of anabolic hormonal activity, the aim of our study was to investigate if maintaining intraoperative normothermia using external and/or internal warming methods could influence stress hormonal response in patients underwent major open abdominal surgical procedures.

Methods
Study population consists of 60 patients who underwent major open abdominal surgical procedures (duration between 2 and 4 hours). Investigation was conducted in Military Medical Academy in Belgrade, designed as single-centre prospective controlled
interventional study and approved by the local Ethics Committee. Each participant signed informed consent. The study included adult patients with American Society of Anesthesiologists (ASA) score I or II, who underwent elective colorectal surgical procedures for malignancy. Of 124 patients initially considered for enrolment, 64 were excluded according to criteria as follows: other indication than colorectal malignancy, ASA score III or IV, duration of intervention less than 2 hours or more than 4 hours and administration of blood transfusion during surgery.

In all patients same method of general balanced anaesthesia (GBA) was used. For premedication, 10 mg of diazepam (intramuscular injection) was administered one hour before anaesthesia induction. Midazolam [0.05–0.15 mg/kg of body weight (BW)], fentanyl (2–6 μg/kg BW), propofol (1–2.5 mg/kg BW) and rocuronium (0.6–1mg/kg BW) were used for induction of GBA. Anaesthesia and analgesia were maintained with 2-4 vol% of volatile aesthetic sevoflurane (respiratory volume of 6-8 ml/kg BW) with intermittent bolus of 25-50 μg of fentanyl. Neuromuscular blockade was maintained with intermittent bolus of 0.15 mg/kg BW of rocuronium. There was no difference between groups regarding hemodynamic parameters, nor volume loading, regardless the warming method; every patient was treated identically, according to contemporary guidelines.

Detailed description of methods of body temperature measurements (oesophageal and skin temperatures) is presented in our previous study (3). Patients were randomly divided in 4 groups: control group (C) consisted of 15 non-warmed patients, while in other 3 groups the same number of patients were either warmed externally (W group) using forced-air warming mattress as described in previous study (3), either received intravenous amino acids intraoperatively (A group), or combination of amino acids and external warming (A+W group). In latter 2 groups commercial solution of 18 amino acids (Aminosol 15%, Hemofarm AD, Serbia) was administered via central venous catheter at rate of 125 ml/hour immediately after anaesthesia induction in order to provide internal thermogenesis (2).

Blood samples for hormone measurement were obtained from each patient in 2 time points for epinephrine and norepinephrine: 90 minutes before and 120 minutes after finishing the surgery; and in 4 time points for cortisol, prolactin and testosterone: 90 minutes before and 120 minutes, 24 hours and 48 hours after surgery. Mean core (oesophageal) temperatures were recorded at the moment of anaesthesia induction and after 30, 60, 90 and 120 minutes.
Concentrations of epinephrine and norepinephrine were measured by competitive ELISA tests (Labor Diagnostika Nord), while concentrations of cortisol, prolactin, and testosterone were measured by ECLIA method (Elecsys 2010, Roche).

Statistical analysis: after tested for normality (by Kolmogorov-Smirnov test), data were presented as means ± standard deviation (SD) for continuous data, or median followed by interquartile range. The significance of differences between groups and between time points were tested using t-test or Mann-Whitney U test (comparison of two groups), ANOVA of Kruskal-Wallis test; post hoc Mann Whitney or Tukey test (multigroup comparison). The statistical significance was accepted at p<0.05.

Complete statistical analysis was performed using SPSS 18 package (Chicago, USA). The sample size was calculated using test power of 0.8 and Type I (alpha) error of 0.05, which revealed that sample size of 15 per group is able to detect the statistically significant difference between independent groups (GPower 3.1).

**Results**

Baseline characteristics of the patients in all groups as well as the environmental conditions in operation theatre are presented in Table 1. There were no significant differences between groups.

| Table 1. |  |
| --- | --- |

There was statistically significant difference between average intraoperative oesophageal temperatures regarding time points, as well as between groups. In W and A+W group the temperatures did not significantly differ between time points, but in C and A groups decreased constantly, with statistically significant difference between the anaesthesia induction and 120th minute (35,61±0,42 vs 33,86±0,71 °C; p<0,000 and 35,81±0,54 vs 34,45±0,41 °C; p<0,000 , respectively) (Fig. 1).

