Koncentracija glukoze i laktata u serumu bolesnika operiranih u totalnoj intravenskoj anesteziji propofolom-fentanilom i u balansiranoj anesteziji izofluranom-fentanilom

Serum levels of glucose and lactate in patients treated under total intravenous anesthesia with propofol-fentanyl and under balanced anesthesia with isoflurane-fentanyl

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Sažetak

Uvod: Cilj studije bio je utvrditi prije-, intra- i poslijeoperacijske koncentracije glukoze i laktata u serumu bolesnika podvrgnutih operacijskom zahvatu u donjem dijelu trbuha pod totalnom intravenskom anestezijom (TIVA) propofolom-fentanilom odnosno općom izbalansiranom anestezijom izofluranom-fentanilom.

Materijali i metode: U ovu prospektivnu studiju bilo je uključeno 50 bolesnika obaju spolova, u dobi od 35 do 60 godina, podvrgnutih operaciji donjeg dijela trbuha. Bolesnici su nasumce podijeljeni u dvije skupine: eksperimentalnu skupinu od 25 bolesnika s ASA I/II (klasifikacija Američkog udruženja anesteziologa) operiranih pod TIVA i kontrolnu skupinu od 25 bolesnika s ASA I/II operiranih pod izbalansiranom anestezijom. Dvije skupine nisu se značajno razlikovale prema duljini operacije i stupnju kirurške traume. Uzorci krvi za mjerenje glukoze i laktata uzimali su se u točno određenim vremenskim točkama: 30 minuta prije početka operacije (T0), 30 minuta od početka operacije (T1), na kraju operacije (T2), 2 sata nakon završetka operacije (T3) i 24 sata nakon završetka operacije (T4). Serumske koncentracije glukoze i laktata mjerile su se pomoću testova dostupnih na tržištu. Rezultati su se analizirali pomoću Mann-Whitneyevog testa.

Rezultati: Serumske koncentracije glukoze izmjerene u vremenskim točkama T1, T2 i T3 bile su značajno niže ($P = 0,03$, $P = 0,001$ odnosno $P < 0,001$) u bolesnika operiranih uz TIVA propofolom-fentanilom nego u onih operiranih uz opću balansiranu anesteziju izofluranom-fentanilom. Srednja koncentracija laktata u krvotoku izmjerena u točki T4 bila je značajno niža ($P = 0,001$) kod bolesnika operiranih uz TIVA nego u bolesnika operiranih uz balansiranu anesteziju, dok je laktat u T1 bio niži u bolesnika operiranih uz balansiranu anesteziju ($P = 0,01$). U skupini bolesnika operiranih uz balansiranu anesteziju srednje serumske koncentracije glukoze i laktata izmjerene u T1, T2 i T3 bile su značajno više od njihovih bazalnih koncentracija ($P < 0,001$). Koncentracije

Abstract

Background: To determine pre-, intra- and postoperative serum glucose and lactate concentrations in patients subjected to low abdominal surgery under total intravenous anesthesia (TIVA) with propofol-fentanyl, and in those under general balanced anesthesia with isoflurane-fentanyl.

Materials and Methods: This prospective study included 50 patients of both sexes, aged between 35 and 60 years, subjected to low abdominal surgery. Patients were randomly divided into two groups: experimental group of 25 ASA I/II (American Society of Anesthesiologists I/II classification) patients treated under TIVA, and control group of 25 ASA I/II patients treated under balanced anesthesia. The length of surgery and the degree of surgical trauma did not differ significantly between the two anesthesia groups of patients. Blood samples for glucose and lactate measurements were drawn at exact time points: 30 minutes before the beginning of the surgery (T0), 30 minutes after the beginning of the surgery (T1), at the end of the surgery (T2), 2 hours after the surgery (T3), and 24 hours after the surgery (T4). Serum levels of glucose and lactate were measured using commercially available kits. The results were evaluated with nonparametric Mann-Whitney test.

