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**ORIGINAL ARTICLE**

# A comparative study on the effect of infusion of 0.3 and 0.6 µg / kg dexmedetomidine during surgery on changes in hemodynamic parameters and pain in patients undergoing spinal surgery under general anesthesia: A 3-blind clinical trial

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## ABSTRACT

**Introduction:** Dexmedetomidine is a drug used widely in recent years to reduce complications during and after surgery, but there is a disagreement about the optimal dose of this drug. The aim of present study was to compare the effects of infusion of two doses of 0.3 and 0.6 µg / kg dexmedetomidine during surgery on changes in hemodynamic parameters and pain in patients undergoing spinal surgery under general anesthesia.

**Methods:** In a clinical trial study, 81 patients, who were candidates for spinal surgery, were randomly assigned to three groups (27 patients in each group). The first group received 0.3 µg / kg dexmedetomidine and the second group received 0.6 µg / kg dexmedetomidine intravenously and the third group (control) received normal saline. Hemodynamic parameters during surgery and recovery and postoperative stage complications such as pain severity and the first time of receiving opioids were evaluated and compared in three groups.

**Results:** Patients who received 0.6 µg / kg dexmedetomidine had lower blood pressure, lower heart rate and lower oxygen saturation during surgery. Also, the severity of postoperative pain was lower in this group. However, the first time of receiving opioid, received drug, length of stay in recovery and extubation time were not significantly different among the three groups.

**Conclusion:** The use of 6 µg / kg dexmedetomidine intravenously is associated with reduced postoperative pain and appropriate hemodynamic stability during surgery. Therefore, it seems that this dose of drug to be effective in preventing acute postoperative pain.

**Keywords:** Postoperative pain, Hemodynamics, Dexmedetomidine

## INTRODUCTION

Complete intravenous anesthesia is widely used in spinal surgery (1). Some α2-adrenoreceptor agonists have been used as the only analgesic agent during and after surgery (2). Dexmedetomidine is a highly selective agonist for the α2-adrenoreceptor that has sedative, anxiolytic, and analgesic properties without respiratory suppression (3, 4). Its shorter duration of action (half-life of plasma ~ 2-3 hours) compared to clonidine and its anesthetic maintaining effect have led to the use of dexmedetomidine as an adjuvant in general anesthesia (5). Dexmedetomidine is currently widely used as an adjuvant for intravenous propofol-based intravenous anesthesia (6,7). In addition to its sedative properties, it increases respiratory stability, reduces the need for opioids to relieve pain, and helps in early postoperative recovery. It also stabilizes the patient's hemodynamics by inhibiting excessive sympathetic activity (8-18).

Hemodynamic changes associated with blood loss during surgery and postoperative pain due to the involvement of multiple neural pathways in spine surgery has challenged the optimal management of these patients during and after surgery (19). In recent years, continuous injections of dexmedetomidine have long been used during spinal surgery and outpatient procedures, especially those performed with local anesthesia (22-22). Several studies have shown that dexmedetomidine is more effective than opioids in controlling pain in post-anesthesia care unit (PACU) (22, 23). However, the effect of different doses of dexmedetomidine as an adjuvant in propofol-based intravenous anesthesia on postoperative pain severity and hemodynamic stability of patients after recovery has not been investigated. Thus, the present study was conducted to compare the effects of two different doses of dexmedetomidine infusion on heart rate, blood pressure and postoperative pain severity at different time points after spinal surgery, especially spinal laminectomy.

## METHODS AND MATERIALS

The present study is a clinical trial conducted in Al-Zahra Hospital in Isfahan in 2020 after the approval of the proposal and obtaining permission from the Medical Ethics Committee of Isfahan University of Medical Sciences with ethics code of IR.MED.REC.1399.195 and code of research of IRCT20130311012782N47 from Iran Clinical Trial Registration Center. This study was designed as a single-center randomized study with three parallel arms. The study population included elective patients candidates for spinal surgery under general anesthesia, in the age range of 18 to 65 years, according to the Class 1 and Class 2 ASA classification. Their written consent form was obtained after explaining about the research objectives by one of the research team.

