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Original Article / Özgün Araştırma

The Influence of Oral Carbohydrate Solution Intake on Stress Response before Total Hip Replacement Surgery during Epidural and General Anaesthesia

Total Kalça Protezi Ameliyatı Öncesi Oral Karbonhidrat Solüsyonu Alımının Epidural ve Genel Anestezi Sırasında Stres Yanıt Üzerine Etkisi

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Abstract / Öz

Objective: The effects of oral carbohydrate solutions, ingested 2 h prior to operation, on stress response were studied in patients undergoing general or epidural anaesthesia.

Methods: The study was performed on 80 ASA I-II adult patients undergoing elective total hip replacement, which were randomized to four groups (n=20). Group G patients undergoing general anaesthesia fasted for 8 h preoperatively; Group GN patients undergoing general anaesthesia drank oral carbohydrate solutions preoperatively; Group E patients undergoing epidural anaesthesia fasted for 8 h and Group EN patients undergoing epidural anaesthesia drank oral carbohydrate solutions preoperatively. Groups GN and EN drank 800 mL of 12.5% oral carbohydrate solution at 24:00 preoperatively and 400 mL 2 h before the operation. Blood samples were taken for measurements of glucose, insulin, cortisol and IL-6 levels.

Results: The effect of preoperative oral carbohydrate ingestion on blood glucose levels was not significant. Insulin levels 24 h prior to surgery were similar; however, insulin levels measured just before surgery were 2-3 times higher in groups GN and EN than in groups G and E. Insulin levels at the 24th postoperative hour in epidural groups were increased compared to those at basal levels, although general anaesthesia groups showed a decrease. From these measurements, only the change in Group EN was statistically significant ($p<0.05$). Plasma cortisol levels at the 2nd peroperative hour were higher in epidural groups than in general anaesthesia groups. Both anaesthesia techniques did not have an effect on IL-6 levels.

Conclusion: We concluded that epidural anaesthesia suppressed stress response, although preoperative oral carbohydrate nutrition did not reveal a significant effect on surgical stress response.

Keywords: Stress response, total hip replacement, carbohydrate solution, general anesthesia, epidural anaesthesia

Amaç: Çalışmamızda preoperatif iki saat öncesine kadar alınan oral karbonhidrat solüsyonlarının cerrahi stres yanıta etkisi genel ve epidural anestezi uygulanan hastalarda değerlendirildi.

Yöntemler: Total kalça protezi ameliyatı geçirecek ASA I-II, 80 hasta dört gruba ayrıldı (n=20). Grup G preoperatif 8 saat açlıkla genel anestezi uygulanan, Grup GN preoperatif oral karbonhidrat solüsyonu içirilerek genel anestezi uygulanan, Grup E preoperatif 8 saat açlıkla epidural anestezi uygulanan, Grup EN preoperatif oral karbonhidrat solüsyonu içirilen epidural anestezi altındaki hastalardan seçildi. Oral karbonhidrat solüsyonu içirilerek çalışmaya katılan grup GN ve grup EN hastalarına; elektif cerrahiden önceki gece saat 24:00'da 800 mL, ameliyattan 2 saat önceyse 400 mL %12,5 oral karbonhidrat solüsyonu içirildi. Glukoz, insülin, kortizol ve IL-6 düzeyleri için kan örnekleri alındı.

Bulgular: Ameliyat öncesi oral karbonhidrat nütrisyonu kan glukoz değerleri üzerine anlamlı bir etki oluşturmadı. Gruplar arasında, ameliyattan 24 saat önceki insülin değerleri arasında fark bulunmazken, ameliyat öncesi nutrisyon verilen gruplarda insülin değerlerinin, nutrisyon almayan gruplardan 2-3 kat fazla olduğu belirlendi. Epidural anestezi gruplarında postoperatif 24. saatteki insülin değerlerinin, bazal değerlere göre arttığı, aynı dönemlerde ise genel anestezi gruplarında plazma insülin konsantrasyonlarının azaldığı görüldü. Ameliyat öncesi nutrisyon uygulanan epidural anestezi grubundaki değişim istatistiksel olarak anlamlıydı ($p<0,05$). Cerrahi girişimi takip eden 2. saatteki kan kortizol değerleri, genel anestezi uygulanan gruplarda epidural anestezi gruplarından daha yüksek bulunmuştur. Uyguladığımız genel ve epidural anestezi teknikleri, IL-6 düzeylerindeki değişim üzerine etkili bulunmamıştır.

