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Full Length Research Paper

Sedation with Dexmedetomidine or Propofol for Carotid Endarterectomy, a Randomized Clinical Trial

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Sedation of the patient during operation under regional anesthesia improves the quality of anesthesia and is sometimes mandatory. Many sedative agents like benzodiazepines, narcotic analgesics, propofol, dexmedetomidine have been used for sedation. We aimed to compare sedative and hemodynamic effects of dexmedetomidine and propofol given for sedation to patients undergoing operation under regional anesthesia. After the approval of Local Ethics Committee 28 patients of ASA 1-3 physical status, aged 50-80 years old, scheduled for carotid endarterectomy operation, were enrolled for the study. Patients were randomly allocated into two groups, each containing 14 patients. 0.5 mg/kg/h propofol infusion in the first group (Group P) and 0.2 µg/kg/h dexmedetomidine infusion in the second group (Group D) was given. Systolic, mean, diastolic arterial pressures (SAP, MAP, DAP), heart rates (HR) and Ramsey Sedation Scores (RSS) of the patients were recorded. MAP, DAP and SpO₂ values were significantly different between the groups, but this had no clinical significance. RSS scores achieved targeted values, but two groups revealed no significant difference. Both propofol and dexmedetomidine can be safely used for sedation in patients undergoing carotid endarterectomy under regional anesthesia, if the appropriate monitoring conditions are provided.

Keywords: Dexmedetomidine, propofol, carotid endarterectomy, sedation.

INTRODUCTION

Having the advantages such as continued spontaneous breathing, being conscious, preserved swallowing and coughing reflexes, low analgesic requirement after operation, shorter hospital staying and low costs, regional anesthesia begins to replace general anesthesia in many types of operations (Krugliak et al., 2000; Houltram and Scanlan, 2004). The main disadvantage of this method is its relevance to patient compliance and management,

dependence of patient wish, requirement of experienced provider. In addition, hemodynamic and psychological effects of surgery and operation room stress on patient due to the patient's consciousness are also disadvantages (Reves et al., 2000).

Feeling worry during regional anesthesia due to operation stress cause anxiety in patients. This circumstance on the one hand causes unwanted hemodynamic changes and on the other hand decreases the efficacy of regional anesthesia leading to discomfort for surgeon and patient during operation. In order to achieve a successful regional anesthesia; just ceasing pain is not enough, also it is necessary to suppress

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endocrine response meanwhile by administering appropriate sedation to the patient (Park and Watkins, 1991).

Sedative agents should have properties such as rapid onset of action, easy dose titration and predicted clinical response (Martin et al., 2003). Ideal sedation consists of properties of patient's conscious response with opening eyes to verbal stimuli, less affected hemodynamics and fast recovery (Çelik et al., 1993; Güldiken et al., 1992). Many agents like benzodiazepines, narcotic analgesics, nitrous oxide, propofol, dexmedetomidine have been used for sedation.

Although dexmedetomidine, a central acting α_2 -adrenoceptor, has been used for sedation in intensive care units for many years, frequency of its intraoperative usage has begun to increase in recent years (Turan et al., 2004). It has been shown that, dexmedetomidine dose-dependently decreases motor activity, suppresses reflexes, increases sedation scores and has analgesic effect (Pertovaara et al., 1990).

Propofol, which is usually used for general anesthesia induction and maintenance, is a potent sedative agent, which has a widely acting central nervous system (CNS) depressant effecting via GABA receptors (Smith et al., 1994), and it is very lipophilic and has a wide distribution volume. These properties make it to pass and be eliminated from CNS rapidly. In spite of these pharmacological properties, its onset and ceasing of action is rapid. Generally it has been used in intensive care; recently it has begun to be used frequently for sedation during regional anesthesia.

In this study, we compared sedative and hemodynamic effects of dexmedetomidine and propofol in patients undergoing carotid endarterectomy under regional anesthesia.

MATERIALS AND METHODS

After the approval of Local Ethics Committee of our hospital 28 patients of ASA 1-3 physical status, aged 50-80 years old, scheduled for carotid endarterectomy operation, were enrolled for the study. Patients with bleeding diathesis, taking anti-coagulant medication, hypotensive patients, those having history of alcoholism and drug addiction, psychosis, poor motivation and social status, allergy to local anesthetics and egg, taking α_2 -receptor antagonist or agonist medication and having advanced liver and renal failure were excluded from the study. All patients were visited one day before the surgery to give information about cervical blockade and sedation and to take informed written consents of each patient. None of the patients were premedicated before the operation.