Results: Serum concentrations of glucose measured at T1, T2 and T3 time points in patients treated under TIVA with propofol-fentanyl were significantly lower ($P = 0.03$, $P = 0.001$ and $P < 0.001$, respectively) than those in patients treated under general balanced anesthesia with isoflurane-fentanyl. The mean circulating level of lactate measured at T4 point in patients treated under TIVA was significantly lower ($P = 0.001$) than that in patients treated under balanced anesthesia, while T1 lactate was lower in patients treated under balanced anesthesia ($P = 0.01$). The mean serum concentrations of glucose and lactate measured at T1, T2, and T3 points were significantly higher related to their baseline levels in patients treated under balanced anesthesia ($P < 0.001$). Both T2 and T3 values of glucose were above the normal range.

glukoze izmjerene u T2 i T3 bile su iznad gornje granice normalnog raspona. U bolesnika na TIVA srednje serumske koncentracije glukoze izmjerene u T1, T2, T3 i T4 bile su značajno više ($P < 0,001$ odnosno $P = 0,001$) od njihovih bazalnih vrijednosti, ali su samo one izmjerene u T2 prelazile gornju normalnu vrijednost. U ovih bolesnika su koncentracije laktata u serumu izmjerene u T1, T2, T3 i T4 bile značajno više ($P < 0,001$) od bazalne koncentracije.

Zaključak. Dobiveni rezultati ukazuju na to da je metabolični odgovor na kirurški zahvat vjerojatno ublažen odnosno poboljšan u bolesnika operiranih uz TIVA propofolom-fentanilom u usporedbi s onim kod bolesnika operiranih uz opću balansiranu anesteziju izofluranom-fentanilom.

Ključne riječi: glukoza, laktat, operacija, anestezija propofolom-fentanilom, anestezija izofluranom-fentanilom

The mean serum levels of glucose determined at T1, T2, T3, and T4 in patients under TIVA were significantly higher ($P < 0.001$; $P = 0.001$) than the baseline level, however, only the level measured at T2 point exceeded the upper normal value. Serum lactate levels measured at T1, T2, T3, and T4 were significantly higher than the baseline level ($P < 0.001$) in patients under TIVA.

Conclusions: The results obtained suggested the metabolic response to surgery to be probably attenuated and thus improved in patients treated under TIVA with propofol-fentanyl in comparison with that in patients treated under general balanced anesthesia with isoflurane-fentanyl.

Key words: glucose, lactate, surgery, propofol-fentanyl anesthesia, isoflurane-fentanyl anesthesia

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Uvod

Odgovor na stres za vrijeme operacijskog zahvata mijenja se pod utjecajem mnogih čimbenika, uključujući težinu i trajanje operacijske traume, operacijsku tehniku te vrst anestezije. Podaci o učincima anestetskih i analgetičnih postupaka na metaboličke odgovore na operaciju kod ljudi raznoliki su, pa čak i proturječni. Biokemijski čimbenici koji započinju, reguliraju i održavaju metabolični odgovor na operaciju nisu u potpunosti utvrđeni.

Dokumentirane su promjene u metabolizmu proteina i glukoze tijekom i poslije operacijskog zahvata (1). Studije su pokazale da se oksidacija endogenih aminokiselina i otpuštanje aminokiselina iz mišića pojačavaju nakon abdominalne operacije (1). Hiperglikemija je izrazito obilježje metaboličnog odgovora izazvanog kirurškom traumom (2). Hiperglikemija se povezuje sa stupnjem kirurške traume i na nju vjerojatno utječe anestezijska tehnika. Dok inhalirani anestetici imaju tek minimalan inhibicijski učinak na odgovor na operacijski stres, anestezija propofolom ublažava intraoperacijski porast glukoze u plazmi tijekom operacije (3,4).

Učinak tkivne kirurške traume i vrste anestezije na neposredan metabolični odgovor nije u potpunosti razjašnjen. Stoga je cilj ove studije bio ispitati učinak totalne intravenske anestezije (TIVA) propofolom-fentanilom i balansirane anestezije izofluranom-fentanilom na koncentracije glukoze i laktata u krvotoku kod bolesnika podvrgnutih elektivnoj kirurgiji donjeg dijela trbuha.

