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Comparing Effects of Sugammadex and Neostigmine on Postoperative Bowel Movements After Laparotomic Gynecological Operations

Laparotomi İle Yapılan Jinekolojik Ameliyatlarda Sugammadeks ve Neostigminin Postoperatif Bağırsak Hareketleri Üzerine Etkilerinin Karşılaştırılması

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ABSTRACT Objective: Gastrointestinal system dysfunction is a common postoperative complication. Especially after abdominal surgery it extends the length of stay in the hospital causing morbidity. Sugammadex is a drug being used in anesthesia routine which binds to steroid formed nondepolarizing muscle relaxants with high affinity and antagonizes neuromuscular block by a completely different mechanism from neostigmine which cause cholinesterase inhibition. We aimed to investigate the effect of sugammadex and neostigmine on return of bowel movements in the postoperative period. **Material and Methods:** 60 patients classified as American Society of Anesthesiologists (ASA) I, II aged between 18 and 65 years who underwent total abdominal hysterectomy, total abdominal hysterectomy, bilateral salpingo-oophorectomy and myomectomy operations under general anesthesia were randomized into two groups (Sugammadex, Group S, Neostigmine, Group N). Before the operation. Group S received 2 mg /kg sugammadex after spontaneous respiratory effort after operation, group N received 0.015 mg /kg atropine followed by 0.3 mg /kg neostigmine. Patients were examined by an independent physician at 0, 4, 8, 12, 24 hours postoperatively with a stethoscope for bowel movement. Patients gas release and defecation time were noted. **Results:** There was no statistically significant difference between groups in terms of demographic characteristics and total surgery time. Total anesthesia time was observed to be significantly shorter in group S. There was no difference between the groups in terms of the first gas extraction time, defecation time and patient discharge time. **Conclusion:** As a result, there was no difference between sugammadex and neostigmine in terms of returning time of postoperative bowel movements.

Keywords: Sugammadex; neostigmine; bowel movements

ÖZET Amaç: Gastrointestinal sistem disfonksiyonu sık görülen, hastanede kalış süresini uzatan ve morbiditeye sebep olan bir postoperatif komplikasyondur. Sugammadeks yüksek afiniteyle steroid yapıdaki nondepolarizan kas gevşeticilere bağlanıp neostigminin etki mekanizması olan kolinesteraz inhibisyonundan tamamen farklı bir mekanizma ile nöromüskler blokajı antagonize eden anestezi rutinine girmiş bir ilaçtır. Çalışmamızda sugammadeks ile neostigminin postoperatif dönemde bağırsak hareketlerinin geri dönmesine etkisinin karşılaştırılmasını araştırmayı amaçladık. **Gereç ve Yöntemler:** ASA (American Society of Anesthesiologists) sınıflaması I-II grubundan yaşları 18-65 yıl arasında değişen, genel anestezi altında total abdominal histerektomi, total abdominal histerektomi bilateral salpfingo-ooferektomi ve miyomektomi operasyonu planlanan 60 hasta üzerinde yapıldı. Operasyon öncesi hastalar randomize edilerek iki gruba (Sugammadeks; Grup S, Neostigmin; Grup N) ayrıldı. Grup S'de operasyon bitimi sonrası spontan solunum eforu görüldükten sonra 2mg/kg sugammadeks, Grup N'de 0,015 mg/kg atropini takiben 0,3 mg/kg neostigmin intravenöz olarak yapıldı. Hastalar araştırmadan bağımsız bir hekim tarafından postoperatif 0, 2, 4, 8, 12, 24 saatlerde stetoskop ile 4 kadranda dinlenerek bağırsak hareketi olup olmadığı kontrol edildi. Hastalara ilk çıkardıkları gaz ve defekasyon zamanını servis hemşiresine haber vermeleri söylendi. **Bulgular:** Hastaların demografik özellikleri, toplam cerrahi açısından fark gözlenmedi. Toplam anestezi süresi bakımından Grup S istatistiksel olarak anlamlı olacak şekilde daha kısa olarak gözlendi. İlk gaz çıkarma zamanı ve defekasyon zamanı açısından gruplar arasında fark gözlenmedi. Taburculuk zamanı açısından gruplar arasında fark gözlenmedi. **Sonuç:** Çalışmamızda sugammadeks ve neostigmin arasında postoperatif bağırsak hareketlerinin geri dönme zamanı arasında fark gözlenmemiştir.

