Research Article

# Efficacy of dexmedetomidine infusion of two different doses in patients undergoing laparoscopic surgeries

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## Abstract

**Introduction:** Dexmedetomidine is an α-adrenoceptor agonist with dose dependent $\alpha_2$-adrenoceptor selectivity. Clinical trials indicate that patients treated with dexmedetomidine required either no additional sedative medication or only small doses of add-on medications. This was significantly different from the add-on medication requirements of patients who did not receive dexmedetomidine. **Aims and objectives:** to study the Efficacy of dexmedetomidine infusion of two different doses in patients undergoing laparoscopic surgeries. **Materials and method:** in the present study three groups were compared (control, dex 0.3 and dex 0.6). Sedation using Ramsay sedation score, pain using Visual analogue score (VAS), incidence of post operative nausea and vomiting and use of any drug for pain, vomiting and any other side effect were measured and compared. **Results:** It was observed that duration of surgery, duration of infusion and use of Fentanyl (µg) was statistically insignificant in all the three groups. The mean time of eye opening in Control, Dex 0.3 and Dex 0.6 was 2.83 ± 0.67 min, 4.35 ± 0.68 min and 4.71 ± 0.61 min respectively. The mean time to follow verbal commands in Control, Dex 0.3 and Dex 0.6 group was 3.32 ± 0.70 min, 4.84 ± 0.68 min and 5.29 ± 0.69 min respectively. The mean time to extubate was maximum (5.94 ± 0.66 min) in Dex 0.6 group as compare to control (3.87 ± 0.62 min) and Dex 0.3 (5.25 ± 0.73 min). The use of antiemetic and analgesics was highest in Control followed by Dex 0.3 and least in Dex 0.6. **Conclusion:** The perioperative infusion of dexmedetomidine has good efficacy during laparoscopic surgery as it, offered decreased postoperative pain level and better sedation scores, decreased the total amount of analgesic and antiemetics requirements as compared with control. Continuous infusion at 0.3µg/kg/hour is recommended over the 0.6µg/kg/hour.

**Keywords:** dexmedetomidine, efficacy, eye opening, analgesics.

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## INTRODUCTION

The use of $\alpha_2$-adrenoceptor agonists as anesthetics is not new. Veterinarians employed xylazine and detomidine for a long time to induce analgesia and sedation in animals, and much of our knowledge was gained from this application. It has recently become evident that complete anesthesia is possible by employing new, more potent $\alpha_2$ agonists, such as medetomidine and its stereoisomer, dexmedetomidine.[1] The $\alpha_2$-adrenergic receptor mediates its effects by activating guanine-nucleotide regulatory binding proteins (G proteins). Activated G proteins modulate cellular activity by signaling a second messenger system or by modulating ion channel activity. The second messenger system, when activated, leads to the inhibition of adenylate cyclase, which, in turn, results in decreased formation of 3,5-cyclic adenosine monophosphate (cAMP). Specific cAMP-dependent kinases modify the activity of target proteins by controlling their phosphorylation status.[2] Dexmedetomidine is an α-adrenoceptor agonist with dose dependent $\alpha_2$-adrenoceptor selectivity. In animals that receive low to medium doses at slow rates of infusion (10

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to 300 μg/kg), high levels of $\alpha_2$-adrenoceptor selectivity are observed, placing dexmedetomidine in the same therapeutic category as clonidine but with more affinity for the $\alpha_2$ adrenoceptor.[3] At higher doses (>1000 μg/kg) or in rapid infusions of lower doses, both $\alpha_1$- and $\alpha_2$-adrenoceptor activities are observed. The majority of patients receiving dexmedetomidine as a primary therapy experienced clinically effective sedation yet were still easily arousable, a unique feature not observed with other clinically available sedatives.[4] Clinical trials indicate that patients treated with dexmedetomidine required either no additional sedative medication or only small doses of add-on medications. This was significantly different from the add-on medication requirements of patients who did not receive dexmedetomidine.