Sonuç: Çalışmamızda; epidural anestezi tekniğinin cerrahi stres yanıtı baskıladığı ancak ameliyat öncesi uygulanan oral karbonhidrat solüsyonu ile beslenmenin, cerrahi stres yanıt üzerinde anlamlı etkisi olmadığı sonucuna varılmıştır.

Anahtar kelimeler: Stres yanıtı, total kalça replasmanı, karbonhidrat solüsyonu, genel anestezi, epidural anestezi

Introduction

Exposure of the human body to surgical or other trauma leads to a neurohumoral response in the body and activates a catabolic process (1). The characteristics of the process include the increase in the metabolisms of lipids, proteins and carbohydrates; the retention of water and sodium and the decrease in insulin sensitivity along with the increase

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in blood glucose. The changes occurring within this process increase the risk for postoperative complications and mortality (2, 3). The surgical stress response of the organism, type of anaesthesia and surgery, duration of preoperative fasting and perioperative bleeding are correlated with the level of postoperative analgesia, and they affect the duration of hospitalization (4). Several previous studies indicated that surgical catabolic responses may vary with the anaesthesia technique. Therefore, some researchers have conducted studies to evaluate the superiority of anaesthesia techniques by applying general, epidural and combined skills (5-7).

Oral carbohydrate solutions have been developed to shorten the preoperative fasting duration. These solutions pass through the stomach in a short time; therefore, they can be used even 2 h before the operation (8). The present study aimed to investigate the effects of oral carbohydrate solutions received up to the preoperative 2nd hour on the surgical stress response of patients undergoing total hip replacement surgery under general or epidural anaesthesia.

Methods

After obtaining informed written consents and the approval of the local Ethics Committee of the İstanbul University Cerrahpaşa Medical School (protocol no: 5289), 80 ASA I-II patients undergoing total hip replacement surgery due to coxarthrosis were included in the study. The exclusion criteria consisted of patients using steroids and/or beta-adrenergic blockers and those with rheumatologic, endocrine, metabolic, renal and liver disease; tumours; obesity; fever and infection. Patients were randomly divided into four groups (n=20). They were randomized using the sealed opaque envelope method.

The first group (Group G) included patients who underwent surgery under general anaesthesia after an 8-h preoperative fasting period. The second group (Group GN) included patients who underwent surgery under general anaesthesia after drinking carbohydrate solutions during the preoperative period. The third group (Group E) included patients who underwent surgery under epidural anaesthesia following an 8-h preoperative fasting period. The fourth group (Group EN) included patients who underwent surgery under epidural anaesthesia after drinking oral carbohydrate solutions during the preoperative period. The patients in Group GN and Group EN were given 800 mL and 400 mL (12.5%) of oral carbohydrate solution (PreopQ, Nutricia, Holland) 8 h and 2 h before their elective surgery, respectively.

Patients were monitored in the operating room using electrocardiography (ECG), non-invasive arterial blood pressure and peripheral oxygen saturation (SpO_2). For the patients in Group E and Group EN, a lumbar epidural catheter was inserted at the L3-L4 intervertebral disc space, using an 18-G epidural needle by the loss of resistance technique. To achieve analgesia in T9 dermatome, 3 mL of 2% lidocaine was first administered as the test dose and then 1 mL of 0.25% bupivacaine and 0.05 mg kg^{-1} morphine (1 mg mL^{-1}) was administered per dermatome through the epidural catheter. For sedation during surgery, 1–3 mg kg^{-1} h^{-1} propofol infusion was administered. To ensure perioperative analgesia, continuous epidural infusion of a mixture of 100 mL 0.9% NaCl, 100 mg 0.5% bupivacain (1 mg mL^{-1}) and 5 mg morphine (0.05 mg mL^{-1}) was administered at a rate of 4 mL h^{-1}. When HR and MAP exceeded 20% of control values during surgery, patients received a 4-mL bolus of epidural solution.