Anahtar Kelimeler: Sugammadeks; neostigmin; bağırsak hareketleri

An important step in general anesthesia practice is to provide muscle relaxation. Since Harold Griffith published the results of his research in 1942 using a curare extract during anesthesia, muscle relaxants have entered the world of anesthesia and rapidly become a routine part of general anesthesia.[1]

Muscle relaxation facilitates both the anesthetist's intubation procedure, patient ventilation, and surgical intervention during anesthesia.

Muscle relaxants are divided into two groups, nondepolarizer and depolarizing. However, in both adults and children, the routine use of depolarizing muscle relaxants has been abandoned. Nondepolarizan muscle relaxants are being used more safely and frequently in routine general anesthesia application after selective antagonists being offered for use. These pharmacological agents act as acetylcholine (Ach) competitive antagonists. When muscle relaxant binds postsynaptic Ach receptors alpha subunit, it prevents the ion channel from opening and the muscle being depolarize. When the surgical procedure is terminated, appropriate pharmacological antagonist agents must be administered in order for this muscle blocker-generated block to be removed. This can be done in two ways. The first method is to reduce the amount of drug in synaptic cleft and increase the amount of Ach. Ach in the synaptic cleft can be increased by anticholinesterase drugs inhibiting the enzyme acetylcholinesterase that rapidly breaks the Ach in the synaptic range.[2] The most commonly used anticholinesterase drug for this purpose is neostigmine. Another new method of reducing the amount of muscle relaxant in the synaptic cleft is sugammadex, the gamma-cyclodextrin derivative, which has been increasingly used in recent years. Sugammadex is a selective antagonist that binds to steroid formed nondepolarizing muscle relaxants with high affinity to neutralize them.[3]

Gastrointestinal system dysfunction is a common postoperative complication. Especially after the abdominal surgery it extends the length of stay in the hospital. Although there is no study of economic consequences in our country, it is reported that the effect on the US health system is $ 1 billion annually.[4] Postoperative gastrointestinal system complications are one of the most important conditions that prolongs the hospital stay. In addition to the effects on patient morbidity, many studies have been carried out on this complication due to the financial burden on the health system.

In this study, we aimed to compare the effects of neostigmine and sugammadex on the postoperative bowel movements which are frequently used in our practice in order to antagonize the effect of the muscle relaxant used in our daily practice.

MATERIAL AND METHODS

The study was carried out in accordance with the ethical standards of the Helsinki Declaration, and was approved by GOP Taksim Training and Research Hospital Ethics Committee Istanbul, Turkey. After receiving patient informed consent 60 ASA I-II patients aged between 18 and 65 years who underwent total abdominal hysterectomy (TAH), total abdominal hysterectomy bilateral salpingo-oophorectomy (TAH-BSO) and myomectomy operations were randomly divided into two groups in our study planned to be performed in Obstetrics and Gynecology Clinic. Because we could not find a similar study in literature we were unable to perform a power analysis for case enrollment.

The patients were randomly divided into two groups by closed envelope method. The closed envelopes that determine which group the patient belongs to were randomly selected by the patient.

Postoperative patient examination was carried out by an anesthesiologist and reanimation resident independent from research.

