Türk Göğüs Kalp Damar Cerrahisi Dergisi 2013;21(4):966-971
doi: 10.5606/tgkdc.dergisi.2013.7641

The analgesic and hemodynamic effects of dexmedetomidine and remifentanil during chest tube removal

Göğüs tüpü çekilmesi sırasında deksmedetomidin ve remifentanilin analjezik ve hemodinamik etkileri

Funda Gümüş,[1] Sıtkı Nadir Şinikoğlu,[1] Kerem Erkalp,[1] Nalan Şanlı,[1] Berk Özkaynak,[2] Adil Polat,[2] Ayşin Alagöl[1]

[1]Department of Anesthesiology and Reanimation, Bağcılar Training and Research Hospital, İstanbul, Turkey
[2]Department of Cardiovascular Surgery, Bağcılar Training and Research Hospital, İstanbul, Turkey

Background: This study aims to investigate the effects of remifentanil and dexmedetomidine in alleviating pain during chest tube removal and these effects were compared in terms of sedation levels, pulmonary and hemodynamic responses.

Methods: The study was designed as a prospective, randomized, double-blinded study. Between February 2011 and July 2011, 41 consecutive patients (31 males, 10 females; mean age 55.7±10.3 years; range 27 to 77 years) who underwent coronary artery bypass graft (CABG) surgery were enrolled. All chest tubes were removed in postoperative 48th hour. The patients were randomized into two groups as dexmedetomidine (0.5 µg/kg) group (group D) and remifentanil (0.5 µg/kg) group (group R). The pain and sedation levels were assessed by numerical rating scale (NRS) and Ramsay scores. Blood pressures [systolic (SAP), diastolic (DAP) and mean (MAP) pressures], peripheral oxygen saturation (SpO_2), respiratory rate (RR) and heart rate (HR) were recorded before and after the agent perfusion and every two minutes after the tube was removed.

Results: The demographic characteristics of the patients in both groups were similar. The pain scores were lower during the measurements which were recorded at six and 10 minutes after chest tube removal in group D. The Ramsay scores were found to be statistically different at all measurements following perfusion, compared to the baseline measurements ($p<0.05$). Systolic arterial blood pressure, MAP and HR were significantly lower in group D and the difference was more pronounced statistically with repeated measurements.

Conclusion: Dexmedetomidine provides a comparable hemodynamic control along with better sedation and analgesia during and after chest tube removal than remifentanil. These effects can be provided safely without having cardiac or respiratory depression in post-cardiac surgery intensive care patients.

Key words: Chest tube removal; dexmedetomidine; intensive care unit.

Amaç: Bu çalışmada remifentanil ve deksmedetomidinin göğüs tüpü çekilmesi sırasında ağrı giderici etkileri incelendi ve bu etkiler sedasyon seviyeleri ile pulmoner ve hemodinamik yanıtlar açısından karşılaştırıldı.

Çalışma planı: Çalışma prospektif, randomize ve çift kör olarak tasarlandı. Çalışmaya Şubat 2011 - Temmuz 2011 tarihleri arasında koroner arter baypas greft (KABG) cerrahisi yapılan ardışık 41 hasta (31 erkek, 10 kadın; ort. yaş 55.7±10.3 yıl; dağılım 27-77 yıl) dahil edildi. Tüm göğüs tüpleri ameliyat sonrası 48. saatte çekildi. Hastalar deksmedetomidin (0.5 µg/kg) (grup D) ve remifentanil (0.5 µg/kg) (grup R) olmak üzere rastgele iki gruba ayrıldı. Ağrı ve sedasyon seviyeleri numerik dereceleme skalası (NRS) ve Ramsay skorları ile değerlendirildi. Kan basınçları [sistolik (SAB), diyastolik (DAB) ve ortalama (OAB)], periferik oksijen satürasyonları (SpO_2), solunum hızları (SH) ve kalp hızları (KH) ilaç perfüzyonu öncesinde, sonrasında ve tüp çekildikten sonra ikişer dakika ara ile kaydedildi.