Patients included in the study were admitted to the operation room 30 minutes before operation. Routine monitorization consisted of non-invasive blood pressure

(NIBP), electrocardiogram (ECG) at DII and V5 derivations, peripheral oxygen saturation (SpO_2) by finger probe. After vascular access was provided by a 16 G cannula on forearm, 10-15 mg/kg 0.9% NaCl infusion was initiated. Another 20 G cannula was placed on the other arm of the patient for vascular access to administer sedative agent. Invasive arterial blood pressure (IBP) was also monitorized via an 18-20 G cannula placed into radial or brachial artery. The basal heart rate (HR), diastolic and systolic arterial pressures (DAP and SAP), SpO_2 values and Ramsey Sedation Scores (RSS) were recorded.

After basal values were recorded, patients were randomly allocated into two groups, each containing 14 patients. Randomization was done by closed envelope method. 0.5 mg/kg/h propofol infusion in first group (Group P) and 0.2 μ g/kg/h dexmedetomidine infusion in second group (Group D) was initiated. Afterwards, patients' head was turned to opposite direction of the operation site in mild extension position. After disinfecting with 10% povidone iodine, blockade site was clothed with sterile clothes. When the injection sites were identified, in order to make C_2 blockade, a 25 gauge needle was placed vertically to the skin and pushed forward until touching C_2 vertebrae's transverse process. At this point, needle was pulled back 1 mm and after testing with negative blood aspiration, 7 mL of 0.5 % bupivacaine was injected. C_3 and C_4 cervical roots were also blocked by the same procedure. After deep cervical blockade, 10 mL of 2% prilocaine was administered to the operation site to provide local anesthesia. Surgery was permitted to start after appropriate sensorial blockade was achieved in the patient. Sedative infusion was discontinued at the end of the operation.

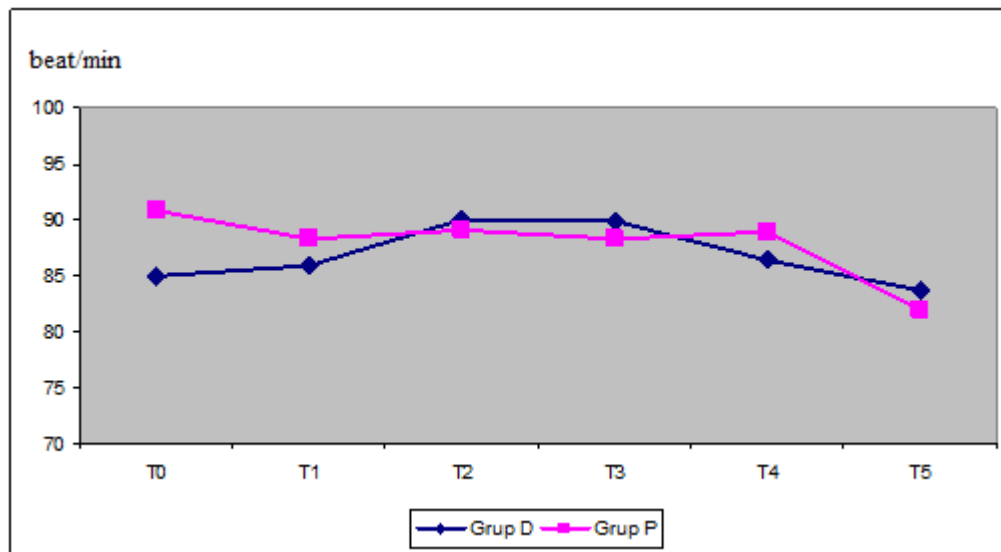
HR, SAP, DAP, mean arterial pressure (MAP), RSS, SpO_2 values of the patients were recorded before blockade (T_0), at 20th minute of blockade (T_1), before carotid artery cross-clamping (T_2), after cross-clamping (T_3), at the end of the operation (T_4) and at the postoperative 1st hour (T_5).

Patients were followed up for potential complications, systemic toxic reactions, nausea, vomiting, hypotension, bradycardia, urine retention, headache, shivering and neurological sequelae. Hypotension was accepted as; decrease in SAP more than 25% of basal value or SAP value less than 90 mmHg. Patients having hypotension were treated with intravenous (iv) fluid and 5 mg ephedrine. Decrease in HR values more than 20% of basal value and severe bradycardia (<50 beat/min) were treated with 0.5-1 mg iv atropine. SpO_2 <90% was accepted as desaturation and patients with desaturation were treated with 4 L/min oxygen given via face mask. Patients had nausea and vomiting, were treated with iv 10 mg metochlopramide.

After the operation was finished, patients were admitted to the intensive care unit (ICU). ECG, SpO_2 , invasive blood pressures were monitorized. Patients were

Table 1. Demographic properties

		Group D	Group P	P
Age		64,35±7,63	65,57±8,12	0,687
Gender	Female	5 (35,7%)	4 (28,6%)	1,000
	Male	9 (64,3%)	10 (71,4%)	

**Figure 1.** Heart rate alteration

discharged to the ward after a 24-hour follow up period, if any complication had not occurred.