ECG (electrocardiography), SpO2 (pulse oximeter), NIBP (noninvasive blood pressure) monitorizations were performed after the patients in both groups were taken to the operating room. Fluid resuscitation with Isolyte-S was initiated after opening the peripheral vein with an 18-gauge intravenous cannula. General anesthesia is planned for all groups. After sedation with 0.03 mg / kg iv midazolam, induction was started following 2 min preoxygenation with 4 l / min O2. 1 mcg / kg fen-

tanyl citrate, 2 mg /kg propofol, 0.06 mg /kg rocuronium. After confirming the location of the exercise tolerance testing (ETT), patients were connected to the Mindray Wato Ex 65 Pro brand anesthesia machine with VT (tidal volume): 8 ml /kg, f (frequency): 12 /min, I / E (inspiratory expiratory ratio) (fractionated oxygen in inspired air): 40%, peep (expiration end positive pressure): 5 cmH2O. Anesthesia maintenance was provided with sevoflurane 1.5 MAC (minimum alveolar concentration), followed by etCO2 (end tidal carbon dioxide) monitoring.

Group N: When spontaneous respiratory effort was observed after the surgical procedure was terminated, 0.01 mg / kg of atropine was administered followed by intravenous administration of 0.03 mg / kg of neostigmine.

Group S: When spontaneous respiratory effort was observed after the surgical procedure was terminated, 2 mg / kg sugammadex was administered intravenously after the surgical procedure was terminated.

After taking the patients into the recovery room, the bowel movements were recorded by listening with auscultation at 0, 2. 6, 12 hours postoperatively, and the patient's gas extraction time and defecation time and discharge time were noted.

The inclusion criteria of the volunteers were:

- In the age range 18-65 years,
- ASA I, II,
- Who signed patient informed consent form
- Who did not have previous abdominal surgery.

STATISTICAL ANALYSIS

Student t test for continuous variables between groups and Pearson Chi square test for categorical variables were analyzed in the SPSS for Windows (version 21) (SPSS Corp., Chicago, IL).

RESULTS

There were no significant differences in age, body weight and ASA data among the 60 patients included in the study (Table 1).

There was no statistically significant difference between the two groups in terms of surgery types (Table 2).

HEARTH RATE

There was no statistically significant difference between the groups in terms of heart rate (Figure 1).

MEAN ARTERIAL PRESSURE BETWEEN GROUPS

When the mean arterial pressure (MAP) values of the groups were compared, there was no statistically significant difference between the groups (Figure 2).

The average duration of the operation is 99 minutes in the sugammadex group, 102 minutes in the neostigm group. The duration of the anesthesia is 104 minutes in the group of sugammadex and 105 minutes in the neostigmine group. Although there was no statistical difference in the duration of surgery, there was a significant difference in the duration of anesthesia (Table 3).

GAS RELEASE TIME

In the sugammadex group, the first degassing time is 355 minutes on average between 228 and 480 minutes, with an average of 348 minutes between 232 and 460 minutes in the neostigmine group. There was no statistically significant difference between the groups (Figure 3).

DEFECATION TIME

The mean defecation time in the Sugammadex group, was 1015 minutes between 716 and 1350

TABLE 1: Comparison of individual and general characteristics of the groups (Mean ± SD).

		Group S (N=30)	Group N (N=30)	P
Age (years)		42±5	41±5	0.68
Weight (kg)		65±6	63±7	0.45
ASA	I	15 (%50)	18 (%60)	0.43
	II	15 (%50)	12 (%40)	

TABLE 2: Surgery type (Mean ± SD).

	TAH	18 (%60)	15 (%50)	0.99
Surgery Type	**TAH-BSO**	8 (%26)	10 (%26)	
	MYOMECTOMY	4 (%14)	5 (%14)	

TAH: Total abdominal hysterectomy.

TAH-BSO: Total abdominal hysterectomy bilateral salpingo-oophorectomy.