Bulgular: İki gruptaki hastaların demografik özellikleri benzerdi. Grup D'de ağrı skorları tüp çekildikten sonra altı ve 10. dakikalarda kaydedilen ölçümlerinde daha düşüktü. Başlangıç ölçümleri ile karşılaştırıldığında, Ramsay skorları perfüzyon sonrası tüm ölçümlerde anlamlı olarak farklı bulundu ($p<0.05$). Sistolik arteriyel kan basıncı, OAB ve KH ölçümleri grup D'de daha düşük olup tekrarlayan ölçümlerde saptanan farklılık istatistiksel olarak daha anlamlı idi.

Sonuç: Göğüs tüpü çekilmesi sırasında ve sonrasında deksmedetomidin, remifentanile kıyasla, daha iyi sedasyon ve analjezinin yanı sıra, benzer hemodinamik kontrol sağlar. Bu etkiler, kardiyak cerrahi sonrası yoğun bakım hastalarında kardiyak veya solunum depresyonu olmadan güvenle sağlanabilir.

Anahtar sözcükler: Göğüs tüpü çekilmesi; deksmedetomidin; yoğun bakım ünitesi.

Available online at
www.tgkdc.dergisi.org
doi: 10.5606/tgkdc.dergisi.2013.7641
QR (Quick Response) Code

Received: September 03, 2012 *Accepted:* February 02, 2013

Correspondence: Funda Gümüş, M.D. Bağcılar Eğitim ve Araştırma Hastanesi, Anesteziyoloji ve Reanimasyon Kliniği, 34200 Bağcılar, İstanbul, Turkey.
Tel: +90 212 - 440 40 00 e-mail: fgumus@hotmail.com

Chest tubes are routinely used after cardiac surgery in order to facilitate fluid and air drainage postoperatively. In more conservative practice, the tubes are removed on the second or third day after surgery as the postoperative drainage ceases and the lungs are fully expanded.[1] Unfortunately, patients frequently have pain associated with chest tube removal. Several pharmalogical [non-steroidal anti-inflammatory drugs (NSAIDS), morphine, fentanyl, propofol, etc.)[2-6] or non-pharmalogical (deep breathing relaxation exercises)][7] methods have been recommended to alleviate the pain caused by this procedure.

Remifentanil is a potent synthetic μ-opioid receptor agonist with a rapid onset and short duration of action due to its metabolism by nonspecific esterases.[8] It is widely used for the sedation of intensive care patients. Dexmedetomidine is a highly selective alpha-2 (α-2) adrenergic agonist that has recently been gaining popularity. The primary aim of this study was to compare the efficacy of remifentanil and dexmedetomidine for alleviating pain both during and after chest tube removal. The secondary aims were to evaluate tolerability in terms of sedation, respiratory rate, oxygen saturation (OS), heart rate, and arterial pressure.

PATIENTS AND METHODS

The institutional ethics committee approved the study, and written consent was obtained from each patient for their participation. The study was conducted in a prospective, randomized, double-blinded fashion, and 50 patients who underwent elective isolated coronary bypass surgery were enrolled. In addition, all of the patients were informed about the chest tube removal procedure preoperatively. Patients were excluded if they lacked the ability to understand and speak the Turkish language, had an ejection fraction (EF) of <40%, or had left bundle branch block , hepatic, renal, or pulmonary failure. A neurological disorder, chronic opioid usage, allergies to opioids or paracetamol, a prolonged need for mechanical ventilation, or the need for vasoactive drug support. In addition, patients under the age of 30 or over the age of 90 were also not included.