Figure 1.

Temperatures in these two groups have had slower recovery after surgery, i.e. postoperative oesophageal temperatures were significantly lower comparing to other two groups in all time points (Fig. 2). On 90th minute average temperatures were 34,38±1,17 (C) and 35,41±0,79 °C (A) comparing to 36,07±0,86 (W) and 36,4±0,66 °C (A+W); p<0,000.
Average concentrations in all groups in 4 time points are presented in Table 2.

Table 2

Statistical analysis by Wilcoxon Signed Ranks revealed highly significant difference between epinephrine concentrations pre- and postoperatively in all 4 groups: (Z= -3.408, p<0.01 in C group; Z= -3.181, p<0.01 in A group; Z= -3.351, p<0.01 in W group, and Z= -3.408, p<0.01 in A+W group). Despite the highest postoperative values recorded in control group, the differences were not statistically significant (Fig. 3).

The similar trend was noticed concentrations of norepinephrine (Fig. 4). Basic levels of norepinephrine were similar in all 4 groups, i.e. there were no statistically significant differences between groups. In all 4 groups highly significant increase was recorded in postoperative values compared to preoperative (Z= -3.181, p<0.01 in C group; Z= -2.556, p<0.01 in A group; Z= -3.237, p<0.01 in W group, and Z= -2.358, p<0.01 in A+W group). These values did not differ between groups.

Peak values of cortisol concentrations were recorded 120 minutes after surgery in all groups. After that the values decreased toward basic levels in following 2 days (Fig 5). There was highly significant difference between 4 time points (Wilks Lambda=0.338; F=35.323, Partial Eta Squared=0.662; p<0.01) and between 4 groups (F=6.002, Partial Eta Squared=0.243; p<0.01).
Multiple comparison analysis (Tukey test) revealed highly significant difference between internal warming (A group) compared to C and W groups (Table 3).

Table 3.

Basic levels of prolactin showed no statistically significant differences between groups. Levels of prolactin were highest 120 minutes postoperatively in all groups (Fig 6). There was statistically significant difference between 4 time points (Wilks Lambda=0,604; F=11,795, Partial Eta Squared=0,396; \( p<0,01 \)) and between groups (F=4,857, Partial Eta Squared=0,206; \( p<0,01 \)). Multiple comparison (Tukey test) revealed the statistically significant difference between A group and all other groups (\( p<0,05 \)).

Figure 6.

Concentrations of testosterone decreased in all groups during the surgical procedures and remained lower after 24 and 48 hours after surgery (Fig 7). The difference is statistically significant in W and A+W groups. Tukey test: in W group: 90 minutes prior to surgery compared to 120 minutes after surgery, \( p=0,043 \); 24 hours after, \( p=0,016 \); and 48 hours after, \( p=0,032 \); in A+W group: 90 minutes prior to surgery vs 120 minutes after, \( p=0,013 \); 24 hours after, \( p=0,008 \); 48 hours after, \( p=0,022 \). There was no significant difference between groups (F=0,992; Partial Eta Squared=0,051; \( p=0,403 \)).

Figure 7.

Discussion

Intraoperative hypothermia is multi factorial and complex condition. It is inadvertent and very common. Induction and maintenance of general anaesthesia change normal protective response to hypothermia. Because of anaesthesia-induced vasodilation, impairment of normal thermoregulation (reduction of thermogenesis, both shivering and non-shivering) there is significant redistribution of heat from core to periphery (1). Effector response to hypothermia is also altered (6). Heat loss is influenced by environmental conditions in operating theatre. Very important factor in intraoperative heat loss is surgical procedure.
itself. We enrolled patients who underwent large and long abdominal surgical procedures, with exposed abdominal cavity. In this setting, hypothermia is significant problem (6). One of end-points of our study was to evaluate efficacy of external warming, amino acid-induced endogenous thermogenesis and their combination in patients undergoing major open abdominal surgical procedures. We noted that there has been increased interest regarding this topic in recent years. In our investigation, after first 30 minutes of surgery, lowest oesophageal temperature was recorded in C group. In this time point, highest temperature was in A+W group, and the same trend was sustained throughout the entire surgical procedure and up to 90 minutes after surgery.