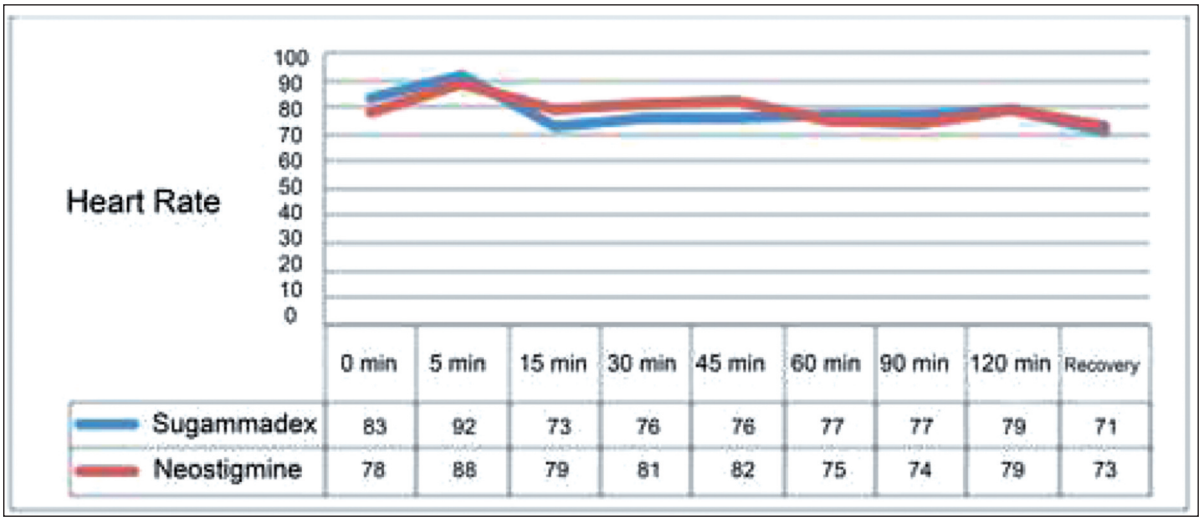

FIGURE 1: Heart rate comparison between groups (Mean ± SD).

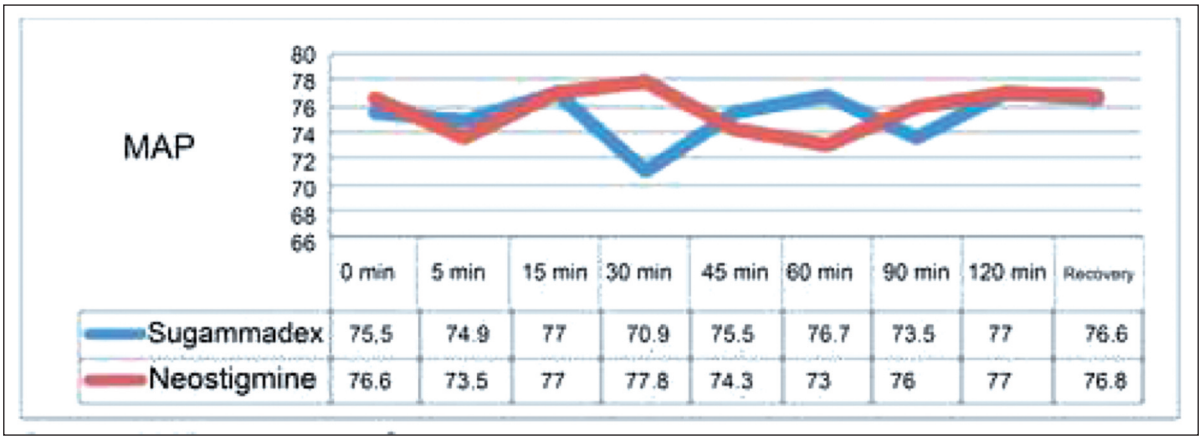

FIGURE 2: Mean arterial pressure comparison between groups (Mean ± SD).

TABLE 3: Operation time (minute, mean ± SD).

	Surgery time	Anestesia time
Sugammadex	99±17	105±17
Neostigmine	102±15	114±15
	P>0.05	P<0.05

minutes, and 1087 minutes between 730 and 1398 minutes in the neostigmine group. Although this period was longer in the neostigmine group, no statistically significant difference was found between the two groups (Figure 4).

PATIENT DISCHARGE TIME

There was no statistically significant difference between the groups in terms of discharge time from hospital (Figure 5).