All of the patients were operated via a median sternotomy. The left internal thoracic artery (LITA) was harvested from each participant, and the left pleurae were opened. Furthermore, the patients were operated on using cardiopulmonary bypass (CPB). Two chest tubes were inserted, and a 36F silicone mediastinal tube (Bıçakcılar, İstanbul, Turkey) was placed at the midline 2-3 cm inferior to the sternotomy incision. A 32F silicone left thoracic tube (Bıçakcılar, İstanbul, Turkey) was also placed at the anterior axillary line through the fifth intercostal space. All of the tubes were fixed with 2/0 silk sutures and removed at the postoperative 48th hour. The patients were randomized into two groups by a closed envelope method. In group D, dexmedetomidine (Precedex™ 200 μg vial, Hospira Inc., Lake Forest, IL, USA) was administered at a dose of 0.5 μg/kg in 100 mL saline solution for 10 minutes with a perfusion pump. One vial was used for each patient. In group R, remifentanil (Ultiva 1 mg vial, GlaxoSmithKline, Brentford, Middlesex, UK) was also administered at the same dosage. Both drugs were administered via the peripheral venous route, and the venous line was flushed with 10 mL saline solution after the perfusion was finished. All of the patients had nasal oxygen delivered at 2 L/minute, and they were coached regarding what to expect regarding the levels of pain before and after the perfusions. In order to compare the efficacy of the two drugs, the pain levels were assessed using a numerical rating scale (NRS) that ranged from zero to 10 with 0 representing no pain and 10 unbearable pain.[9] Additionally, the Ramsay sedation scale (RSS) was used to assess the sedation levels of the patients as follows: 1= anxious and agitated, restless, or both (1 point), 2= cooperative, oriented, and tranquil (2 points), 3= responds to command only (3 points), 4= brisk response (4 points), 5= sluggish response (5 points) and 6= no response (6 points)].[10] The following parameters were also noted: arterial pressure measurements [systolic (SAP), diastolic (DAP) and mean (MAP)], respiratory rate (RR), peripheral oxygen saturation (SpO_2), and heart rate (HR). These measurements were made at the following time points: T_1: before perfusion of the drugs; T_2: at the end of the perfusion of the drugs; T_3: after the first chest tube removal; T_4: after the second chest tube removal; T_5: the second minute after chest tube removal; T_6: the fourth minute after chest tube removal; T_7: the sixth minute after chest tube removal; T_8: the eighth minute after chest tube removal; and T_9: the 10th minute after chest tube removal. To ensure that the patients benefited from conventional analgesia, all received 75 mg diclofenac sodium (Diclomec/ampoule, Abdi İbrahim İlaç Sanayi ve Tic. A.Ş, İstanbul, Turkey) intramuscularly within the last 24 hours. None of them received any additional analgesia in the two hours prior to the chest drain removal. A separate registrar who was blinded to the group of patients recorded all of the parameters.

The data was collected prospectively in a database. The continuous data was compared using

an independent t-test, and a chi-square or Fisher's exact test was employed to compare the discreet data where appropriate. The pain levels and sedation scores were compared with the Mann-Whitney U test for the measurements at the same time points. The cost of the drugs used was also compared with the Mann Whitney U test. In addition, the power of the study was calculated prospectively by accepting a median NRS pain score reduction of 2 cm as being a clinically meaningful reduction in pain for this procedure. The previous literature[2,4] that focused on patients with chest drains in situ indicated that the standard deviation (SD) for the visual analog scale (VAS) pain scores on chest tube removal was approximately 2 cm. Therefore, taking a type 1 error of 0.05 and a type 2 error of 0.15, each group needed to have 18 patients to detect this level of difference with 85% power.

RESULTS

Originally, 50 patients were enrolled in the study, but nine of them were excluded (five from group D and four from group R). Two of these were not included because of prolonged ventilator support, six because of the need for vasoactive drugs, one because of renal failure. The demographic characteristics of the two groups were similar. In group R, 14 patients were male (70.0%) and six were female (30.0%) while in group D, 17 patients were male (81.0%) and four were female (19.0). The difference between the groups was not statistically different (p=0.484). The average ages in group R were 55.0±12.9 (range, 30-77); whereas they were slightly older for group D at 56.4±7.4 (range, 41-70) (p=0.664). Furthermore, the body mass indices (BMIs) were 25.5±3.2 for group R (range, 20-30) and 26.5±2. for group D (range, 41-70), which was statistically insignificant (p=0.250).

The comparisons of pain and sedation scores are summarized in Table 1. The target pain reduction was achieved in all of the patients. The pain scores were significantly lower in group D at the T_7 (p=0.033) and T_9 (p=0.033) time points. The sedation scores were higher in group D at all of the time points, but the median values were similar, and the differences became more pronounced with repeated measurements.