Dexmedetomidine was approved by the Food and Drug Administration at the end of 1999 for use in humans as a short-term medication (<24 hours) for analgesia and sedation in the intensive care unit (ICU). Its unique properties render it suitable for sedation and analgesia during the whole perioperative period. Its applications as a premedication, as an anesthetic adjunct for general and regional anesthesia and as a postoperative sedative and analgesic are similar to those of the benzodiazepines, but a closer look reveals that the $\alpha_2$-adrenoceptor agonist has more beneficial side effects.

## AIMS AND OBJECTIVES

To study the Efficacy of dexmedetomidine infusion of two different doses in patients undergoing laparoscopic surgeries.

## MATERIAL AND METHOD

The present study was conducted at Chhatrapati Shahuji Maharaj Medical University, Lucknow, UP. Following inclusion and exclusion criteria was used to select the study subjects.

**Inclusion criteria**

- Patients aged 20-50 years belonging to ASA physical status I or II planned for laparoscopic surgery.

**Exclusion Criteria**

- An allergy to $\alpha_2$ adrenergic agonist or antagonist,
- A history of uncontrolled hypertension, Heart block greater than first degree,
- A history of alcohol or drug abuse,
- Clinically significant neurologic, cardiovascular, renal, hepatic, or gastrointestinal diseases, and
- Pregnant or breast-feeding

Thus using the above mentioned inclusion and exclusion criteria 60 patients were selected for the study. After getting approval from Ethical Committee of the college, informed consent was taken from the patient.

The patients were randomly allocated to 3 different groups using the computer generated random table.

**Group 1(control):** Received saline infusion during procedure

**Group 2(DEX 0.3):** Received infusion of dexmedetomidine 0.3 μg/kg/hour.

**Group 3(DEX 0.6):** Received infusion of dexmedetomidine 0.6 μg/kg/hr.

A baseline cardio-respiratory measures including heart rate (HR), pulse oximetry ($SPO_2$), Non-invasive Systolic blood pressure (SBP), Diastolic Blood pressure (DBP), Mean Arterial pressure (MAP) and End tidal $Co_2$ ($Etco_2$) were recorded once the patient came to operating room. Patients were monitored continuously during the surgery. Duration of surgery, Duration of infusion and use of Fentanyl (μg) were recorded. During the post operative period of 24 hours patient was monitored at intervals of 2 hours for first 6 hours and then at interval of 6 hours till 24 hours, sedation using Ramsay sedation score, pain using Visual analogue score (VAS), incidence of post operative nausea and vomiting and use of any drug for pain, vomiting and any other side effect. Rescue medication in post operative room for pain were injection tramadol and injection voveran (diclofenac sodium) while for vomiting included injection emeset (ondansetron).

## RESULTS

**Table 1:** Baseline summary of subjects of three groups

| Characteristics | Control (n=20) | Dex 0.3 (n=20) | Dex 0.6 (n=20) | P value |
|---|---|---|---|---|
| Sex (male/female) | 6/14 | 8/12 | 6/14 | $0.60^{ns}$ |
| Age (yrs) | 33.95 ± 6.67 | 34.20 ± 10.75 | 34.30 ± 7.95 | $0.01^{ns}$ |
| Weight (kg) | 57.20 ± 8.57 | 61.00 ± 11.21 | 58.70 ± 8.19 | $0.83^{ns}$ |
| SBP (mmHg) | 121.40 ± 10.85 | 128.50 ± 12.28 | 126.95 ± 10.67 | $2.19^{ns}$ |
| DBP (mmHg) | 82.55 ± 7.10 | 82.90 ± 9.41 | 83.20 ± 6.35 | $0.04^{ns}$ |
| MAP (mmHg) | 95.50 ± 7.86 | 98.10 ± 8.38 | 97.78 ± 7.03 | $2.62^{ns}$ |
| HR (beat/min) | 81.65 ± 8.36 | 83.95 ± 7.50 | 81.75 ± 4.25 | $0.70^{ns}$ |
| ASA Grade (I/II) | 11/9 | 13/7 | 9/11 | $1.62^{ns}$ |

ns- p>0.05

 

A total of 60 patients (male=20 and female=40) were randomized equally to treat either with Control, Dex 0.3 and Dex 0.6. The age of all patients ranged from 20-50 yrs. The baseline demographic characteristics (sex, age, weight, SBP, DBP, MAP, HR and ASA Grade) of three groups of patients were compared and it was observed that there was no statistically significant.