Postoperative nausea and vomiting were observed at 3 patients in neostigmine group and 4 patients in sugammadex group, and not repeated after methoclopramide treatment.

DISCUSSION

In 1942, after Harold Griffith published the results of his research using purified curare (South American arrow poison) during anesthesia, muscle relaxants quickly became routine medications for anesthesia. As Griffith notes, it is emphasized that agents that block the neuromuscular junction do not cause anesthesia, and that these drugs cause paralysis.[5]

With ongoing studies since the introduction of curare in daily practice it has been a crucial ele-

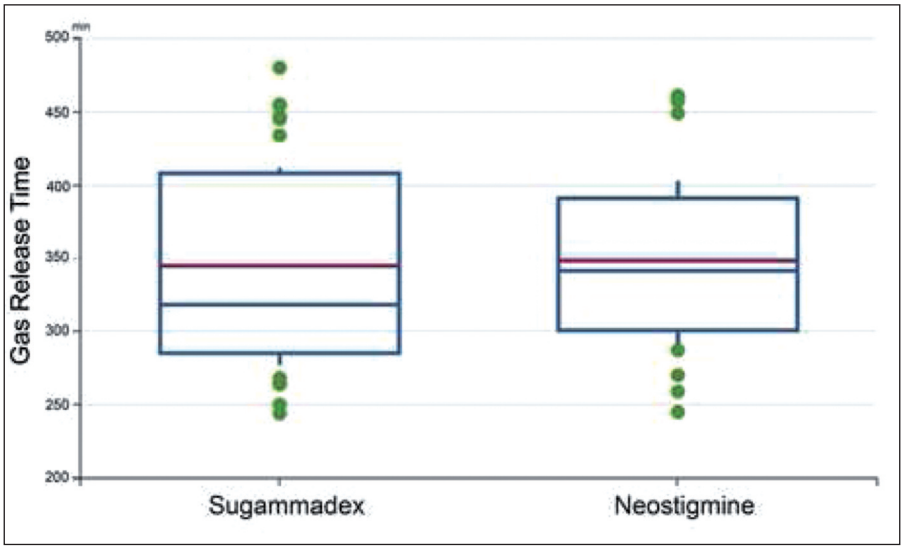

FIGURE 3: Comparison of gas release times between groups.

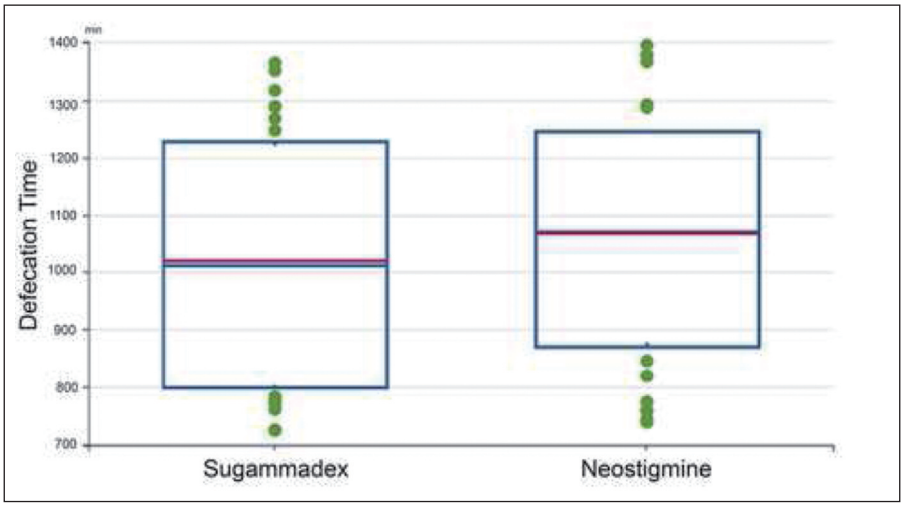

FIGURE 4: Comparison of defecation time between groups.

ment in general anesthesia and intensive care units. At the same time, complications related to their use and drug interactions, differences in individual responses and brought some hesitations and concerns about the use of these drugs.[6] Due to these hesitations, the effects of the drugs to body sysytems have been examined in detail. As a result there are many studies about the pharmacodynamics of sugammadex, which is an antagonizing drug that is routinely used with curare.