Patients with allergies to any anesthetic drugs, history of kidney and liver disease, drug and alcohol addiction, heart failure, history of heart attack, pregnant women,

patients used opioid use before the intervention, and in the cases of changes in anesthesia technique or surgery technique for any reason and in case of complications during the operation that required medical intervention were excluded from study. The sample size required for the study was estimated to be 29 people for each group using the formula of estimating the sample size to compare the means and considering 95% confidence level, 80% test power, standardized effect size of 0.4 (22) and 6 post-intervention observations and correlation between observations of 0.6. a convenient sampling method was used and patients were allocated to three groups using random permuted block allocation method according to the time of entering the operating room.

The drug used was 200 mg Vial Dex (100 µg/ ml) made in Iran by Exir Pharmaceutical Company. It was diluted in 50 ml of distilled water so that each ml contained 4 µg of the drug. Then, the drugs were injected into similar coded syringes (A, B, and C) by an anesthesiologist who was not involved in the study and were given to an anesthesiologist who collected the data for injection. The drugs contained 0.6 and 0.3 µg / kg dexmedetomidine per kg body weight, and normal saline, injected into syringes at equal volume and shape.

The anesthesiologist and the data analyst were unaware of the type of drug used in the three groups. The codes were kept by the anesthesiologist until the end of the data analysis, and after analysis, the codes were opened and the results were written based on of drug doses and placebo. All groups were given propofol 2.5-3 mg / kg, atracurium 0.5 mg / kg and fentanyl 2µ g / kg along with one of the drugs injected into the syringe by the anesthetist. To collect data, a researcher-made form including hemodynamic parameters, duration of anesthesia, time of first opioid request, time of extubation, incidence of drug complications were used. The VAS (visual acuity scale) was used to determine pain. Hemodynamic parameters were measured and recorded every 15 minutes during surgery and recovery and 2, 8, 16, and 24 hours after entering the ICU. Stable hemodynamics, O2 Sat above 90%, and normal body temperature were essential for removing endotracheal tube. If the patient felt pain after opening the eyes, the pain severity was measured by VAS and if it was higher than 4, 0.05 mg / kg morphine was injected and then pain was then measured and recorded again.

Pain severity was measured at the beginning of recovery and 2, 8, 24 and 48 hours after surgery. Also, the time of the first opioid request, incidence of drug complications, the length of stay in recovery and at the end of 24-hour hospitalization, the duration of the operation, time of extubation, and the level of the operated vertebra were determined and recorded in all patients. Data were analyzed using SPSS-24 software. Chi-square, one-way analysis of variance, Kruskal-Wallis and repeated measures analysis of variance were used to analyze the data at a significant level of $P < 0.05$. In Group 1, anesthesia was induced with propofol 2.5 to 3 mg per kg body weight and atracurium (0.5 mg / kg) and fentanyl (2 µg / kg) along with infusion of dexmedetomidine at a dose of 0.3 µg / kg simultaneously with beginning of propofol maintenance. In Group 2, anesthesia was induced with propofol 2.5 to 3 mg per kg body weight along with dexmedetomidine infusion at a dose of 0.6 µg / kg. In Group 3, the same amount of maintenance serum infusion was used as placebo. In Groups 1 and 2, dexmedetomidine was discontinued at the onset of skin closure. It should be noted that the same dose of dexmedetomidine was administrated to patients in the ICU. Postoperative pain severity was measured by using Visual Acuity Scale (VAS).

## RESULTS

In the present study, 81 patients underwent laminectomy in three groups (27 in each group). Six participants were excluded from the study due to unpredicted problems. (Figure 1).

According to Table 1, the three groups did not differ significantly in terms of distribution of demographic and general variables and all three groups were almost homogeneous ($P \geq 0.05$).Charts 1 to 5 show the trend of changes in hemodynamic parameters of patients before surgery until the time of admission to ward in 3 groups. Systolic, diastolic, mean arterial blood pressure and heart rate during the stay in recovery were significantly different among the three groups, and the group that received 0.6 µg / kg dexmedetomidine had lower systolic blood pressure and lower heart rate ($P < 0.001$). Also, the percentage of blood oxygen saturation in recovery and ward was significantly different among the three groups and in the 0.6 µg / kg dexmedetomidine group, SPO2 index was lower than that of the control group ($P < 0.001$). However, diastolic blood pressure, mean arterial pressure, and heart rate did not differ significantly among the three groups at any of the times.