Materijal i metode

Ispitanici

U ovu prospektivnu studiju bilo je uključeno 50 bolesnika (22 muškaraca i 28 žena, bijelaca, stanovnika tuzlanske

Introduction

Stress response to surgery is modulated by several factors, including severity and duration of surgical trauma, surgical technique, and type of anesthesia. Data on the effects of anesthetic and analgesic regimens upon metabolic responses to surgery in humans are varying and even controversial. The biochemical factors initiating, regulating and sustaining the metabolic response to surgery have not been fully identified.

Changes in the protein and glucose metabolism during and after surgery have been documented (1). Endogenous amino acid oxidation and amino acid release from the muscle after abdominal surgery have been shown to increase (1). Hyperglycemia is a prominent feature of the metabolic response induced by surgical trauma (2). Hyperglycemia is related to the degree of surgical trauma and can be, probably, influenced by the anesthetic technique. Whereas inhaled anesthetics exert only minimal inhibitory influence on the surgical stress response, propofol anesthesia attenuates the intraoperative increase in plasma glucose (3,4).

The effects of surgical tissue trauma and type of anesthesia on the immediate metabolic response have not yet been fully clarified. Hence, the aim of the present study was to investigate the effect of total intravenous anesthesia (TIVA) with propofol-fentanyl and the effect of balanced anesthesia with isoflurane-fentanyl on the circulating levels of glucose and lactate in patients subjected to elective low abdominal surgery.

Materials and methods

Patients

The prospective study included 50 patients (22 male and 28 female, Caucasians, residents of the narrow region in

regije). Svi su bolesnici podvrgnuti kirurškom zahvatu u donjem dijelu trbuha (40 operacija raka debelog crijeva i 10 histerektomija) na Klinici za kirurgiju i traumatologiju te na Klinici za ženske bolesti Kliničkog bolničkog centra u Tuzli, Bosna i Hercegovina.
Kriteriji za uključenje bolesnika u studiju bili su: elektivni operacijski zahvat u donjem dijelu trbuhu, dob između 35 i 60 godina, status ASA I/II (klasifikacija I/II Američkog udruženja anesteziologa), podjednako trajanje operacije i podjednak stupanj kirurške traume.
Kriteriji za isključenje bili su: metabolična, jetrena ili bubrežna bolest, uzimanje lijekova koji utječu na metabolizam glukoze.
Studiju je odobrio stručni savjet Medicinskog fakulteta Sveučilišta u Tuzli. Prije uključenja u studiju svi su bolesnici potpisali obrazac za obaviješteni pristanak.
Bolesnici su nasumce podijeljeni u dvije skupine: eksperimentalnu skupinu od 25 bolesnika s ASA I/II operiranih uz TIVA propofolom-fentanilom i kontrolnu skupinu od 25 bolesnika s ASA I/II operiranih uz opću balansiranu anesteziju izofluranom-fentanilom.

Protokol anestezije

Protokol balansirane anestezije: za predmedikaciju midazolam 0,1 mg/kg i.m.; za indukciju tiopental natrij 5 mg/kg, uz fentanil 0,1 mg prije intubacije, u ukupnoj dozi od 0,005 mg/kg prije kirurške incizije; za održavanje anestezije izofluran 1,2-2,4 vol% pomiješan s oksidulom i kisikom u omjeru 1:1; suksametonium hidroklorid 1,5 mg/kg i Tracrium 0,5-0,8 mg/kg za intubaciju i miorelaksaciju.
Protokol za TIVA: za predmedikaciju midazolam 0,1 mg/kg i.m.; za indukciju propofol 2 mg/kg i fentanil 0,1 mg prije intubacije, u ukupnoj dozi od 0,005 mg/kg prije kirurške incizije; za održavanje anestezije infuzija propofola 6-12 mg/kg/h uz ventilaciju naizmjeničnim pozitivnim tlakom (IPPV) mješavine zraka, kisika i FiO_2 33-50%; opetovane doze fentanila od 0,1 mg ovisno o kliničkim pokazateljima; suksametonium hidroklorid 1,5 mg/kg i Tracrium 0,5-0,8 mg/kg za intubaciju i miorelaksaciju.
Tijekom operacijskog zahvata u svih se je bolesnika provodio hemodinamski nadzor (srčani ritam, sistolični i dijastolični krvni tlak) i praćenje CO_2 u izdahu. Tijekom operacije bolesnici su primali izbalansiranu otopinu elektrolita te Ringerovu otopinu laktata i 5%-tnu otopinu glukoze 24 sata poslije operacije. Srčani ritam, krvni tlak i proširenost zjenica bili su važni pokazatelji u praćenju tijeka anestezije. Anestetici i miorelaksansi dodavani su prema protokolu tijekom operacijskog zahvata.