The hemodynamic and respiratory parameters are summarized in Tables 2 and 3, respectively. The systolic and mean blood pressures were significantly lower in group D, and the differences became more pronounced with repeated measurements. The average heart rates were also significantly lower in group D in all of the measurements. Although it was not clinically significant, the average OS levels were significantly higher in group D after perfusion (T_2) and after the removal of each drain (T_3 and T_4) (Table 3). However, when we compared the respiratory rates, no statistical significance was found, and none of the patients had respiratory depression (Table 3). The average cost of the drugs was 29.9 Turkish liras (TL) for remifentanil and 40.5 TL for dexmedetomidine, and the difference in cost was statistically significant (p=0.0001).

DISCUSSION

The most important finding in this study was the achievement of better sedation and analgesia levels with remifentanil and dexmedetomide, but comparable control of hemodynamic parameters was achieved only with the latter drug, which could lead to more favorable outcomes in patients that might have serious hemodynamic disabilities in such a clinical setting.

Chest tube removal, which is routinely performed after cardiac surgery, is a painful procedure. Gift et al.[11] reported that a burning or pulling sensation were common after the procedure, but pain was the

Table 1. Median values of the analgesia and sedation scores

Time	NRS	*p*	Ramsay	*p*
T_1				
Group D	3	0.276	2	1.000
Group R	3		2	
T_2				
Group D	0	0.281	2	0.001
Group R	0		2	
T_3				
Group D	0	0.078	2	0.021
Group R	1		2	
T_4				
Group D	2	0.524	2	0.011
Group R	2		2	
T_5				
Group D	0	0.215	2	0.021
Group R	0		2	
T_6				
Group D	0	0.069	3	0.0001
Group R	0		2	
T_7				
Group D	0	0.033	3	0.0001
Group R	2		2	
T_8				
Group D	0	0.069	3	0.0001
Group R	0		2	
T_9				
Group D	0	0.033	3	0.0001
Group R	2		2	

NRS: Numerical rating scale.

Table 2. Hemodynamic parameters

Group	SAP		DAP		MAP		HR	
	Mean±SD	*p*	Mean±SD	*p*	Mean±SD	*p*	Mean±SD	*p*
T_1								
Group D	131.2±17.2	0.543	71.1±11.6	0.493	91.8±10.1	0.858	101.5±9.0	**0.021**
Group R	128.0±16.1		73.5±10.1		91.2±11.7		108.7±10.0	
T_2								
Group D	116.7±16.8	0.536	66.5±10.7	0.401	82.9±11.6	0.214	96.6±9.3	**0.039**
Group R	119.8±14.1		69.3±10.2		87.2±9.8		102.0±6.7	
T_3								
Group D	109.8±18.5	0.058	63.5±11.8	**0.041**	76.4±12.2	**0.008**	94.0±11.6	**0.032**
Group R	120.0±14.6		71.1±11.1		86.3±10.2		101.2±8.7	
T_4								
Group D	112.2±14.8	0.072	65.5±11.6	0.195	79.3±12.6	**0.040**	94.1±11.4	**0.018**
Group R	120.9±15.2		70.3±11.5		87.1±10.9		101.9±8.5	
T_5								
Group D	109.7±16.0	**0.007**	62.0±11.7	0.067	78.8±13.1	**0.046**	93.6±9.3	**0.011**
Group R	122.5±12.6		68.9±11.9		86.4±10.1		100.8±7.9	
T_6								
Group D	102.1±14.4	**0.002**	60.1±6.4	**0.003**	72.7±8.7	**0.0001**	92.0±9.0	**0.009**
Group R	116.3±13.5		68.4±10.0		83.8±9.7		99.6±8.7	
T_7								
Group D	103.1±17.5	**0.002**	62.1±8.7	0.103	76.8±11.5	**0.037**	91.2±9.8	**0.005**
Group R	119.2±12.0		66.6±8.4		83.8±8.9		99.5±8.1	
T_8								
Group D	105.1±13.3	**0.003**	64.4±9.0	.0356	75.0±11.1	**0.046**	91.2±8.5	**0.006**
Group R	118.1±13.3		67.5±11.6		82.7±11.6		99.2±8.9	
T_9								
Group D	102.3±11.3	**0.0001**	61.2±8.1	0.143	74.1±10.2	**0.021**	91.3±8.5	**0.009**
Group R	118.2±14.1		65.8±11.2		82.3±11.4		98.7±8.7	