Sugammadex, a cyclodextrin derivative used in the reversal of the effects of neuromuscular blocking agents (NMBAs) in steroid form, is a reversible agent for a new generation of muscle relaxation. It incorporates NMBAs in the lipophilic structure with high affinity (molecular encapsulation) to form inclusion complexes. Thus, the receptor binding of NMBA in the steroidal construct is inhibited. The diffusion of this water-soluble complex into the plasma is by diffusion thus the concentration of NMBA in the nerve-muscle junction is reduced.[7] Sorgenfrei et al. examined the dose response relationship, safety and pharmacokinetics of sugammadex declining the neuromuscular block

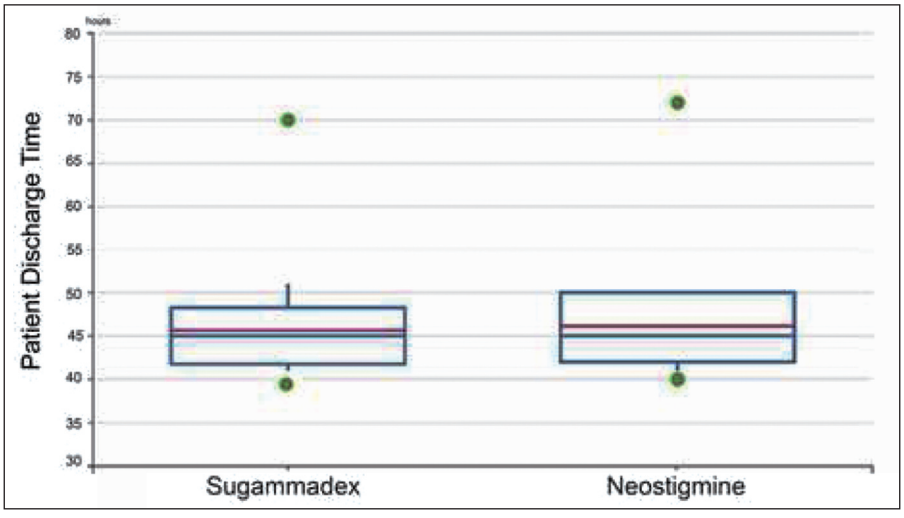

FIGURE 5: Comparison of patient discharge time between groups.

formed with rocuronium and found that the 2 mg / kg dose of sugammadex was safe.[8] In a study conducted by Shields et al., sugammadex was compared at different doses to remove rocuronium-delivered neuromuscular block. 1 mg / kg, 2 mg / kg, 4 mg / kg, 6 mg / kg of rocuronium was given at the beginning of the study and the deep block was provided for at least two hours, sugammadex were given and the times to reach the TOF ratio of 0.9 were found to be 6.4, 2.4, 2.3, 1.4, 1.2, min, respectively.[9]

We studied the effect of sugammadex which began to become a routine of anesthesia practice on postoperative gastrointestinal system dysfunction, in this study.

Gastrointestinal system dysfunction is a common postoperative complication. It is an important condition that affects the length of stay in the hospital, especially after abdominal surgery. These problems are more frequent in open major abdominal surgery and after laparoscopic abdominal operations performed with general anesthesia . The return of gastrointestinal function in the postoperative period is clinically important. Because the patient can develop pain, nausea, vomiting, respi ratory dysfunction and paralytic ileus. For this reason, many studies have been carried out regarding the acceleration of postoperative bowel movements. In a study by Patolia et al. post-cesarean diet 4-8 hours after the cesarean section return of bowel movements was significantly earlier than the group starting at the traditional time which is 12-24 hours.[10] Similarly, in a study by Ahmed comparing the effect of early and late feeding after cesarean section, the gas release time of the group that started early oral intake (2nd hour) was found to be significantly shorter than the late feeding group (24th hour).[11] Askarpour et al. studied the effects of early feeding, chewing gum and laxative use after open cholecystectomy, early feeding and gum-chewing group showed earlier onset of bowel movements other group. there were no differences between the gum-chewing group and the early-feeding group in terms of the onset of bowel movements in the study.[12]