Uzorci

Uzorci krvi za mjerenje koncentracije glukoze i laktata uzimali su se u točno određeno vrijeme, tj. 30 minuta prije početka operacije (T_0), 30 minuta od početka operacije (T_1), na kraju operacije (T_2), 2 sata nakon operacije (T_3) i 24

Tuzla surrounding). All of them were subjected to the low abdominal surgery (40 colon cancer operations and 10 hysterectomies) at University Department of Surgery and Traumatology and University Department of Gynecology, Tuzla University Clinical Center, Tuzla, Bosnia and Herzegovina.
The inclusion criteria for patients were as follows: elective low abdominal surgery; age between 35 and 60 years; ASAI/II status (American Society of Anesthesiologists I/II classification); almost the same length of the surgery, and almost the same degree of surgical trauma.
Exclusion criteria were as follows: presence of a metabolic, hepatic or renal disease, and receiving any medication known to affect glucose metabolism.
The study was approved by the Council of the School of Medicine, University of Tuzla. All patients signed informed consent forms before inclusion in the study.
Patients were randomly divided into two groups: experimental group of 25 ASA I/II patients treated under TIVA with propofol-fentanyl, and control group of 25 ASA I/II patients treated under general balanced anesthesia with isoflurane-fentanyl.

Anesthesia protocol

The protocol of balanced anesthesia was as follows: premedication with midazolam 0.1 mg/kg i.m.; induction with thiopental sodium 5 mg/kg, with fentanyl 0.1 mg before intubation with the overall dose of 0.005 mg/kg before surgical incision; maintenance of anesthesia with isoflurane 1.2-2.4 vol% mixed with nitrous oxide and oxygen at a ratio of 1:1; suxamethonium hydrochloride 1.5 mg/kg and Tracrium 0.5-0.8 mg/kg for intubation and myorelaxation.
The protocol for TIVA was as follows: premedication with midazolam 0.1 mg/kg i.m.; induction with propofol 2 mg/kg and fentanyl 0.1 mg before intubation with the overall dose of 0.005 mg/kg before surgical incision; maintenance of anesthesia with propofol infusion 6-12 mg/kg/h with ventilation by intermittent positive pressure (IPPV) with a mixture of air, oxygen and FiO_2 33-50%; repetitive fentanyl doses of 0.1 mg depending on clinical parameters; suxamethonium hydrochloride 1.5 mg/kg and Tracrium 0.5-0.8 mg/kg for intubation and myorelaxation.
Hemodynamic monitoring (heart rate, systolic and diastolic blood pressure) and expired air CO_2 monitoring were performed in all patients during surgical treatment. Patients received electrolyte-balanced solution during the operation, and Ringer-lactate solution and 5% glucose solution 24 hours after the operation. Heart rate, blood pressure and pupillary dilatation were relevant parameters for the anesthesia course follow up. Anesthetics and myorelaxants were added according to the protocol during the operation.

Samples

Blood samples for glucose and lactate measurements were drawn at exact time points: 30 minutes before the

sata nakon operacije (T_4). Koncentracija glukoze u serumu mjerila se pomoću testa Glucose Flex™ (Dade Behring), a koncentracija laktata pomoću testa Lactic Acid Flex™ (Dade Behring) dostupnih na tržištu.

Statistička analiza

Raspodjela kvantitativnih varijabla utvrđena je pomoću distribucijskih histograma uz unošenje vjerojatnosti i vjerojatnosti lišenih trenda. Rezultati su se procjenjivali pomoću neparametrijskog Mann-Whitneyevog testa, uz izračunavanje srednjih vrijednosti, standardnih devijacija (SD) i standardnih pogrješaka (SE). Razina statističke značajnosti utvrđena je kao vrijednost P = 0,05. Sve statističke analize provedene su pomoću statističkog programa SPSS verzija 10.