Intraoperative hypothermia is defined as oesophageal temperature below 36 °C. After 30 minutes of surgery, frequency of hypothermia was 100% in group C and 93% in groups A and W. Lowest frequency of hypothermia (80%) was in group A + W. After 120 minutes of surgery, all patients in groups C and A were hypothermic. Frequency of hypothermia in group W was 86.6%. Again, lowest frequency of hypothermia was in A+W group (66.6%).

It is evident that in our study more than half of the patients remained hypothermic despite air warming mattress and/or amino-acid infusion both 30 min and 120 min after anesthesia induction. This is in accordance with results from a large retrospective study regarding intraoperative core temperature patterns in patients warmed with forced air (7). Authors demonstrated that more than 60% of the patients were hypothermic 45 minute after induction and that 20 % of them continued to be hypothermic for more than 120 minutes.

Administration of intravenous nutrients, such as amino acids, has been investigated in normothermia maintenance setting due to endogenous metabolic heat production as well as increase of whole-body heat content by 20% (8). Salem and co-authors investigated 42 cancer patients who underwent pelvi-abdominal surgery, randomized to receive either amino-acid infusion or warm Ringer solution infusion 2 hours before anaesthesia induction. Authors concluded that amino-acid infusion before anaesthesia and surgery restored core body temperature: in the first 120 minutes in this group there was no hypothermia (9). These results are at odds with ours regarding A group: after 120 minutes all patients were hypothermic. Different results are to be expected due to a difference in a study design: in our study infusion started immediately after anaesthesia induction; in their study 2 hours before.
Amino acids infusion might be intraoperatively beneficial for surgical patients because it can counteract the disadvantageous fasting metabolism; metabolic fate is two-fold: oxidation for energy production and/or building blocks for protein synthesis. In both cases large amounts of energy are needed for amino acid metabolism and eventually heat production (10). In recent systematic review and meta-analysis regarding perioperative amino acid infusion for preventing hypothermia, it was demonstrated that, based on 626 participants from 14 randomized controlled trials, amino acid infusion led to a +0.46 °C increase in temperature. Authors concluded that this small difference is of clinical significance and that this method of normothermia maintenance has similar effect as conventional warming systems and may serve as a viable alternative (11). In several studies, various methods of perioperative prewarming and warming were investigated in surgical procedures other than exclusively major open abdominal ones (12, 13, 14). Authors concluded that, active warming is more efficient than passive in hypothermia prevention. Yet, even with active warming, hypothermia persisted in some patients. Authors also emphasized that continued innovation in active warming technology and research in different methods of active warming is necessary. Given that, one would expect investigation of various methods of intraoperative warming. Yet, interestingly, in literature available to us, we did not find any studies regarding combination of external warming and amino acid-induced endogenous thermogenesis in prevention of inadvertent intraoperative hypothermia. One recent investigation included combination of forced-air warming and warmed intravenous fluid consisting of lactated Ringer solution, but not amino acids (1). Our results showed that mean core temperature was highest in group A+W at 120th minute after anaesthesia induction. At that time-point, the lowest frequency of hypothermia was again in group A+W. It would seem that combination of endogenous amino acid-induced thermogenesis and external warming mattress is most effective in preventing intraoperative hypothermia.

The primary aim of our study was to investigate stress hormone response in patients unerwent major surgery and the effects of various warming methods. Our results show substantial increase in concentrations of catecholamines in postoperative period in all groups. Highest values were recorded in non warmed patients, but we found no significant difference compared to other groups. Also, despite the notably higher basic values in groups C and A compared to other two groups, these differences did not reach the
statistical significance. Frank and coworkers indicated that decrease in core temperature by 1.5 °C is related to higher epinephrine concentration in early postoperative period, while maintenance of normothermia shows little effect on epinephrine and norepinephrine concentrations (15). Earlier investigations also failed in attempts to relate the effects of intraoperative hypothermia to catecholamine response, probably due to insufficient number of participants, confounding influence of age, lack of randomization and lack of standardized postoperative analgesion (16, 17). Other investigators also reported that mild intraoperative hypothermia does not have important effect on stress hormones concentrations in hypothermic patients (18, 19). In the same study, authors simultaneously investigated cortisol response and did not found any intraoperative increase of its concentrations. Frank and coworkers found that patients who received general anaesthesia showed higher postoperative concentrations of cortisol compared to those received combined or regional anaesthesia, and concluded that cortisol response is determined by anaesthesiology technics rather than hypothermia (15). In our investigation peak values of cortisol levels were achieved in all groups 120 minutes after surgery. We found statistically significant difference regarding the warming method. In group in which we simulated endogenous thermogenesis by intravenous administration of amino acid solution we recorded the lowest changes in cortisol levels both intraoperatively and postoperatively compared to other groups. In all groups cortisol concentrations tend to normalize in following 48 hours.