In intragroup investigations, the trend of changes in systolic, diastolic blood pressure, mean arterial pressure, heart rate and blood oxygen saturation percentage during the intervention was significantly different in all three groups, so that the trend of these parameters from the time of injection to the end of the procedure showed a decreasing trend, but in recovery and wards, the trend increased and approached the baseline values. In intergroup investigations, the trend of changes in blood pressure and heart rate during the study period was not significantly different among the three groups and patients in all three groups showed the same trend. However, changes in blood oxygen saturation percentage were significantly different among the three groups ($P = 0.02$) and the 0.6 µg / kg dexmedetomidine group had a lower SPO2 level than other two groups, and there was no significant difference between the two groups of 0.3 µg / kg dexmedetomidine and the control.

Evaluation of postoperative pain severity in the three groups showed that patients received 0.6 µg / kg dexmedetomidine had lower pain severity than the control group from the beginning of recovery to time of hospitalization ($P<0.001$). Also, the mean pain severity of the group received 0.3 µg / kg dexmedetomidine from entering the recovery to the time of hospitalization was lower than the control group. Moreover, after 30 minutes of recovery, the pain severity of the 0.6 µg / kg dexmedetomidine group was lower than that of the 0.3 µg / kg dexmedetomidine group. Finally, based on the results, the trend of changes in postoperative pain severity was

significantly different among the three groups and in all stages of study, patients who received 0.3 and 0.6 µg / kg dexmedetomidine had a lower pain severity than the control group. Also, pain severity was lower in group 0.6 µg / kg dexmedetomidine than 0.3 µg / kg dexmedetomidine group (Chart 6).