Rezultati

Prema testovima upotrebljenim za određivanje glukoze i laktata normalan raspon za glukozu bio je 3,9-6,1 mmol/L, a za laktat 0,4-2,0 mmol/L. Srednje serumske koncentracije glukoze izmjerene u T_1, T_2 i T_3 bile su iznad normalnog raspona za glukozu u bolesnika operiranih uz balansiranu anesteziju izofluranom-fentanilom, dok su koncentracije izmjerene u T_0 i T_4 bile unutar normalnog raspona. U bolesnika operiranih uz TIVA propofolom samo je serumska koncentracija glukoze izmjerena u T_2 bila iznad normalnog raspona, dok su sve ostale vrijednosti bile unutar normalnog raspona za glukozu.

U bolesnika operiranih uz balansiranu anesteziju srednja serumska koncentracija laktata izmjerena u T_2 bila je iznad normalnog raspona za laktat, dok su sve ostale izmjerene vrijednosti bile unutar referentnog raspona. U bolesnika operiranih uz TIVA propofolom sve srednje koncentracije laktata u serumu izmjerene u T_1, T_2, T_3 i T_4 bile su unutar normalnog raspona za laktat.

Srednje serumske koncentracije glukoze izmjerene u T_1, T_2 i T_3 bile su značajno niže u skupini bolesnika operiranih uz TIVA propofolom-fentanilom u usporedbi s bolesnicima koji su operirani uz balansiranu anesteziju izofluranom-fentanilom (P = 0,03, P = 0,001 odnosno P < 0,001) (tablica 1.).

Srednja koncentracija laktata u krvotoku izmjerena u T_4 u skupini bolesnika operiranih uz TIVA bila je značajno niža u usporedbi s onom kod bolesnika operiranih uz balansiranu anesteziju izofluranom (P = 0,001), dok je koncentracija laktata izmjerena u T_1 bila niža u skupini bolesnika na balansiranoj anesteziji nego u onih na TIVA (P = 0,01) (tablica 2.).

beginning of the surgery (T_0), 30 minutes after the beginning of the surgery (T_1), at the end of the surgery (T_2), 2 hours after the surgery (T_3), and 24 hours after the surgery (T_4). Serum levels of glucose were measured using a commercially available Glucose Flex™ kit (Dade Behring). Serum levels of lactate were measured using a commercially available Lactic Acid Flex™ kit (Dade Behring).

Statistical analysis

The distribution of quantitative variables was determined by using distribution histograms with probability plots and de-trended probability plots. The results were evaluated with nonparametric Mann-Whitney test, with mean values, standard deviations (SD), and standard errors (SE) calculated. The value of P = 0.05 was considered statistically significant. All statistical analyses were performed with SPSS statistical software, version 10.

Results

According to the kits used for glucose and lactate determination, the normal range for glucose was 3.9-6.1 mmol/L, and for lactate 0.4-2.0 mmol/L. The mean serum concentrations of glucose measured at time points T_1, T_2, and T_3 were all above the normal range for glucose in patients treated under balanced anesthesia with isoflurane-fentanyl, while the T_0 and T_4 values were within the normal range. Only the T_2 glucose concentration was above the normal range in patients treated under TIVA with propofol, while other values were within the normal range for glucose.

The mean serum level of lactate measured at T_2 was above the normal range in patients treated under balanced anesthesia, while lactate values at other points were within the reference range. Lactate concentrations measured at T_1, T_2, T_3 and T_4 were within the normal range in patients treated under TIVA with propofol.

The mean serum levels of glucose measured at T_1,T_2, and T_3 time points in patients operated under TIVA with propofol-fentanyl were significantly lower than those in patients treated under general balanced anesthesia with isoflurane-fentanyl (P = 0.03, P = 0.001 and P < 0.001, respectively) (Table 1).

The mean circulating levels of lactate measured at T_4 in TIVA group of patients was significantly lower in comparison with that in patients treated under balanced anesthesia with isoflurane (P = 0.001), while serum lactate determined at T_1 point in the balanced anesthesia group was lower than that in TIVA group (P = 0.01) (Table 2).