NCSS (Number Cruncher Statistical System) 2007 & PASS 2008 Statistical Software (Utah, USA) were used to analyze study data. While assessing the study data; as well as using identifying statistical methods (mean, standard deviation), in comparison of quantitative data Student-t test and Mann Whitney U test were used to compare normal and abnormal distribution parameters between groups, respectively. Comparing normal distribution parameters and abnormal distribution parameters in each group paired sample t-test and Wilcoxon signed rank test were used, respectively. In comparison of qualitative data Chi-Square and Fisher's Exact Chi-Square tests were used. Significance was accepted with $P < 0.05$. When we accepted $\alpha = 0.05$, $\beta = 0.2$ in power analysis, it was calculated at least 20 patients should have been included in each group. However, when time and our hospital's conditions have been taken into consideration, 14 patients for each group were included in the study.

RESULTS

This study was carried out on 28 patients aged 53-78 years, consisting of 9 (32%) women and 19 (67.8%) men. Demographic data is demonstrated at Table 1. Demographic data of the patients did not differ significantly between the groups ($P > 0.05$).

There were no significant differences between the groups regarding HR values measured at identical times, ($P > 0.05$). In in-group analysis there were no significant differences regarding HR values compared with T0 values, ($P > 0.05$), (Figure 1).

SAP values at the corresponding T0, T1, T2, T3, T4 and T5 times were not significantly different between the groups ($P > 0.05$). The in-group comparisons showed significantly lower SAP values at T4 and T5 in Group D and at T2, T3, T4 and T5 in Group P compared with T0 values in either group ($P < 0.05$), though it didn't have clinical relevance, (Figure 2).

In comparison of DAP, MAP, SpO₂ values between the groups; DAP values measured at T2 and T5 times in