Group G and Group GN received 10 mg kg^{-1} h^{-1} propofol infusion followed by 2–3 μg kg^{-1} fentanyl infusion for general anaesthesia. Tracheal intubation was performed with 0.2 mg kg^{-1} iv cisatracurium. Subsequently, mechanical ventilation was started with the following ventilator settings: tidal volume 6–8 mL kg^{-1}, respiratory frequency 12/min and FiO_2 0.4 (oxygen-air mixture) (AMS 2000 Anesthesia Delivery Unit, Sweden). Maintenance of anaesthesia was provided with 6–8 mg kg^{-1} h^{-1} propofol infusion, while neuromuscular blockage was maintained with periodical administration of 0.03 mg kg^{-1} cisatracurium. Patients whose HR and MAP went beyond 20% of control levels were administered 0.05 mg kg^{-1} morphine. At the end of the surgery, the neuromuscular block was antagonized by intravenous administration of 0.015 mg kg^{-1} atropine and 0.03 mg kg^{-1} neostigmine. Normal saline was used for perioperative liquid replacement. Intraoperative blood loss was measured, and all patients having a blood loss of 20% received whole blood transfusion.

For postoperative pain control, Group E and Group EN received patient-controlled analgesia with 1 mg mL^{-1} bupivacaine, 0.05 mg mL^{-1} morphine, 3 mL h^{-1} basal infusion, a bolus of 3 mL and a lockout of 30 min. Group G and Group GN patients were administered iv patient-controlled analgesia using 1 mg mL^{-1} morphine and a bolus of 1 mL with a lockout time of 7 min. HR, SpO_2 and mean arterial blood pressure values of all patients were recorded before intubation, 5 min after the intubation and at 5-min intervals during the surgery.

Blood samples were obtained on the first preoperative day, in the preparation room before surgery, 5 min after the skin incision and at the 1st, 2nd, 6th and 24th hour after the incision to determine the serum glucose and insulin levels. We also collected blood samples 1 day before the surgery, in the surgery preparation room and at the 6th and 24th hour after the skin incision for measuring Interleukin 6 (IL-6) levels.

Serum glucose levels were measured with the 'Accutrend Alpha' instrument (Roche, Switzerland) using the glucose oxidase method. Blood glucose levels measured at 60–110 mg dL^{-1} while the patient was fasting and below 140 mg dL^{-1} 2 h after the food intake were considered normal in this method.

Insulin levels were measured in serum using DPC insulin kits (Catalogue Number: LKIN 1, LKIN 5) and the 'IM-

MULITE 2-site chemiluminescent immunometric assay' method (DPC, 1997, the USA). In this method, insulin levels between 2.6 μU mL^{-1} and 24.9 μU mL^{-1} were considered normal. Cortisol levels were determined with the DPC cortisol kits (Catalogue No: LKCO 1, LKCO 5) and the IMMULITE analyser (DPC, 1997, USA) via the 'Competitive immunoassay' method. According to these measurements, normal cortisol values were as follows: 5–25 μg mL^{-1} in the morning, 8–20 μg mL^{-1} in the afternoon and lower than 6 μg mL^{-1} in the evening. IL-6 levels were also measured in serum using Anogen IL-6 kits (Catalogue No: EL10023) by the enzyme-linked immunosorbent assay (ELISA). The levels below 12.5 pg mL^{-1} were considered normal in the measurements performed using the ELISA method. The severity of postoperative pain was analysed in the recovery room 6 h and 24 h after the skin incision using the Visual Analogue Scale (VAS) with the range 0–10 (0: no pain, 10: extreme pain). During this time, the presence of nausea and vomiting was also recorded.