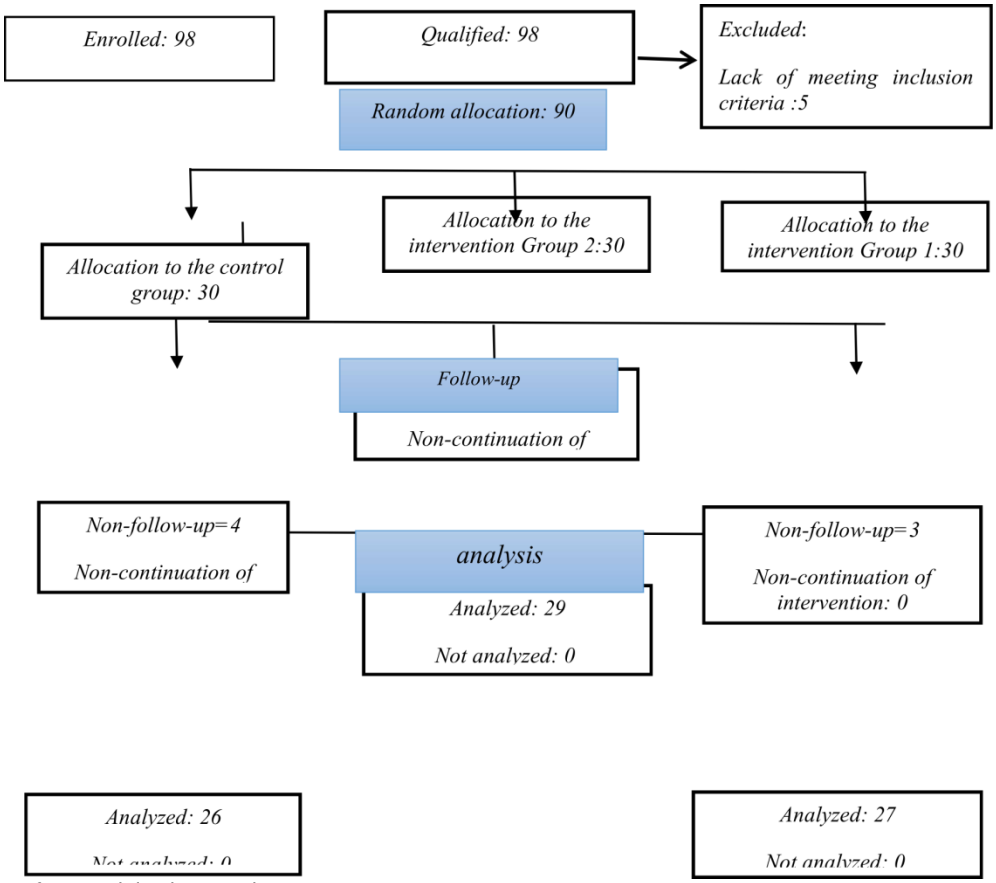


Figure 1- Algorithm of research implementation

Table 1: Distribution of demographic and general variables in three groups

| Variable | | Study groups with different doses of dexmedetomidine | | | |
|---|---|---|---|---|---|
| | | Control | 0.3 µg / kg | 0.6 µg / kg | P |
| Mean age (year) | | 2. 14±3 .46 | 6.4 ± 14.46 | 9. 13±3 .51 | 35.0 |
| Gender | Male | 3).14(58 | 7).18(66 | 6).15(55 | 69.0 |
| | Female | 7).10(41 | 3).9(33 | 4).12(44 | |
| ASA | 1 | 2).12(52 | 17(63) | 1).13(48 | 55.0 |
| | 2 | 8).11(47 | 10(37) | 8).14(51 | |
| Duration of surgery (minutes) | | 3. 44±7 .156 | 6. 53±2 .164 | 4. 41±6 .149 | 53.0 |
| Duration of anesthesia (minutes) | | 9. 44±1 .182 | 3. 60±7 .189 | 7. 47±1 .174 | 55.0 |

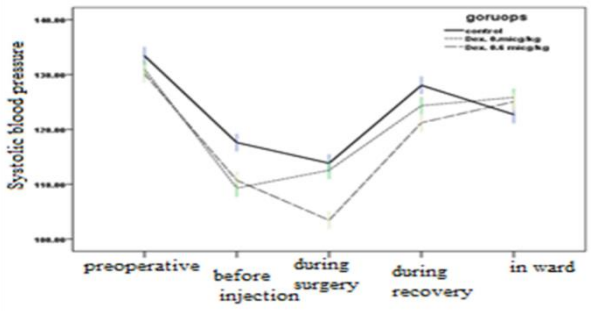


Chart 1: Changes in systolic blood pressure from preoperative stage to hospitalization stage in three groups (P = 0.11)

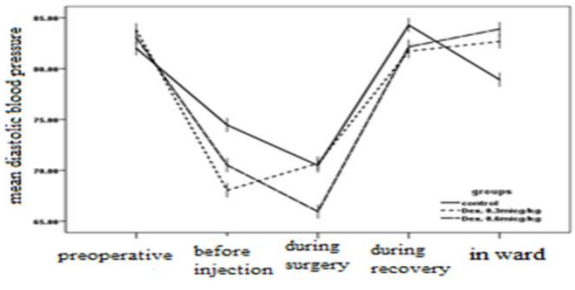


Chart 2: trend of changes in diastolic blood pressure from preoperative stage to hospitalization stage in three groups (P = 0.91)

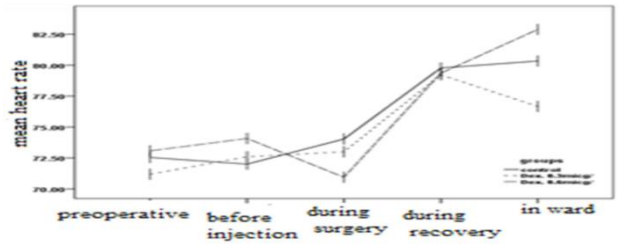


Chart 3: trend of changes in heart rate from preoperative stage to hospitalization in three groups (P = 0.81)

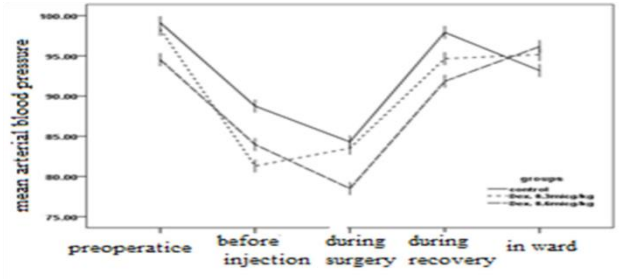


Chart 4: Trend of changes in mean arterial blood pressure from preoperative stage to hospitalization stage in three groups (P = 0.22)