SAP: Systolic arterial pressure; DAP: Diastolic arterial pressure; MAP: Mean arterial pressure; HR: Heart rate; SD: Standard deviation.

most frequent complaint. Opioids have been used as analgesics in these patients, but the results have not always been satisfactory.[12] Considering the drawbacks of opioids, different approaches have been tried by other authors.[2-4,6,7] Remifentanil is one of the most widely used agents for this purpose, and it has been recommended for its efficacy and short duration of action.[2,8] Therefore, we used remifentanil as our positive control group in order to evaluate the effects of dexmedetomidine, a well known agent used for intensive care sedation.

One of the most striking features of dexmedetomidine is the attenuating need for opioid analgesia.[13] Herr et al.[14] also reported that dexmedetomidine had similar effects on the various blood pressures, and it was accompanied by a decreased need for morphine. In contrast to their study, we used lower doses of dexmedetomidine and aimed for relatively lower sedation scores since the patients in our study had already been extubated. In spite of this, the sedation scores were higher in group D. Doğan et al.[15] reported that dexmedetomidine provided a rapid onset of sedation in monitored anesthesia patients, thus lending credence to the positive effects of this drug.

Along with the analgesic and sedative effects, dexmedetomidine also favorably affected the hemodynamics, which subsequently caused a decrease in the rate of myocardial ischemia (MI).[13,16] Table 2 outlines the similar positive hemodynamic effects in our study, which were more prominent with the systolic and mean blood pressures and HRs. The hemodynamic benefits of this drug have been attributed to the decrease that occurs in the plasma catecholamine levels through the central sympathetic system.[17] In addition, we utilized dexmedetomidine in order to have better control of the hypertension in the patients without the occurrence of hypotensive periods. Günay et al.[18] also showed that dexmedetomidine provided better hemodynamic stability compared with esmolol during intubation.

Table 3. Respiratory parameters

Group	SpO_2		RR	
	Mean±SD	p	Mean±SD	p
T_1				
Group D	97.5±2.0*	0.118	26±7	0.062
Group R	96.6±2.6*		22±4	
T_2				
Group D	97.0±1.9*	0.029	23±6	0.058
Group R	96.4±2.7*		20±3	
T_3				
Group D	97.0±1.3*	0.013	24±5	0.194
Group R	96.6±2.4*		20±4	
T_4				
Group D	97.1±1.4*	0.007	25±5	0.396
Group R	96.7±2.6*		21±4	
T_5				
Group D	97.2±1.3*	0.071	24±6	0.267
Group R	96.9±2.2*		21±4	
T_6				
Group D	97.3±1.4*	0.146	24±6	0.294
Group R	97.0±2.2*		21±4	
T_7				
Group D	97.3±1.4*	0.192	24±5	0.052
Group R	97.1±2.1*		21±3	
T_8				
Group D	97.4±1.4*	0.051	24±5	0.023
Group R	97.2±2.5*		20±3	
T_9				
Group D	97.0±1.4*	0.254	24±5	0.125
Group R	97.0±2.0*		21±3	

SpO_2: Oxygen saturation; RR: Respiratory rate; SD: Standard deviation; * Percent.