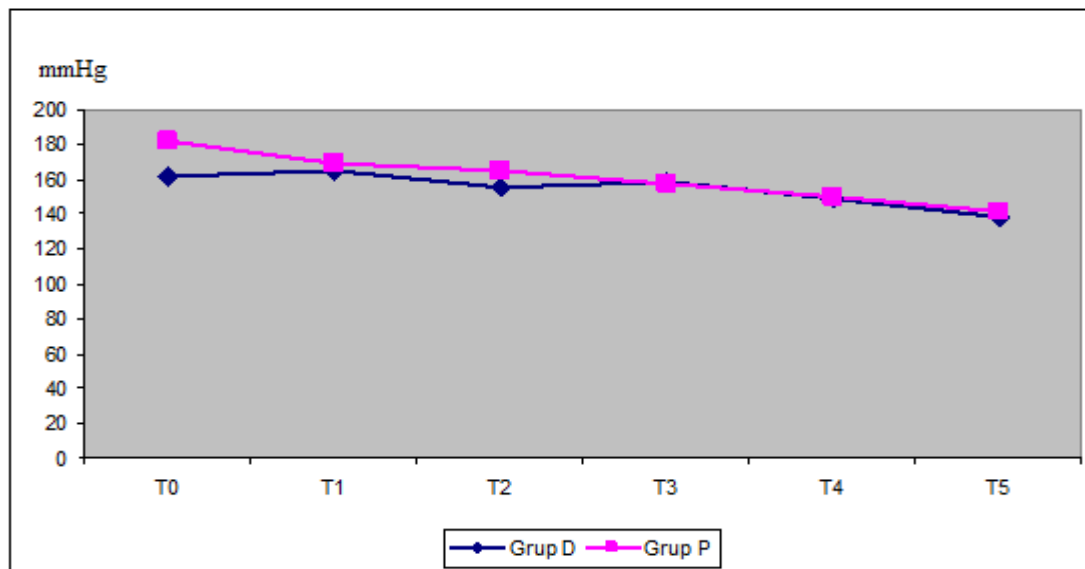


Figure 2. Systolic arterial pressure alteration

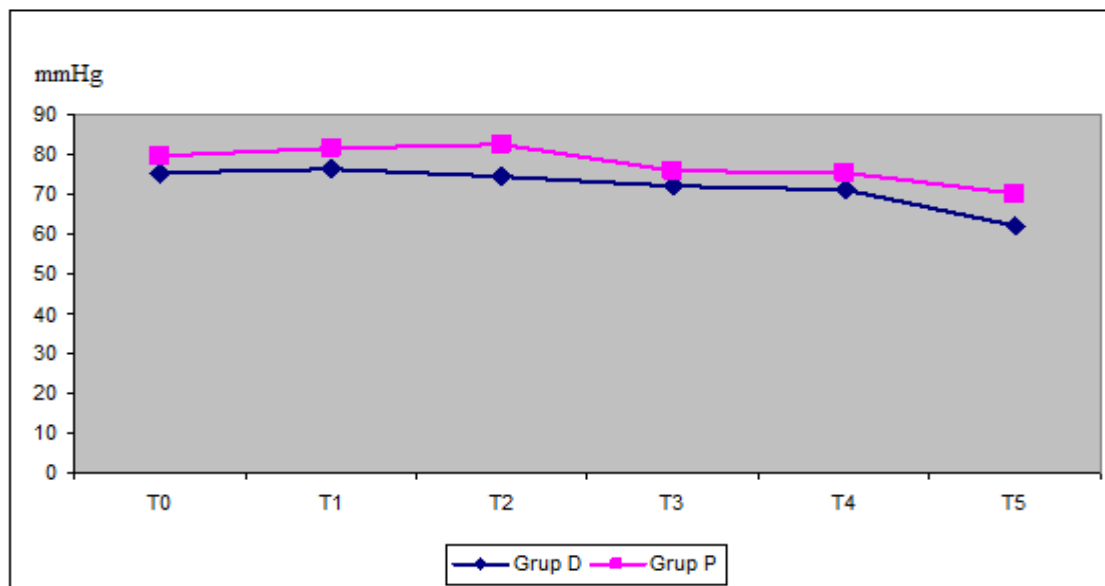


Figure 3. Diastolic arterial pressure alteration

Group P were significantly higher than corresponding values in Group D ($P < 0.05$); the MAP values at T2 and T5 times in Groups D were significantly lower than those in Group P ($P < 0.05$) and the SpO_2 values in Group D at T1 and T5 times were significantly lower than those in Group P ($P < 0.05$), whilst all of these differences had no clinical significance.

The in-group comparisons showed that, DAP values measured at T5 time in either group ($P < 0.05$); the MAP values measured at T5 time in Group D and at T3, T4, T5

times in Group P ($P < 0.05$); the SpO_2 values measured at T2, T3, T5 times in Group D and at T2, T3, T4 times in Group P ($P < 0.05$) were all significantly lower than the ones measured in T0 times of all parameters in both the groups ($P < 0.05$), however all these differences had no clinical significance, (Figure 3 and 4).

There were no significant differences in corresponding RSS values measured at T0, T1, T2, T3, T4 and T5 times between the groups ($P > 0.05$). The in-group comparisons showed that, the increase in RSS values