Along with other stress hormones, surgical stress and intraoperative hypothermia also induce prolactin secretion (20), probably via central dopaminergic mechanism. In our investigation we recorded increase in prolactin concentration in all four groups with peak values measured 120 minutes after surgery. We also noted the statistically significant difference between groups warmed with amino acids and combination of amino acids and forced-air mattress compared to other two groups. This may lead to conclusion that amino acids were responsible to observed difference. Interestingly, we recorded somewhat higher basic levels of prolactin in A group compared to other three groups, but the difference was not statistically significant. After 48 hours, concentrations of prolactin were decreased toward baseline levels, which is in agreement with results of previously mention investigation (20).
Finally, when we analyzed testosterone response, we found decrease in concentrations after surgery in all groups, and lower levels were sustained throughout the entire observation, i.e. following 48 hours. The differences between baseline levels and postoperative measurements were statistically significant in W and A+W groups, but there was no difference between groups in any time point. Lindh and coworkers recorded maintenance of low concentration of testosterone up to 16th postoperative day (20), with inevitable impairment of anabolic processes necessary for recovery. According to our findings, as well as results reported in other studies, we may notice that major surgical trauma and perioperative hypothermia impose rapid, intensive and long-lasting effect on gonadal activity (reflected by decreased testosterone levels), while the effect on suprarenal activity is rather mild.

There are several limitations in our study: although the sample size was sufficient for correct statistical analysis, reported patterns and trends in stress hormone profile and methods of hypothermia should be confirmed in larger population. In addition, our results are obtained in patients underwent specific surgical intervention in general anaesthesia, hence further investigations need to be conducted in other types of surgery and other types of anaesthesia.

**Conclusion**

Prevention of intraoperative hypothermia is of major importance in reduction of complications associated with avoidable hypothermia in surgical patients. This study demonstrates effects of intraoperative hypothermia and three warming methods on stress hormone response in patients who underwent major open abdominal surgical procedures. Both external and internal warming methods were effective in attenuation of intraoperative and postoperative hyperthermia, and the most effective was forced-air mattress per se, or in combination with internal warming. Comparison of catecholamine concentrations measured 90 minutes before and 120 minutes after surgical procedures revealed significant increase during surgery, with highest values recorded in non-warmed group. Concentrations of cortisol and prolactin also showed significant increase at the same time point, with tendency to normalization after 48 hours. Contrary, testosterone concentrations showed decrease after 120 minutes without normalization throughout the entire period of
observation. Except for testosterone, changes in all stress hormones were attenuated in warmed groups compared to controls, and internal warming (amino acid solution) with or without forced-air mattress was the most effective. Regarding both features of surgical stress investigated in this study (hypothermia and stress hormone response), combination of endogenous amino acid-induced thermogenesis and external air warming mattress is most effective.