Statistical analysis

The characteristics of patients and surgery and the presence of nausea and vomiting were analysed using the 'chi-square test'. The levels of serum glucose, insulin, cortisol, IL-6, HR and MAP were compared between the groups using the 'Multiple Variance Analysis' (ANOVA and post hoc test Tukey HSD). The VAS values of the groups were compared with the 'Kruskal–Wallis test'. Obtained data were expressed with the mean (±) and standard deviation values. P<0.05 was considered statistically significant.

Results

Considering their sex, age, height, body weight and duration of surgery, there was no significant difference between groups (Table 1). Additionally, no significant difference could be found between the heart rates of groups. When the mean arterial pressure was compared between groups, the values in Group E and Group EN measured at the 1st preoperative day, were found to be significantly higher than those in Group GN (p<0.013) (94.20±9.33 and 95.30±11.44 vs 85.25±8.64). There was no statistically significant difference between other groups.

The preoperative blood glucose levels in Group G were significantly higher than those in Group GN in the morning of the surgery (p<0.05). We also observed that glucose levels at the postoperative 24th hour were significantly lower in Group G and Group EN than in Group GN and Group E (p<0.05). No statistically significant difference was observed between other groups (Table 2).

According to the comparison of the insulin levels between the groups, the postoperative insulin levels in Group E were significantly higher than those in Group G; the preoperative insulin levels in Group EN were statistically higher than those in Group G and Group E in the morning of the surgery and the levels measured at the 1st hour after the skin incision were significantly higher in Group EN and Group GN than those in Group G and Group E (p<0.05) (Table 3). The comparisons of the groups also indicated that cortisol levels measured 2 h after skin incision were significantly higher in Group G and Group GN than in Group EN (p<0.05) (Table 4). No statistically significant difference was found between the groups considering IL-6 values, blood loss and transfusions.

There was no statistically significant difference between groups regarding the incidence of nausea and vomiting. One patient from Group E and two patients from Group EN had nausea and vomiting. None of the study subjects experienced aspiration of gastric contents. The VAS values at the 6th postoperative hour were found to be significantly higher in Group G and Group E than in Group GN and Group EN (p<0.05). The VAS values, however, did not show any statistically significant difference between other groups (Table 5).

Discussion

In this study, the preoperative oral carbohydrate intake did not have a significant effect on the surgical stress response of patients undergoing total hip replacement surgery. The response of the organism against surgical stress was correlated

Table 1. Patient demographics

	Group G n=20		Group GN n=20		Group E n=20		Group EN n=20		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	p
Age (years)	47.95	16.28	52.70	15.21	57.65	18.05	53.30	14.69	0.310
Height (cm)	162.35	7.39	161.00	9.02	157.75	35.88	162.55	11.09	0.858
Body weight (kg)	69.95	9.91	68.65	11.46	72.80	8.26	75.75	17.81	0.281
Time (min)	141.00	40.48	148.75	51.30	126.00	34.40	139.25	36.93	0.376
Male	4	20.0	3	15.0	8	40.0	8	40.0	
Female	16	80.0	17	85.0	12	60.0	12	60.0	0.167

ANOVA and Tukey HSD (age and height), Kruskal–Wallis (time), Chi-square (gender)

Table 2. The comparison of glucose levels between groups

	Group G n=20		Group GN n=20		Group E n=20		Group EN n=20		
Glucose	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**p**
Preop 1	110.00	18.53	109.20	22.20	103.95	17.39	98.90	30.92	0.390
Preop 2	108.35	20.52	86.60	20.58	101.85	23.00	96.60	30.82	0.040
Glucose 3	95.45	18.10	96.70	28.51	89.35	22.01	86.10	20.90	0.407
Glucose 4	115.45	33.68	108.85	19.99	105.80	19.91	100.00	35.73	0.383
Glucose 5	125.85	31.35	124.75	31.09	114.80	24.53	115.90	43.75	0.618
Glucose 6	139.35	30.66	123.65	40.47	129.25	32.93	124.95	43.00	0.534
Glucose 7	130.55	22.75	138.95	46.55	140.90	34.64	120.70	21.08	0.204
Glucose 8	130.20	27.23	147.95	29.22	156.05	37.56	126.25	22.72	0.005