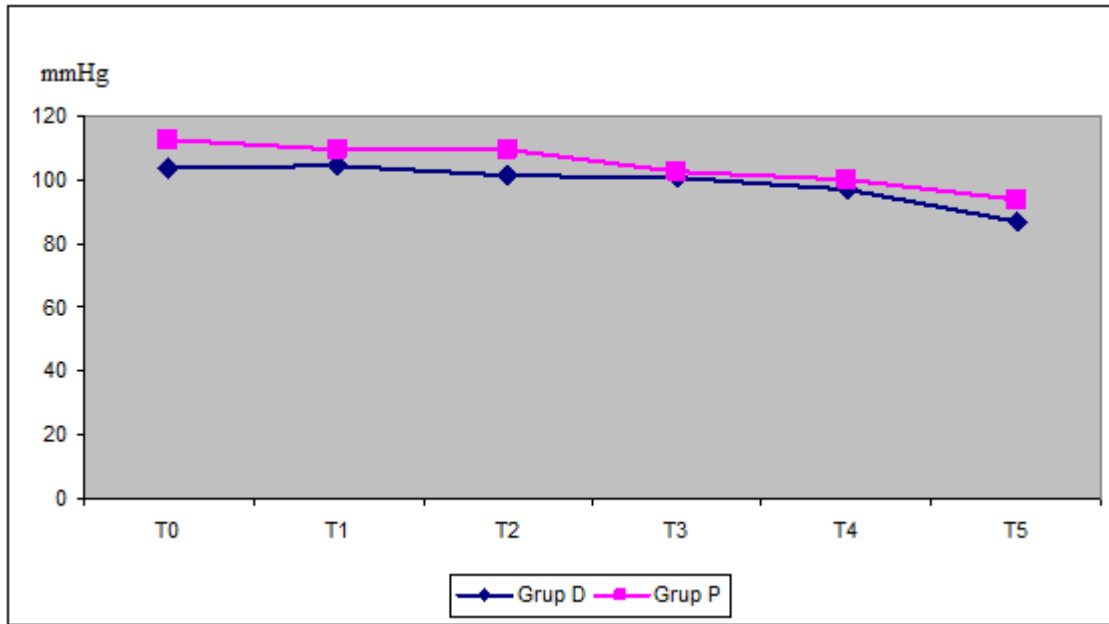


Figure 4. Mean arterial pressure alteration

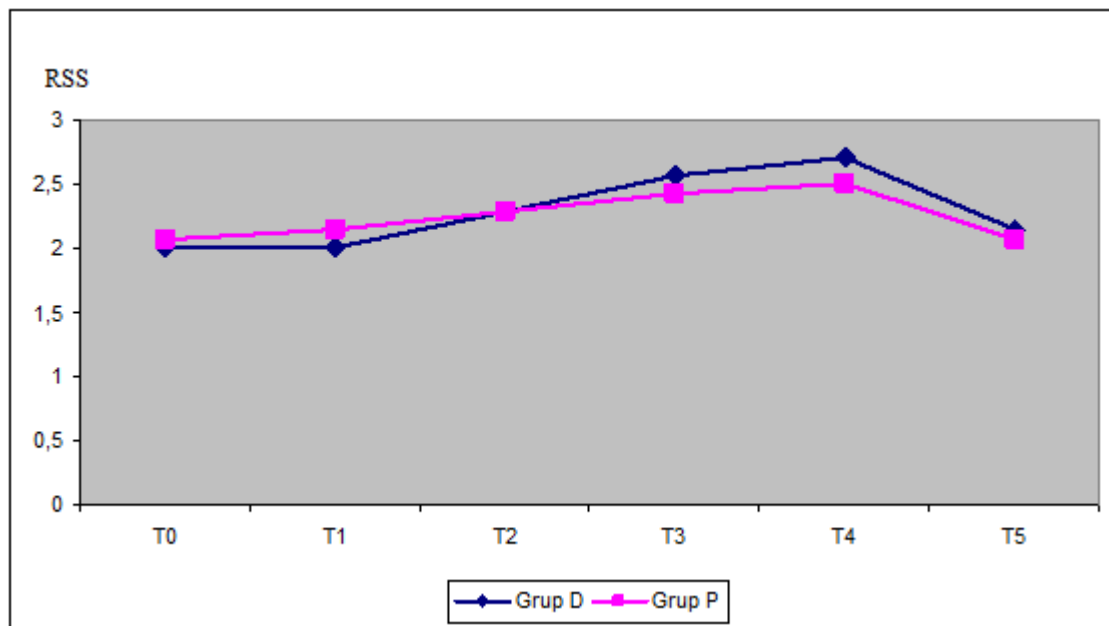


Figure 5. Ramsey Sedation Score alteration. RSS: Ramsey Sedation Score.

measured at T3 and T4 times compared to T0 time values in either group was significant, ($P < 0.01$), (Figure 5).

Four of the 28 patients included in the study had experienced hypotension and bradycardia during the operation due to vagal nerve stimulation. 3 mL of 2 % prilocaine was administered to the surgical site to prevent

vagal stimulus in these patients. Patients had hypotension and bradycardia were positioned in trendelenburg position and treated with 5-10 mg ephedrine and 0.5-1 mg atropine iv respectively. After hemodynamic parameters had come into stable levels, operation was continued on. Intraoperative facial nerve paralysis and voice hoarseness occurred due to cervical

blockade in four of the patients. Neurological deficits were disappeared at postoperative 1st day of follow up period. One of the patients complicated with postoperative aphasia, confusion and right hemiplegia, another patient become right hemiplegic. After intensive care treatment period, these patients were referred to concerned rehabilitation centers.

DISCUSSION

The main consequence of our study is that, both dexmedetomidine and propofol, administered for sedation in regional anesthesia, provide adequate increase in sedation levels. There was no superiority of any of them regarding sedation levels. Hemodynamic and respiratory parameters were altered with either agent, whereas these were not significant clinically.

Aho et al. used dexmedetomidine and diclofenac for analgesia in patients undergoing laparoscopic tubal ligation and found morphine requirement of patients as 33% and 83%, respectively (Aho et al., 1991). No patients had any additional analgesic requirement during intraoperative and early postoperative periods in our study. Superficial and deep cervical blockade would have also had significant effect on this result.

If dexmedetomidine is administered by intravenous bolus injection, it reduces heart rate and blood pressure (Reves et al., 2000). This effect is partly due to its sympatholytic activity; however it can be associated with vagal stimulation (Nelson et al., 2003; Kallio et al., 1989). Shehabi et al. administered dexmedetomidine infusion (0.2-0.7 µg/kg/h) for approximately 71.5 hours for sedation of intensive care patients and found that dexmedetomidine can be used in critical patients for effective sedation and as a backup analgesic without causing any significant changes in vital symptoms for 24 hours (Shehabi et al., 2004). Ickeringill et al. administered dexmedetomidine (0.2-0.4 µg/kg/h) in mechanically ventilated ICU patients and determined statistically significant, but clinically insignificant reduction in systolic blood pressure and heart rate in the first six hours (Ickeringill et al., 2004).