References
1. Jun JH, Chung MH, Jun IL, Kim Y, Kim H, Kim JH et al. Efficacy of forced-air warming and warmed intravenous fluid for prevention of hypothermia and shivering during cesarean delivery under spinal anesthesia Eur J Anaesthesiol 2019;36(6):442-8.
2. Zeba S, Surbatovic M, Jevtic M, Filipovic N, Popovic N, Radakovic S, et al. Influence of perioperative administration of amino acids on thermoregulation response in patients underwent colorectal surgical procedures. Vojnosanit Pregl 2007;64(6):421-4.
3. Zeba S, Surbatovic M, Marjanovic M, Jevdjic J, Hajdukovic Z, Karkalic R, et al. Efficacy of external warming in attenuation of hypothermia in surgical patients. Vojnosanit Pregl 2016;73(6):566-71.
4. Goldestein DS. Catecholamines and stress. Endocrine regulations 2003;37:69-80.
5. Nicholson G, Hall GM. Stress response during surgery. In: Kumar CM Bellamy M, eds. Gastrointestinal and colorectal anaesthesia. New York: Informa Healthcare USA, 2007:33-44.
6. Matika R, Ibrahim M, Patwardhan A. The importance of body temperature: An anesthesiologist’s perspective. Temperature (Austin) 2016;4(1):9-12.
7. Sun Z, Honar H, Sessler DI, Dalton JE, Yzng D, Panjasawatwong K, et al. Intraoperative core temperature patterns, transfusion requirement and hospital duration in patients warmed with forced air. Anesthesiology 2015; 122(2):276-85.
8. McSwain JR, Yared M, Doty JW, Wilson SH. Perioperative hypothermia: causes, consequences and treatment. World J Anesthesiol 2015; 4(3):58-65.
9. Salem WT, El-din Helaly MK, Hassan MM, Radwan NH, Samy SF. Effect of perioperative amino acid infusion on intraoperative hypothermia and postoperative
15. Frank SM, Higgins Ms, Breslow MJ, Fleisher LA, Gorman RB, Sitzman JV, et al. The catecholamine, cortisol and hemodynamic responses to mild perioperative hypothermia: a randomized clinical trial. Anesthesiology 1995; 82(1):83-93.

16. Breslow MJ, Parker SD, Frank SM, Norris EJ, Yates H, Raff H, et al. The PIRAT Study Group: Determination of catecholamine and cortisol response to lower extremity revascularization. Anesthesiology 1993; 79:1202-09.

17. Holcher C, can Aalten L, Sutherland C. Anesthesia generates neuronal insulin resistance by inducing hypothermia. BMC Neuroscience 2008; 9:100-6.

18. Yi JW, Choi YK. The hemodynamic changes and stress hormone responses to mild intraoperative hypothermia during intravenous anesthesia (in neurosurgical patients). Korean J Anesthesiol 2003; 45(6):702-9.

19. Chi OZ, Choi JK, Lee DI, Kim YS, Lee I. Intraoperative mild hypothermia does not increase the plasma concentration of stress hormones during neurosurgery. Can J Anesth 2001;48(8):815-8.
20. Lindh A, Carlstrom K, Eklund J, Wilking N. Serum steroids and prolactin during and after major surgical trauma. Acta Anaesthesiol Scand 1992; 36:119-24.
Table 1.

Characteristics of patients and environments

| Characteristic                        | Control group (C) | Amino acid group (A) | Warming mattress group (W) | Combined warming group (A+W) |
|---------------------------------------|-------------------|----------------------|---------------------------|-----------------------------|
| Age (yrs.)                            | 65,19±4.89        | 63,89±4,34           | 63,25±5,8                 | 62,23±3,87                  |
| Males (%)                             | 60                | 40                   | 53,33                     | 46,66                       |
| Females (%)                           | 40                | 60                   | 46,66                     | 53,33                       |
| Body weight (kg)                      | 74,28±5,16        | 73,89±5,65           | 72,9±6,12                 | 73,24±5,87                  |
| Duration of anaesthesia (min)         | 141,28±16.13      | 139,55±13,59         | 133,46±12,02              | 137,21±14,12                |
| Temperature in operation theatre (ºC) | 21,25±1,52        | 21,22±1,47           | 21,14±1,64                | 21,18±1,56                  |
| Relative humidity (%)                 | 57,13±6,28        | 56,35±5,59           | 55,6±5,55                 | 56,25±5,84                  |
| Wind speed (m/s)                      | 0,21±0,04         | 0,21±0,02            | 0,22±0,04                 | 0,22±0,02                   |
Table 2