ANOVA and Tukey HSD. Preop 1: 1 day before surgery, Preop 2: preoperative recovery room, Glucose 3: 5 min after skin incision, Glucose 4: 1 h after skin incision, Glucose 5: 2 h after skin incision, Glucose 6: 3 h after skin incision, Glucose 7: 6 h after skin incision, Glucose 8: 24 h after skin incision

Table 3. The comparison of insulin levels between groups

	Group G n=20		Group GN n=20		Group E n=20		Group EN n=20		
Insulin	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**p**
Preop 1	11.71	5.44	9.31	3.18	10.71	5.09	11.40	6.07	0.448
Preop 2	18.40	5.90	17.11	7.29	17.42	7.26	17.89	7.67	0.944
Cortisol 3	23.17	8.52	20.68	10.54	17.81	10.58	12.53	8.62	0.006
Cortisol 4	20.62	9.01	21.46	7.45	23.26	10.85	27.68	33.97	0.640

Kruskal–Wallis. Preop 1: 1 day before surgery, Preop 2: preoperative recovery room, Insulin 3: 5 min after skin incision, Insulin 4: 1 h after skin incision, Insulin 5: 2 h after skin incision, Insulin 6: 3 h after skin incision, Insulin 7: 6 h after skin incision, Insulin 8: 24 h after skin incision

Table 4. The comparison of cortisol levels between groups

	Group G n=20		Group GN n=20		Group E n=20		Group EN n=20		
Cortisol	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**p**
Preop 1	11.71	5.44	9.31	3.18	10.71	5.09	11.40	6.07	0.448
Preop 2	18.40	5.90	17.11	7.29	17.42	7.26	17.89	7.67	0.944
Cortisol 3	23.17	8.52	20.68	10.54	17.81	10.58	12.53	8.62	0.006
Cortisol 4	20.62	9.01	21.46	7.45	23.26	10.85	27.68	33.97	0.640

Kruskal–Wallis. Preop 1: 1 day before surgery, Preop 2: preoperative recovery room, Insulin 3: 5 min after skin incision, Insulin 4: 1 h after skin incision, Insulin 5: 2 h after skin incision, Insulin 6: 3 h after skin incision, Insulin 7: 6 h after skin incision, Insulin 8: 24 h after skin incision

with the type of anaesthesia and surgery, duration of preoperative fasting, intra-operative bleeding and postoperative analgesia level. These factors also had an influence on the hospitalization time (9). Surgical catabolic response may vary based on the technique of anaesthesia.

The comparison of stress hormones between the groups showed significant differences at specific times; however, only IL-6 showed no significant difference between groups. It was observed in the study that the glucose levels measured on the morning of the surgery were lower in patients receiving nutrients than those who did not. Our study bears a resemblance to the results of the study conducted by Thorell et al. (10). As in the study of Maruyama et al. (11), serum glucose levels increased in all groups when the surgery started. However, unlike our study, they administered steroids to the first group

Table 5. The comparison of Visual Analogue Scale levels between groups

	Group G n=20		Group GN n=20		Group E n=20		Group EN n=20		
VAS	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**p**
VAS 1	2.85	0.93	2.45	1.15	3.35	1.14	2.90	1.29	0.106
VAS 2	1.80	0.77	1.30	0.73	1.85	0.75	1.25	0.79	0.019
VAS 3	0.90	0.79	0.80	0.70	0.50	0.76	0.65	0.75	0.357