Tablica 1. Serumske koncentracije glukoze (mmol/L) u bolesnika operiranih uz TIVA propofolom-fentanilom i bolesnika operiranih uz balansiranu anesteziju izofluranom-fentanilom u određenim vremenskim točkama

Table 1. Circulating glucose levels (mmol/L) in patients treated under TIVA with propofol-fentanyl and patients treated under balanced anesthesia with isoflurane-fentanyl at different time points

Patient group	-30 min	+30 min	+180 min	+300 min	+1440 min
TIVA (N = 25)	4.6 ± 0.09**	5.79 ± 0.13	6.63 ± 0.17	5.82 ± 0.10	5.08 ± 0.07
Balanced anesthesia (N = 25)	5.005 ± 0.14	6.19 ± 0.16	7.53 ± 0.18	8.57 ± 0.30	5.18 ± 0.15
p*	0.6	0.03	0.001	< 0.001	0.7

TIVA, total intravenous anesthesia; *Mann-Whitney test; **$\overline{x}$ ± SE

Tablica 2. Serumske koncentracije laktata (mmol/L) u bolesnika operiranih uz TIVA propofolom-fentanilom i bolesnika operiranih uz balansiranu anesteziju izofluranom-fentanilom u određenim vremenskim točkama

Table 2. Circulating lactate levels (mmol/L) in patients treated under TIVA with propofol-fentanyl and patients treated under balanced anesthesia with isoflurane-fentanyl at different time points

Patient group	-30 min	+30 min	+180 min	+300 min	+1440 min
TIVA (N = 25)	1.14 ± 0.04**	1.62 ± 0.05	2.10 ± 0.06	1.52 ± 0.06	0.67 ± 0.03
Balanced anesthesia (N = 25)	0.87 ± 0.5	1.37 ± 0.05	2.10 ± 0.09	1.68 ± 0.09	0.89 ± 0.04
p*	0.06	0.01	0.6	0.1	0.001

TIVA, total intravenous anesthesia; *Mann-Whitney test; **$\overline{x}$±SE

Rasprava

Rezultati ovoga ispitivanja su pokazali da su srednje serumske koncentracije glukoze i laktata za vrijeme i neposredno nakon operacije značajno niže u bolesnika operiranih uz TIVA propofolom-fentanilom u usporedbi s bolesnicima operiranim uz opću balansiranu anesteziju izofluranom-fentanilom (tablice 1. i 2.). Dobiveni rezultati ukazuju na to da se metabolični odgovor na kirurški zahvat vjerojatno ublažava i time poboljšava u bolesnika operiranih uz TIVA propofolom-fentanilom u odnosu na onaj u bolesnika operiranih u općoj balansiranoj anesteziji izofluranom-fentanilom. Rezultati nekih drugih sličnih studija sukladni su rezultatima dobivenim u ovom našem ispitivanju. Za razliku od inhalirane anestezije, anestezija propofolom uz dodatak sufentanila obuzdava intraoperacijski porast koncentracije glukoze u plazmi (4). Inhibicijski učinak propofola na simpatoadrenalni sustav dokumentiran je u bolesnika podvrgnutih operaciji srca (5), kao i *in vitro* kad su koncentracije propofola, slično onima zabilježenim za vrijeme uvođenja u anesteziju, smanjile bazalno i nikotinom poticano otpuštanje katekolamina iz kromafinskih stanica (5). TIVA propofolom ublažava perioperacijski metabolični i endokrini odgovor u usporedbi s inhaliranom anestezijom sevofluranom (6). Intraoperacij-

Discussion

The results of this study showed the mean serum concentrations of glucose and lactate during the operation and shortly after the operation to be significantly lower in patients treated under TIVA with propofol-fentanyl in comparison with those in patients treated under general balanced anesthesia with isoflurane-fentanyl (Tables 1 and 2). The results suggested the metabolic response to surgery to be probably attenuated and thus improved in patients treated under TIVA with propofol-fentanyl as compared with that in patients treated under general balanced anesthesia with isoflurane-fentanyl. Results of some other similar studies are comparable with those obtained in our study. Propofol anesthesia supplemented with sufentanil, in contrast to inhaled anesthesia, suppressed the intraoperative increase in plasma glucose concentration (4). Inhibitory effects of propofol on the sympathoadrenal system have been documented in patients undergoing cardiac surgery (5), and documented *in vitro* when propofol concentrations, similar to those observed during the induction of anesthesia, decreased the basal and nicotine-stimulated release of catecholamines from chromaffin cells (5). TIVA with propofol blunts perioperative metabolic and endocrine response when compared