Despite many studies showing that propofol decreases heart rate, there are some studies showing that it has no effect on heart rate. Harris et al. had administered propofol at 1-3 mg/kg/h dose in critical care patients and found decrease in MAP with no changes in HR (Harris et al., 1990). Marşan et al. administered propofol and midazolam at sub-anesthetic doses to patients undergoing surgery with spinal anesthesia, found much more decrease in HR, although it was statistically insignificant (Marşan et al., 1999). Nokaigawa et al. had infused different doses of propofol in dogs and showed that 6 mg/kg/h dose of propofol decreased MAP with no changes in HR, whereas doses over 15 mg/kg/h propofol began to decrease HR (Nakaigawa et al., 1995). Ground

et al. compared 2 mg/kg/h propofol and 3 mg/kg/h thiopental administered for sedation; although the difference in sedation between groups was not significant, they stated that, propofol had more reducing effect on HR compared to thiopental (Grounds et al., 1985).

In our study the effects of dexmedetomidine and propofol on HR were minimal and the difference between the groups was not significant. Although either agent caused significant difference in SAP, DAP, MAP and HR values compared to the basal values, these differences had no clinical significance.

Dexmedetomidine doesn't cause rebound hypertension and tachycardia after rapid cessation of the infusion (Geyskes et al., 1979). Martin et al. had administered 0.2-0.7 µg/kg/h dexmedetomidine infusion following a bolus dose of 1 µg/kg in 10 minutes to postoperative patients in ICU and observed that arterial blood pressure values were remained in normal ranges without rebound effect in most of the patients (Martin et al., 2003). Venn et al. didn't observe any evidence of rebound in patients receiving dexmedetomidine longer than 24 hours (Venn et al., 2000). We haven't observed any rebound effect in any of the patients during our study.

Sakarya et al. had compared the sedative effects of propofol and midazolam and reported that, bolus injection of dexmedetomidine is not appropriate for preventing sudden hemodynamic responses (Sakarya et al., 1999). Weinbroum et al. and Roekaerts et al., have determined hypotension following bolus administration of propofol (Weinbroum et al., 1997; Roekaerts et al., 1993). We haven't observed sudden blood pressure decreases owing to not administering bolus loading dose.

Although SAP values were detected significantly different between the groups, both of the agents caused reduction in SAP. However, propofol caused more rapid decrease in SAP than dexmedetomidine. In comparison of DAP, dexmedetomidine caused significantly more decrease in DAP at the T2 and T5 times than propofol. Comparison of each group in itself showed significant decrease in DAP in either group. Regarding MAP, both of the agents decreased MAP, but dexmedetomidine caused significantly more decrease at T2 and T5 times than propofol. We suggest that, keeping arterial pressures high and treating pressure decreases with intraoperative inotropic support during carotid artery clamping is necessary to prevent these differences at T3 and T4 times.

Studies show that, dexmedetomidine has dose-dependent sedative and analgesic effects (Aantaa et al., 1990). It is established that endogenous sleep pathways has role in the sedation mechanism of dexmedetomidine (Khan et al., 1999; Nelson et al., 2003). Stimulation of α₂-adrenoceptors in locus ceruleus makes sedation via adenylate cyclase inhibition (Nelson et al., 2003). Virkkila et al. administered 1 µg/kg dexmedetomidine intramuscularly for premedication and observed mild

sedation without marked hemodynamic changes (Virkkila et al., 1993).

Having the properties like wide distribution volume, high tissue affinity, rapid clearance, and early and high quality recovery makes propofol a preferred agent, particularly in out-patient anesthesia (Ariboğan et al., 1999). Balci et al. compared dexmedetomidine and propofol in terms of sedation and reached to desired level of sedation score two times longer with dexmedetomidine. If compared with short acting propofol, the authors determined that, the effects of dexmedetomidine sustain in postoperative period and sedation scores were significantly lower in dexmedetomidine group (Balci et al., 2006). Arain et al. compared sedative effects of dexmedetomidine and propofol and reported more rapidly achieved sedation with propofol (Arain and, Ebert, 2002).

Ramsey Sedation Score was used to compare sedation levels of patients in our study. We had appropriate levels of sedation with either agent and we didn't observe significant difference between the two agents regarding RSS.