In our study, patients who had total abdominal hysterectomy, total abdominal hysterectomy bilateral salpingo-oophorectomy and myomectomy operations were examined and compared in terms of the effect of neostigmine and sugammadex on return time of postoperative intestinal movements in reversing of rocuronium induced neuromuscular block in 60 cases. The results were evaluated in a 95% confidence interval and a significance level of <0.05.

Patients were between 18-60 year olds with a mean age of 42±5 in group S and 41±5 in group N. No statistically significant difference was found in

terms of the other demographic characteristics, the average of operation and anesthesia time.

There was no difference between the experimental and control groups in terms of the length of hospital stay in our study (p> 0.05) (Figure 5). In addition, it was determined that there was no significant relationship between gas and gaita removal times and discharge time of patients; at the hospital where the study is performed, gas removal of the patients after the surgical interventions is taken as a criterion for the discharge of the patients and discharged by the physician about 48 hours after the operation.

In our study, when the first gas release times of the patients after surgery were examined, it was found that patients in the Sugammadeks group had an average of 348±87 and patients in the control group had gas in average 355 ± 80 hours.

Akhlaghi and colleagues conducted a research on patients with cesarean section; the first gas release time was 769±312 minutes in the control group (n=200).[13] In the research that Harma and his colleagues have done on patients with cesarean section, (n=23) in the first gas release time was 960±410 minutes in control group.[14] The shorter duration of gas extraction in our groups can be attributed to earlier mobilization and oral feeding compared to the above studies. In the hospital where the work is done, patients are routinely mobilized on the 2nd hour of postoperative day and the patients are given warm water.

In our study, when patients were examined for the first defecation time after surgery, the mean defecation time of patients in the experimental group was 1015±235 minutes, and patients in the control group was 1087±244 minutes. In a survey conducted by Abd al-Maeboud and his colleagues; The first gaita removal time was 1260±280 minutes.[15] Akhlaghi et al. found the first gaita removal time was to be 1308±266 minutes.[13] Harma et al. stated that the first gaita removal time was 1460 ± 345 minutes.[14]

There are no data to compare in the literature since there is no study for the effect of sugammadex at gas extraction and defecation.

RESULT

In our study, we investigated whether sugammadex, which has managed to become a part of the anesthesia routine quickly in recent years, has any effect on the gastrointestinal system which has not been investigated previously. When our findings were examined, it was statistically shown that sugammadex had no effect on the return of postoperative intestinal motility when compared with neostigmine. More prospective studies involving major intestinal surgeries may provide more information about bowel movements since they have greater effect on intestinal motility.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Yavuz Demiraran;* ***Design:*** *Fatih Çiftçi, Tayfun Aldemir, Yavuz Demiraran;* ***Supervision/Consultancy:*** *Fatih Çiftçi, Tayfun Aldemir, Yavuz Demiraran;* ***Data Collection and/or Processing:*** *Fatih Çiftçi, Tayfun Aldemir, Yavuz Demiraran;* ***Analysis and/or Interpretation:*** *Fatih Çiftçi, Tayfun Aldemir, Yavuz Demiraran;* ***Source Search: F****atih Çiftçi, Tayfun Aldemir, Yavuz Demiraran;* ***Article Writing:*** *Fatih Çiftçi, Tayfun Aldemir, Yavuz Demiraran;* ***Critical Review:*** *Fatih Çiftçi, Tayfun Aldemir, Yavuz Demiraran;* ***Resources and Funding:*** *Fatih Çiftçi, Tayfun Aldemir, Yavuz Demiraran;* ***Ingredients:*** *Fatih Çiftçi, Tayfun Aldemir, Yavuz Demiraran.*

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