Kruskal–Wallis. Preop 1: 1 day before surgery, Preop 2: preoperative recovery room, Insulin 3: 5 min after skin incision, Insulin 4: 1 h after skin incision, Insulin 5: 2 h after skin incision, Insulin 6: 3 h after skin incision, Insulin 7: 6 h after skin incision, Insulin 8: 24 h after skin incision

showing glucose intolerance and thus found that the increase in glucose level was significantly greater in that group than the ones abstaining from any kind of food and liquid intake before the surgery. In our study, however, although Group G and Group E were not allowed the oral intake of liquids or solids 8 h prior to the surgery, Group GN and Group EN were given 800 mL carbohydrate solution 8 h before the elective procedure and 400 mL of 12.5% carbohydrate solution before the surgery. When Group GN was compared with the groups that did not have any food and liquid intake before the surgery, no statistically significant difference could be observed in those groups regarding the increase of serum glucose levels at the beginning of the surgery. Similarly, we made a comparison between Group EN and other groups abstaining from any food and liquid intake. According to that comparison, there was no statistically significant difference between those groups regarding the increase of serum glucose levels at the start of the surgery. However, the glucose increase in Group EN was found to be higher than in the other groups.

In the study by Nygren et al. (9), serum glucose levels were highest at the 40th minute and returned to the basal level at the 120th minute. In our study, however, serum glucose levels increased to the highest level at the 2nd hour after the skin incision and were higher than the basal level. That difference may have been due to the fact that there was more surgical stress and bleeding, and the duration of the surgery was longer in total hip replacement than in laparoscopic cholecystectomy and parathyroid surgery.

In this study, as in the studies by Hausell et al. (12) and Soop et al. (13), insulin levels in the epidural anaesthesia group showed an increase at the postoperative 24th hour compared with the basal insulin levels, but there was a decrease in the plasma insulin concentration level in the general anaesthesia group. The present study also indicated that the increase in the cortisol level was higher in the groups that did not have any food and liquid intake before the surgery than in the groups receiving preoperative oral carbohydrate nutrition; nevertheless, oral carbohydrate administration did not have any effect on the blood cortisol level. The blood cortisol levels in the groups receiving general anaesthesia reached the highest level at the postoperative 2nd hour. During this time, the cortisol increase was observed to be lower in the groups receiving only epidural anaesthesia. However, we did not observe any increase in the cortisol levels of the group receiving preoperative nutrition together with epidural anaesthesia.

The comparison of IL-6 levels in the general anaesthesia group with the epidural group did not show any significant difference. Our study, on that sense, was similar to the study by Hogevold et al. (14), conducted among patients undergoing total hip replacement, and with the study by Naito et al. (15), which analysed patients undergoing upper abdominal surgery. Also, it was indicated in the study that VAS scores of the patients receiving oral nutrition before the surgery was significantly lower 6 h after the skin incision than those who did not receive preoperative nutrition solution. Conversely, patients who received nutrition and those abstaining from oral food or fluid intake had similar VAS levels at the postoperative 24th hour.

In several studies, the efficacy of the epidural technique proved to be superior than general anaesthesia in terms of reducing the surgical stress. In a study comparing general and epidural anaesthesia in 60 ASA 1-2 patients, the surgical trauma-related stress response was evaluated by determining the levels of serum CRP, TSH, cortisol and glucose. Heart rate and cortisol values were found to be significantly higher in the general anaesthesia group at the 30th minute (16). In a comparative study, it was concluded that when epidural anaesthesia is combined with general anaesthesia for patients undergoing major spinal surgery, the epidural group demonstrated lower levels of glucose, cortisol, IL-1β, IL-6 and IL-10 during the postoperative period. (17). Surgical trauma produces a neuroendocrine response mediated by the release of proinflammatory cytokines and hormones (18). The role of preoperative oral carbohydrate intake is related with a reduction in the inflammatory response to surgical stress because the insulin-stimulated glycogen synthase activity is attenuated by surgery and the glycogen stores in the liver, skeletal muscle and adipose tissue decrease (19).

On the other side, similar with our findings, the oral carbohydrate intake showed no effect on stress response for patients undergoing laparoscopic cholecystectomy (20). No sig-

nificant change was obtained in the levels of cortisol, glucose and insulin resistance.

Study limitations

The major limitation of this study is the number of participants in each group. To compare larger groups, further studies are needed.

Conclusion

We concluded from the study that the epidural anaesthesia technique could suppress the surgical stress response, but the oral carbohydrate solution diet applied in the preoperative period did not have a significant effect on surgical stress response.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of İstanbul University Cerrahpaşa School of Medicine.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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