One of the most important characteristic of sedative agents is respiratory depression. Therefore the patients should be monitored closely; if required, respiratory support could be given, especially in deeply sedated patients. The most important parameters showing respiratory depression are; respiratory rate and peripheral oxygen saturation. Many studies have been carried out on this subject showed that, sedative agents cause respiratory depression. Yamakage et al. compared propofol and midazolam for their sedative properties and reported decreased tidal volumes and pO₂ values after propofol infusion (Yamakage et al., 1999). Marşan et al. compared propofol and midazolam for sedation and observed significant reductions in SpO₂ in either group (Harris et al., 1990). Bloor et al. observed minimal change in ventilation frequency, a decrease in minute ventilation and an increase in pCO₂ in patients received dexmedetomidine for sedation (Bloor et al., 1992). It is reported in many studies that, dexmedetomidine usually doesn't cause respiratory depression even at deep sedation levels (Ebert et al., 2000; Jaakola et al., 1991). In our study, there were significant decreases in SpO₂ at T2, T3 and T4 times compared to T0 time with both of the agents. Although dexmedetomidine caused significantly more reduction in SpO₂ than propofol, in clinical view these desaturations due to either agent had no significance. These decreases returned back to T0 basal levels at the postoperative 1st hour.

CONCLUSION

In conclusion, both propofol and dexmedetomidine can be safely used for sedation in patients undergoing carotid endarterectomy under regional anesthesia, if the

appropriate monitoring conditions are provided.

REFERENCES

- Aantaa RE, Kanto JH, Scheinin M, Kallio AM, Scheinin H (1990). Dexmedetomidine premedication for minor gynecologic surgery. *Anesth. Analg.* 70: 407-413.
- Aho MS, Erkola OA, Scheinin H, Lehtinen AM, Korttila KT (1991). Effect of intravenously administered dexmedetomidine on pain after laparoscopic tubal ligation. *Anesth Analg.* 73: 112-118.
- Arain SR, Ebert TJ (2002). The efficacy, side effects, and recovery characteristics of dexmedetomidine versus propofol when used for intraoperative sedation. *Anesth Analg.* 95: 461-466.
- Ariboğan A, Ünlügenç H, Reyhan E (1999). Lokal Anestezi Sırasında "Bilinçli Sedasyon" Uygulaması. *Türk Anesteziyoloji ve Reanimasyon Cemiyeti Mecmuası.* 27: 537-544.
- Balci C, Arıkan Y, Baki E (2006). *Türk Anest Rean Der Dergisi.* 34: 249-254.
- Bloor BC, Ward DS, Belleville JP, Maze M (1992). Effects of intravenous dexmedetomidine in humans. II. Hemodynamic changes. *Anesthesiol.* 77: 1134-1142.
- Çelik M, Köprülü AŞ, Atlan A, Özer E (1993). Rejyonal Anesteziye Sedasyon. *Türk Anest ve Rean Mecmuası.* 21: 59-62.
- Ebert TJ, Hall JE, Barney JA, Uhrich TD, Colino MD (2000). The effects of increasing plasma concentrations of dexmedetomidine in humans. *Anesthesiol.* 93: 382-394.
- Geyskes GG, Boer P, Dorhout Mees EJ (1979). Clonidine withdrawal. Mechanism and frequency of rebound hypertension. *Br. J. Clin. Pharmacol.* 7: 55-62.
- Grounds RM, Twigg AJ, Carli F, Whitwam JG, Morgan M (1985). The haemodynamic effects of intravenous induction. Comparison of the effects of thiopentone and propofol. *Anaesthesia.* 40: 735-740.
- Güldiken G, Pamukçu Z, Karamanlioğlu B, Şengönlü O (1992). Oral Temazepam'ın premedikasyon değerinin araştırılması. *Türk Anest ve Rean Mecmuası;* 20: 408.
- Harris CE, Grounds RM, Murray AM, Lumley J, Royston D, Morgan M (1990). Propofol for long-term sedation in the intensive care unit. A comparison with papaveretum and midazolam. *Anaesthesia.* 45: 366-372.
- Houltam B, Scanlan M (2004). Sedation. *Nurs Stand.* 18: 45-46.
- Ickeringill M, Shehabi Y, Adamson H, Ruettimann U (2004). Dexmedetomidine infusion without loading dose in surgical patients requiring mechanical ventilation: haemodynamic effects and efficacy. *Anaesth Intensive Care.* 32: 741-745.
- Jaakola ML, Salonen M, Lehtinen R, Scheinin H (1991). The analgesic action of dexmedetomidine-a novel α2-adrenoceptor agonist-in healthy volunteers. *Pain.* 46: 281-285.
- Kallio A, Scheinin M, Koulou M, Ponkilainen R, Ruskoaho H, Viinamäki O, et al (1989). Effects of dexmedetomidine, a selective alpha 2-adrenoceptor agonist, on hemodynamic control mechanisms. *Clin. Pharmacol. Ther.* 46: 33-42.
- Khan ZP, Ferguson CN, Jones RM (1999). Alpha-2 and imidazoline receptor agonists. Their pharmacology and therapeutic role. *Anaesthesia.* 54: 146-165.
- Krugliak P, Ziff B, Rusabrov Y, Rosenthal A, Fich A, Gurman GM (2000). Propofol versus midazolam for conscious sedation guided by processed EEG during endoscopic retrograde cholangiopancreatography: a prospective, randomized, double-blind study. *Endoscopy.* 32: 677-682.
- Marşan A, Şen S, Gümüş T, Gümüş H, Göğüş N, Aksu C (1999). Spinal anesteziye sedasyon amacıyla kullanılan propofol ve midazolamın hemodinamik, anksiyolitik ve amnezik etkilerinin karşılaştırılması. *Türk Anesteziyoloji ve Reanimasyon Cemiyeti Mecmuası.* 27: 42-47.
- Martin E, Ramsay G, Mantz J, Sum-Ping ST (2003). The role of the alpha 2- adrenoceptor agonist dexmedetomidine in postsurgical sedation in the intensive care unit. *J. Intensive Care Med.* 18: 29-41.
- Nakaigawa Y, Akazawa S, Shimizu R, Ishii R, Yamato R (1995). Effects of graded infusion rates of propofol on cardiovascular haemodynamics, coronary circulation and myocardial metabolism in dogs. *Br. J. Anaesth.* 75: 616-621.