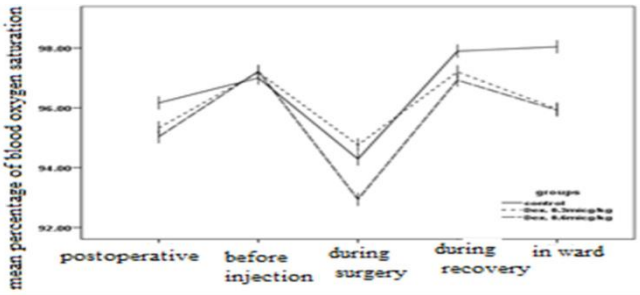


Chart 5: The trend of changes in the percentage of blood oxygen saturation from preoperative stage to hospitalization in three groups (P = 0.002)

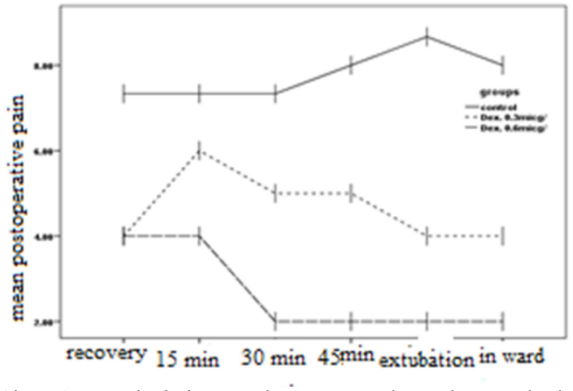


Chart 6: Trend of changes in postoperative pain severity in three groups (P = 0.008)

Table 2: Mean extubation time, length of stay in recovery, receiving opioids and postoperative complications in three groups

| Variable | | Study group (dose of dexmedetomidine) | | | |
|---|---|---|---|---|---|
| | | Control | 0.3 µg / kg | 0.6 µg / kg | |
| Mean extubation time (minute) | | **46±170** | **7. 57±3 .177** | **4. 45±1 .163** | **59.0** |
| Mean recovery time (minutes) | | **9. 24±7 .92** | **1. 14±8 .97** | **20±95** | **38.0** |
| Mean first time of opioid received (minute) | | **4. 2±5 .6** | **5. 3±7 .6** | **1±2 .5** | **08.0** |
| Mean dose of opioid received | | **10** | **10** | **8.9** | **38.0** |
| Hemodynamic complications | Bradycardia | **2).1(4** | **5).5(18** | **9).7(25** | **1.0** |
| | Hypotension | **2).1(4** | **8).4(14** | **6).8(29** | **053.0** |
| | Tachycardia | **8).5(20** | **0(0)** | **0(0)** | **002.0** |
| | Hypertension | **0(0)** | **1).3(11** | **7).1(3** | **32.0** |
| Patient satisfaction | Completely satisfied | **8).5(20** | **6).9(34** | **8).8(30** | **83.0** |
| | Satisfied | **5).15(62** | **8).14(53** | **7).2(57** | |
| | No idea | **7).4(16** | **7).2(7** | **7).2(7** | |
| | Dissatisfied | **0(0)** | **8).1(3** | **8).1(3** | |

Table 2 shows the mean extubation time, length of stay in recovery, taking opioid, and postoperative complications. Based on this table, the mean extubation time, length of stay in recovery, first time of drug request, and received drug dose were not significantly different among the three groups. A total number of 30 patients (38.5%) had hemodynamic complications, including 7 patients (29.2%) in the control group, 10 patients (37%) in the 0.3 µg / kg dexmedetomidine group and 13 patients (48.1%) in the 0.6 µg / kg dexmedetomidine group and no significant difference was observed among the three groups (P = 0.4). The complications included bradycardia (13 cases), hypotension (13 cases), tachycardia (5 cases) and hypertension (4 cases) that the frequency of tachycardia was significantly different among the three groups (P = 0.002).

## DISCUSSION AND CONCLUSION

Nowadays, dexmedetomidine is widely used due to its small complications on hemodynamics of patients undergoing surgery and its analgesic effects on postoperative pain, but a single theory has not been proposed on the optimal dose of this drug. Thus, this study was conducted to compare the effects of two different doses of dexmedetomidine infusion on heart rate, blood pressure and postoperative pain severity at different time points after spinal surgery, especially spinal laminectomy. In this study, three groups of patients underwent surgery. The first two groups received 0.3 and 0.6 µg / kg dexmedetomidine intravenously, and the third group, as control group, received saline. The three groups did not differ significantly in terms of demographic and clinical

variables and no confounding effect of the above factors was observed on the results of the study.