ske koncentracije glukoze, laktata i slobodnih masnih kiselina u plazmi bile su značajno niže uz TIVA u usporedbi s inhalacijskom anestezijom (7). Anestetici mogu utjecati na metabolizam glukoze, barem djelomice, kroz modulaciju simpatičkog tonusa.

Intraoperacijske koncentracije glukoze mjerene 2 sata nakon operacije bile su iznad normalnog raspona u naših bolesnika operiranih uz anesteziju izofluranom-fentanilom, dok je u bolesnika operiranih uz TIVA propofolom samo koncentracija glukoze izmjerena u T_2 bila iznad tog raspona, a sve druge izmjerene koncentracije glukoze bile su ununtar normalnog raspona. Koncentracije laktata mjerene u svim vremenskim točkama u objema skupinama bolesnika bile su unutar referentnog raspona, s iznimkom koncentracije laktata izmjerene u T_2 u skupini bolesnika na balansiranoj anesteziji. Ovi su nalazi sukladni s literaturnim podacima (4,8-12).

Pretpostavlja se da su mehanizmi kojima se posreduju metabolični utjecaji anestezije vjerojatno hormonski (8). Stresni hormon kortizol je snažan promicatelj glukoneogeneze u jetri (13), te djeluje na jetrene zalihe glikogena kao i na smanjenje utroška glukoze u perifernim tkivima. Hormon rasta i prolaktin imaju stanovitu ulogu u stresu, vjerojatno kroz njihovo hiperglikemijsko djelovanje u jetri (13,14). Anestezija propofolom nije značajno utjecala na svetjelesnu sintezu i oksidaciju proteina, ali je uzrokovala manje no značajno sniženje svetjelesne razgradnje proteina, moguće posredovano snižavanjem koncentracije kortizola u plazmi (15).

Nadalje, neki podaci ukazuju na to da anestetske koncentracije propofola inhibiraju stvaranje O^{2-} uslijed preopterećenja glukozom, a to bi se moglo odvijati kroz mehanizme koji uključuju, barem djelomice, suzbijanje staničnog preuzimanja glukoze (16).

Razgradnja proteina u skeletnim mišićima, glikoliza i glukoneogeneza su istaknuta obilježja intermedijarnog metabolizma kod bolesnika u uvjetima kirurškog stresa. Zapažen je izravan odnos između svetjelesne razgradnje proteina i proizvodnje glukoze kod kirurških bolesnika (3,9,17). Mišićni proteini razgrađuju se kako bi osigurali glukoneogenične aminokiseline za *de novo* glukoneogenezu u jetri. Poticanje glukoneogeneze kortizolom u jetri uzrokovano je prvenstveno stimulacijom katabolizma proteina (13,18). Kinetička ispitivanja metabolizma proteina i glukoze za vrijeme abdominalne kirurgije otkrila su sniženje svetjelesnog metabolizma proteina i glukoze, uz hiperglikemijski odgovor uzrokovan smanjenim svetjelesnim klirensom glukoze, kao i značajnim odnosom između proizvodnje glukoze i razgradnje proteina (9). Stopa sveukupnog metabolizma povećana je u stanjima stresa, ali je kapacitet oksidativnog metabolizma ograničen. To je jedan od glavnih razloga zbog kojeg se katabolični putovi počinju odvijati na neaerobičan način i stvarati, između ostalog, laktat.

to inhaled anesthesia with sevoflurane (6). Intraoperative plasma concentrations of glucose, lactate and free fatty acids were significantly lower in TIVA in comparison with inhalation anesthesia (7). Anesthetic agents can affect glucose metabolism through, at least partly, sympathetic tone modulation.