Venn et al.[19] reported that dexmedetomidine sedation had a positive effect on the respiratory system in post-cardiac surgical patients. In our study, the respiratory parameters were analyzed according their relationship with patient discomfort, and the most prominent differences were noted after the perfusion and after the removal of each drain. These outcomes may be explained by the comfort provided by the analgesic and the sedative effects of dexmedetomidine. None of the patients had OS levels of lower than 90%. In fact, both remifentanil and dexmedetomidine were safe in terms of respiratory depression, which was defined as having a respiratory rate of less than 8 or 10 breaths per minute.[20] However, it could be argued that the use of remifentanil is almost always associated with some level of respiratory depression. In order to avoid such a complication, we tried to use the lowest dose possible. Although there were significant differences between the groups, the target NRS and RSS scores were achieved in all patients. The differences in the repeated measurements, especially after T_6, may be explained by the shorter half-life of remifentanil compared with dexmedetomidine. Similarly, Demirhan et al.[21] showed that dexmedetomidine provided sedation and anesthesia after thoracotomies without respiratory depression while also decreasing the need for opioid analgesia.

We preferred to administer the drugs via intravenous perfusion. Although bolus usage has been reported,[2] administering the loading dose with a perfusion pump is preferred, especially for dexmedetomidine.[22] In addition, a fixed dose regimen was analyzed in this study. Other authors reported that they titrated the dose according to the RSS scores.[2,23] We saw no need for this since the procedure was fast, and our results confirmed that adequate analgesia and sedation took place. Another potential drawback may have been the small number of patients in our study. Barnard et al.[24] analyzed seven important studies in this field and found that almost all of them had small sample sizes. Thus, it appears that most studies in this field are underpowered. Some studies on this topic have included groups which were not uniform in order to receive data related to different treatment regimens. However, as previously explained, our analysis was designed to achieve 85% power of analysis; therefore, the groups were uniformly distributed. The number of excluded patients also did not adversely affect our analysis. Another potential objection might concern the evaluation of the arterial blood gas analysis in these patients since this could have contributed to the results of the respiratory analysis of the groups. However, we did not want to measure the blood gases at the indicated time durations in order to be less invasive.

Nevertheless, several drawbacks were apparent in this study. First, the study population was highly selective with relatively large numbers of exclusion criteria, but these criteria were essential in order to avoid complications and to assess the analgesia and sedation effectively. In addition, the timing of the chest tube removal could be argued. Many centers prefer to remove the chest tubes within 24 hours. As a training center, our surgical team prefers to remove the drains on the second postoperative day, and there were no complications related to the time of chest tube removal

in any of our patients. Another possible drawback was that dexmedetomidine is significantly more expensive than remifentanil. As of October 2012, the cost of remifentanil for a single patient was 29.9 TL, whereas it was 40.5 TL for dexmedetomidine. This fact may constitute a major handicap that will prohibit or limit the use of dexmedetomidine.

Conclusions

We believe that dexmedetomidine is similar to remifentanil in that it provides comparable hemodynamic control with added sedation and analgesia during and after chest tube removal. In addition, dexmedetomidine can be administered safely without cardiac or respiratory depression in post-cardiac surgery ICU patients.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding

The authors received no financial support for the research and/or authorship of this article.