Investigation of hemodynamic parameters before, during and after surgery showed that blood pressure, heart rate and percentage of blood oxygen saturation during surgery were lower in the group received 0.6 µg / kg dexmedetomidine. In a study conducted by Gulabani et al. on patients undergoing tonsillectomy, the effect of two doses of 0.1 and 0.5 µg / kg dexmedetomidine in comparison with lignocaine on the hemodynamics of patients was investigated. Blood, heart rate, and percentage of blood oxygen saturation were not significantly different among the three groups (23). Smitha et al. distributed 90 patients who were candidate for surgery under general anesthesia to three groups (30 patients in each group) using 0.5 µg / kg, 1 µg / kg dexmedetomidine and normal saline and examined their effect on hemodynamics of patients during laryngoscopy. Based on the results of the mentioned study, the mean blood pressure of systole, diastole, mean arterial and heart rate in the group received 1 µg / kg dexmedetomidine was significantly lower than that of other two groups. In the mentioned study, it was concluded that 0.1 µg / kg dexmedetomidine is preferable to 0.5 µg / kg dexmedetomidine in maintaining hemodynamic stability during laryngoscopy (24). In another study conducted by Jarineshin et al., the effect of two doses of 0.5 and 0.1 µg dexmedetomidine on hemodynamics of patients during laryngoscopy was compared with the control group. In the mentioned study, the mean systolic, diastolic and heart rate blood pressure was significantly lower in the group received 1 µg / kg dexmedetomidine than the group received 0.5 µg / kg dexmedetomidine and the control group (25). Based on the results of the present study and comparison with other studies, it seems that the use of 0.6 µg / kg dexmedetomidine is associated with fewer changes in blood pressure during and after surgery. The results of our study showed that patients who received 0.6 µg / kg dexmedetomidine had lower postoperative pain severity than the group received 0.3 µg / kg dexmedetomidine and the control group. Also, the group that received 0.3 µg / kg dexmedetomidine experienced lower postoperative pain severity than the control group. Moreover, the first time of drug administration in the 0.6 µg / kg dexmedetomidine group was late, but no significant difference was observed among the groups. Also, there was no significant difference among the three groups in terms of e dose of received opioids.

Park et al. investigated the effect of two intravenous doses of 0.5 and 0.1 µg / kg dexmedetomidine on hemodynamics in elderly patients undergoing spinal anesthesia surgery after surgery. The patients received 0.5 µg / kg dexmedetomidine had lower postoperative pain severity, and other postoperative complications such as nausea and vomiting did not differ significantly among the groups (26). Thus, given the analgesic effects of this drug, its use during anesthesia seems to be associated with a reduction in postoperative pain. Therefore, its use in surgery can be recommended. According to the results of our study, the duration of endotracheal tube removal and the length of stay in recovery were not significantly different among the three groups. In a study conducted by Momeni et al., the effect of 0.2 µg / kg dexmedetomidine on pain and other postoperative complications as well as hemodynamics of CABG patients was investigated. In the mentioned study, in which 40 patients participated in each group, the level of morphine consumption after surgery was significantly different between the two groups and the level of morphine consumption in the dexmedetomidine group was significantly lower than that in the control group. The level of postoperative pain in the dexmedetomidine group was significantly lower than that of the placebo group and the extubation time in the dexmedetomidine group was significantly shorter than that of the placebo group (27). In general, the results of various studies have indicated that the use of dexmedetomidine has a favorable effect in maintaining hemodynamic stability and reducing postoperative complications. According to the results, 0.56 µg / kg dexmedetomidine has more favorable effects and although it has few complications in patients, it seems that 0.6 µg / kg dose of it to be more useful in heavy and long-term surgeries with more postoperative complications, such as spinal surgery. One of the limitations of the study may be the small number of samples in the groups. Due to the small number of samples, more studies are needed in this area. In addition, this study was conducted in one center on spine surgeries and similar studies can be also conducted on other surgeries.

## CONCLUSION

The use of 0.6 µg / kg dexmedetomidine as an intravenous infusion is associated with reduced postoperative pain and appropriate hemodynamic stability during surgery, and this dose seems to be effective in preventing acute postoperative pain.

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