Concentrations of hormones in 4 time points in all groups

| Hormone     | Group       | Mean±SD            | 90 min before surgery | 120 min after surgery | 24 h after | 48 h after |
|-------------|-------------|--------------------|------------------------|------------------------|------------|------------|
| Epinephrine (pg/mL) | C       | 106,13±89,63       | 777,07±800,08         | -                      | -          | -          |
|             | A       | 53,47±52,022       | 388,27±293,48         | -                      | -          | -          |
|             | W       | 79,60±81,06        | 442,07±517,83         | -                      | -          | -          |
|             | A+W     | 80,80±60,99        | 664,33±606,33         | -                      | -          | -          |
| Norepinephrine (pg/mL) | C       | 580,53±465,38      | 1349,67±984,16        | -                      | -          | -          |
|             | A       | 588,73±452,93      | 1265,67±949,13        | -                      | -          | -          |
|             | W       | 313,53±357,68      | 800,53±738,04         | -                      | -          | -          |
|             | A+W     | 318,80±238,16      | 937,80±1063,43        | -                      | -          | -          |
| Cortisol (nmol/L)  | C       | 533,57±199,92      | 1211,23±373,98        | 654,29±221,49          | 494,71±165±39 |
|             | A       | 408,98±201,88      | 542,98±340,96         | 584,15±339,08          | 486,57±418±59 |
|             | W       | 573,22±188,70      | 1351,59±482,12        | 643,31±211,01          | 514,16±183,28 |
|             | A+W     | 400,09±191,49      | 803,64±279,66         | 631,65±399±79          | 495,07±373,74 |
| Prolactin (μIU/mL) | C       | 226,98±138,32      | 624,29±417,18         | 230,51±86,97           | 273,34±140,11 |
|             | A       | 411,64±224,59      | 1106,74±922,42        | 707,51±840,59          | 487,96±280,82 |
|             | W       | 237,36±166,69      | 638,37±335,53         | 258,37±172,69          | 315,56±211,55 |
|             | A+W     | 295,72±257,15      | 1162,44±11,6359       | 363,26±373,29          | 506,52±479,99 |
| Testosterone (nmol/L) | C       | 8,92±7,16          | 6,38±6,01             | 5,67±4,27              | 5,74±5,14  |
|             | A       | 6,31±7,48          | 4,20±4,92             | 5,27±4,00              | 3,49±3,18  |
|             | W       | 10,32±8,29         | 6,41±4,79             | 5,66±4,19              | 5,33±4,41  |
|             | A+W     | 11,67±7,69         | 6,24±4,04             | 6,75±4,18              | 5,89±3,86  |

C – Control group (non-warmed)

W – Group warmed with forced-air mattress

A – Group warmed with amino acids

A+W – Combined warmed group
Table 3.

Multiple comparison of groups (Tukey test)

| Group I | Group II | Mean difference (I-II) | p     |
|---------|----------|------------------------|-------|
| A       | C        | -217.7777              | <0.01 |
|         | W        | -264.8993              | <0.01 |
| A+W     | W        | -187.9583              | <0.05 |

C – Control group (non-warmed)
W – Group warmed with forced-air mattress
A – Group warmed with amino acids
A+W – Combined warmed group
Figure 1.

C – Control group (non-warmed)
W – Group warmed with forced-air mattress
A – Group warmed with amino acids
A+W – Combined warmed group
C – Control group (non-warmed)
W – Group warmed with forced-air mattress
A – Group warmed with amino acids
A+W – Combined warmed group

Figure 2.
C – Control group (non-warmed)
W – Group warmed with forced-air mattress
A – Group warmed with amino acids
A+W – Combined warmed group

Figure 3. Average concentrations of epinephrine pre- and postoperatively
C – Control group (non-warmed)
W – Group warmed with forced-air mattress
A – Group warmed with amino acids
A+W – Combined warmed group

Figure 4.
Figure 5.

- C – Control group (non-warmed)
- W – Group warmed with forced-air mattress
- A – Group warmed with amino acids
- A+W – Combined warmed group
C – Control group (non-warmed)
W – Group warmed with forced-air mattress
A – Group warmed with amino acids
A+W – Combined warmed group

Figure 6.
C – Control group (non-warmed)
W – Group warmed with forced-air mattress
A – Group warmed with amino acids
A+W – Combined warmed group

Figure 7.
Figure legends:

Figure 1. Intraoperative oesophageal temperatures in all groups
Figure 2. Postoperative oesophageal temperatures in all groups
Figure 3. Average concentrations of epinephrine pre- and postoperatively
Figure 4. Average concentrations of norepinephrine pre- and postoperatively
Figure 5. Average concentrations of cortisol in 4 time points
Figure 6. Average concentrations of prolactin in 4 time points
Figure 7. Average concentrations of testosterone in 4 time points

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