- Nelson LE, Lu J, Guo T, Saper CB, Franks NP, Maze M (2003). The alpha2-adrenoceptor agonist dexmedetomidine converges on an endogenous sleep-promoting pathway to exert its sedative effects. *Anesthesiol.* 98: 428-436.
- Nelson LE, Lu J, Guo T, Saper CB, Franks NP, Maze M (2003). The alpha2- adrenoceptor agonist dexmedetomidine converges on an endogenous sleep promoting pathway to exert its sedative effects. *Anesthesiol.* 98: 428-436.
- Park WY, Watkins PA (1991). Patient-controlled sedation during epidural anesthesia. *Anesth Analg.* 72: 304-307.
- Pertovaara A, Kauppila T, Tukeyva T (1990). The effect of medetomidine, an alpha-2 adrenoceptor agonist, in various pain tests. *Eur. J. Pharmacol.* 179: 323-328.
- Reves GJ, Glass SA, Lumbarsky DA (2000). Non-barbiturate Intravenous Anesthetics. In Miller RD (Ed) *Anesthesia*. 5th ed. New York. Churchill Livinstone. pp. 249-256.
- Roekaerts PM, Huygen FJ, de Lange S (1993). Infusion of propofol versus midazolam for sedation in the intensive care unit following coronary artery surgery. *J. Cardiothorac. Vasc. Anesth.* 7: 142-147.
- Sakarya M, Askar F, Derbent A (1999). Miyokard revaskülarizasyonu sonrası propofol ve midazolam ile sedasyon. *Türk. Anest. Rean. Cem. Mec.* 27: 171-176.
- Shehabi Y, Ruettimann U, Adamson H, Innes R, Ickeringill M (2004). Dexmedetomidine infusion for more than 24 hours in critically ill patients: sedative and cardiovascular effects. *Intensive Care Med.* 30: 2188-2196.
- Smith I, White PF, Nathanson M, Gouldson R (1994). Propofol: an update on its clinical use. *Anesthesiol.*; 81: 1005-1043.
- Turan A, Şapolya O, Karamanlioğlu B, Kurt I, Pamukçu Z (2004). Monitörize anestezi bakımında: Propofol ve deksmedetominin karşılaştırılması. *Türk Anest Rean Der Dergisi*; 32: 100-105.
- Venn RM, Hell J, Grounds RM (2000). Respiratory effects of dexmedetomidine in the surgical patient requiring intensive care. *Crit. Care.* 4: 302-308.
- Virkkila M, Ali-Melkkila T, Kanto J, Turunen J, Scheinin H (1993). Dexmedetomidine as intramuscular premedication in outpatient cataract surgery. A placebo-controlled dose-ranging study. *Anaesthesia.* 48: 482-487.
- Weinbroum AA, Halpern P, Rudick V, Sorkine P, Freedman M, Geller E (1997). Midazolam versus propofol for long-term sedation in the ICU: a randomized prospective comparison. *Int. Care Med.* 23: 1258-1263.
- Yamakage M, Kamada Y, Toriyabe M, Honma Y, Namiki A (1999). Changes in respiratory pattern and arterial blood gases during sedation with propofol or midazolam in spinal anesthesia. *J. Clin. Anesth.* 11: 375-379.