Intraoperative glucose levels and that measured two hours after the surgery in our isoflurane-fentanyl anesthesia group were above the normal range for glucose; however, in patients treated under TIVA with propofol, only T_2 glucose concentration was above the normal range while the levels measured at other points were within the normal range. Lactate levels measured at all points in both patient groups, except for T_2 in balanced anesthesia, were within the reference range. These findings are in accordance with some other literature reports (4,8-12).

It has been proposed that the mechanisms by which the metabolic effects of anesthesia are mediated are likely to be hormonal (8). The stress hormone cortisol is a powerful promoter of gluconeogenesis in the liver (13), and acts on the glycogen storage in the liver as well as on the reduction of glucose utilization in peripheral tissues. Growth hormone and prolactin have a role in stress, probably by their hyperglycemic action in the liver (13,14). Propofol anesthesia did not significantly affect whole body protein synthesis and oxidation but caused a small, although significant, decrease in the whole body protein breakdown, possibly mediated through the suppression of plasma cortisol concentration (15). Furthermore, some data indicate that anesthetic concentrations of propofol inhibit O^{2-} generation by D-glucose overload, and that this may occur *via* mechanisms that include, at least in part, the inhibition of cellular glucose uptake (16).

Protein degradation in skeletal muscle, glycolysis, and gluconeogenesis are the prominent characteristics of intermediary metabolism in patients under surgical stress conditions. Direct relationship between the whole body protein breakdown and glucose production in surgical patients have been observed (3,9,17). Muscle proteins are broken down to provide gluconeogenic amino acids for *de novo* gluconeogenesis in the liver. Promotion of gluconeogenesis by cortisol in the liver is caused primarily by the stimulation of protein catabolism (13,18). Kinetics studies of protein and glucose metabolism during abdominal surgery have revealed depression of the whole body protein and glucose metabolism with the hyperglycemic response being caused by a decreased whole body glucose clearance and a significant relationship between glucose production and protein breakdown (9). The rate of the overall metabolism is increased in stress conditions, but the capacity of oxidative metabolism is limited. This is one of the main reasons why catabolic pathways begin to work unaerobically and to produce, among other metabolites, lactate.

Rezultati zabilježeni u ovom istraživanju pokazali su da su serumske koncentracije glukoze i laktata povišene tijekom operacijskog zahvata, te da je taj porast izraženiji u bolesnika koji su operirani uz opću balansiranu anesteziju izofluranom u usporedbi s onima koji su operirani uz TIVA propofolom. Zapažene promjene vjerojatno su uzrokovane kirurškim stresom, katabolizmom proteina i glukoneogenezom. Međutim, u dvjema anestezijskim skupinama bolesnika ispitivali smo samo dva metabolična parametra. To je bilo znatno ograničenje ove naše studije, jer nije bilo moguće točno procijeniti koji je proces odgovorniji za kontrolu glikemije u skupini bolesnika s TIVA.
Metabolični odgovor na operaciju vjerojatno je ublažen i time poboljšan u bolesnika operiranih uz TIVA propofolom u usporedbi s onim u bolesnika operiranih uz opću balansiranu anesteziju izofluranom. Naši su rezultati sukladni literaturnim podacima iz sličnih studija i pokazuju kako višestruki pristupi uz kombinaciju anestetika, analgetika i operacijskih strategija rezultiraju boljom regulacijom glikemije tijekom intra- i perioperacijskog razdoblja, a time i boljim kliničkom ishodom u bolesnika.

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Results obtained in our study showed that serum levels of glucose and lactate were increased during surgical treatment, and that this increase was more pronounced in patients treated under general balanced anesthesia with isoflurane than in those under TIVA with propofol. The observed changes are probably due to surgical stress, protein catabolism and gluconeogenesis. However, only two metabolic parameters were investigated in the two anesthesia groups of our patients. It was a major limitation to our study because it was not possible to precisely evaluate which process was more responsible for the control of glycemia in TIVA group of patients.
Metabolic response to surgery is probably attenuated and thus improved in patients treated under TIVA with propofol in comparison with that in patients treated under general balanced anesthesia with isoflurane. Our results are in accordance with similar data reported in the relevant literature, and they indicate that multimodal approaches combining anesthetic, analgesic and surgical strategies will result in better control of glycemia during the intra- and perioperative periods, and thus in improvement of the clinical outcome of disease.

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