REFERENCES

1. Mueller XM, Tinguely F, Tevaearai HT, Ravussin P, Stumpe F, von Segesser LK. Impact of duration of chest tube drainage on pain after cardiac surgery. Eur J Cardiothorac Surg 2000;18:570-4.
2. Casey E, Lane A, Kuriakose D, McGeary S, Hayes N, Phelan D, et al. Bolus remifentanil for chest drain removal in ICU: a randomized double-blind comparison of three modes of analgesia in post-cardiac surgical patients. Intensive Care Med 2010;36:1380-5.
3. Singh M, Gopinath R. Topical analgesia for chest tube removal in cardiac patients. J Cardiothorac Vasc Anesth 2005;19:719-22.
4. Akrofi M, Miller S, Colfar S, Corry PR, Fabri BM, Pullan MD, et al. A randomized comparison of three methods of analgesia for chest drain removal in postcardiac surgical patients. Anesth Analg 2005;100:205-9.
5. Joshi VS, Chauhan S, Kiran U, Bisoi AK, Kapoor PM. Comparison of analgesic efficacy of fentanyl and sufentanil for chest tube removal after cardiac surgery. Ann Card Anaesth 2007;10:42-5.
6. McMurray TJ, Bhanumurthy S, Groogan F. Low dose propofol for chest tube removal. Anaesthesia 1995;50:566.
7. Friesner SA, Curry DM, Moddeman GR. Comparison of two pain-management strategies during chest tube removal: relaxation exercise with opioids and opioids alone. Heart Lung 2006;35:269-76.
8. Glass PS, Gan TJ, Howell S. A review of the pharmacokinetics and pharmacodynamics of remifentanil. Anesth Analg 1999;89:S7-14.
9. Chapman CR, Syrjala KL. Measurement of pain. In: Bonica JJ, editor. The management of pain. Vol. 1, 2nd ed. Philadelphia: Lea & Febiger; 1991. p. 580-92.
10. Ramsay MA, Savege TM, Simpson BR, Goodwin R. Controlled sedation with alphaxalone-alphadolone. Br Med J 1974;2:656-9.
11. Gift AG, Bolgiano CS, Cunningham J. Sensations during chest tube removal. Heart Lung 1991;20:131-7.
12. Carson MM, Barton DM, Morrison CC, Tribble CG. Managing pain during mediastinal chest tube removal. Heart Lung 1994;23:500-5.
13. Triltsch AE, Welte M, von Homeyer P, Grosse J, Genähr A, Moshirzadeh M, et al. Bispectral index-guided sedation with dexmedetomidine in intensive care: a prospective, randomized, double blind, placebo-controlled phase II study. Crit Care Med 2002;30:1007-14.
14. Herr DL, Sum-Ping ST, England M. ICU sedation after coronary artery bypass graft surgery: dexmedetomidine-based versus propofol-based sedation regimens. J Cardiothorac Vasc Anesth 2003;17:576-84.
15. Doğan Ö, Ünver S, Tunçel Yİ, Keleş S, Süner ZC. Monitörize anestezi bakımında deksmedetomidin ile midazolam/remifentanil kombinasyonunun karşılaştırılması. Türk Anest Rean Der Dergisi 2011; 39:292-301.
16. Venn RM, Grounds RM. Comparison between dexmedetomidine and propofol for sedation in the intensive care unit: patient and clinician perceptions. Br J Anaesth 2001;87:684-90.
17. Jalonen J, Hynynen M, Kuitunen A, Heikkilä H, Perttilä J, Salmenperä M, et al. Dexmedetomidine as an anesthetic adjunct in coronary artery bypass grafting. Anesthesiology 1997;86:331-45.
18. Günay H, Moğol EB, Kaya FN, Türker G, Yavaşcaoğlu B, Ahun F ve ark. Deksmedetomidin ve esmololün derlenme döneminde oluşan artmış hemodinamik yanıt tedavisindeki etkinliklerinin karşılaştırılması. J Clin Exp Invest 2012;3:53-60.
19. Venn RM, Hell J, Grounds RM. Respiratory effects of dexmedetomidine in the surgical patient requiring intensive care. Crit Care 2000;4:302-8.
20. Cashman JN, Dolin SJ. Respiratory and haemodynamic effects of acute postoperative pain management: evidence from published data. Br J Anaesth 2004;93:212-23.
21. Demirhan A, Gül R, Ganidağlı S, Koruk S, Mızrak A, Şanlı M, ve ark. Torakotomi sonrası ağrı tedavisinde tramadol ve deksmedetomidinin kombinasyonu. GKDA Derg 2011;17:34-41.
22. Martin E, Ramsay G, Mantz J, Sum-Ping ST. The role of the alpha2-adrenoceptor agonist dexmedetomidine in postsurgical sedation in the intensive care unit. J Intensive Care Med 2003;18:29-41.
23. Shehabi Y, Ruettimann U, Adamson H, Innes R, Ickeringill M. Dexmedetomidine infusion for more than 24 hours in critically ill patients: sedative and cardiovascular effects. Intensive Care Med 2004;30:2188-96.
24. Barnard J, Thompson J, Dunning J. Can any intervention effectively reduce the pain associated with chest drain removal? Interact Cardiovasc Thorac Surg 2004;3:229-32.