**Table 2:** Distribution of patients according to duration of surgery, duration of infusion and use of fentanyl in subjects of three groups

| Characteristics | Control (n=20) | Dex 0.3 (n=20) | Dex 0.6 (n=20) | P value |
|---|---|---|---|---|
| Duration of surgery (min) | 88.75 ± 17.16 | 87.75 ± 19.63 | 88.00 ± 17.65 | $0.02^{ns}$ |
| Duration of infusion (min) | 102.25 ± 16.66 | 99.75 ± 18.60 | 102.00 ± 16.01 | $0.13^{ns}$ |
| Use of Fentanyl (µg) | 58.75 ± 7.93 | 59.25 ± 8.16 | 62.00 ± 12.18 | $0.66^{ns}$ |

ns- p>0.05

It was observed that duration of surgery was almost equal in control, Dex 0.3 and Dex 0.6 groups. (88.75min, 87.75min and 88min respectively). The duration of infusion in Control, Dex 0.3 and Dex 0.6 ranged from 70-130 min, 60-130 min and 75-135 min respectively with mean (± SD) 102.25 ± 16.66 min, 99.75 ± 18.60 min and 102.00 ± 16.01 min, respectively. When the use of fentanyl was compared it was observed that in control and Dex 0.3 group it was nearly similar (58.75 and 59.25 µg respectively). The mean use of Fentanyl was slightly higher in Dex 0.6 (62 µg) as compared to both Control and Dex 0.3. But the difference in the fentanyl dose in the all the three groups was not statically significant.

**Table 3:** Distribution of patients according to time of eye opening, time to follow verbal commands, time to extubate in subjects of three groups

| Characteristics | Control (n=20) | Dex 0.3 (n=20) | Dex 0.6 (n=20) | ANOVA F value |
|---|---|---|---|---|
| Time of eye opening (min) | 2.83 ± 0.67 | $4.35 \pm 0.68^{**}$ | $4.71 \pm 0.61^{**}$ | $46.55^{**}$ |
| Time to follow verbal commands (min) | 3.32 ± 0.70 | $4.84 \pm 0.68^{**}$ | $5.29 \pm 0.69^{**\S}$ | $44.76^{**}$ |
| Time to extubate (min) | 3.87 ± 0.62 | $5.25 \pm 0.73^{**}$ | $5.94 \pm 0.66^{**\S}$ | $49.27^{**}$ |

$^{*}$p<0.05 or $^{**}$p<0.01- as compared to Control
$^{\S}$p<0.05 or $^{\S\S}$p<0.01- as compared to Dex 0.3

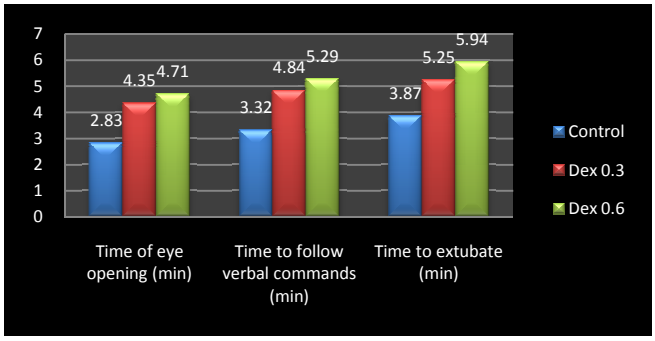


**Figure 1:** Distribution of patients according to time of eye opening, time to follow verbal commands, time to extubate

The mean time of eye opening in Control, Dex 0.3 and Dex 0.6 was 2.83 ± 0.67 min, 4.35 ± 0.68 min and 4.71 ± 0.61 min respectively. The mean time of eye opening was slightly higher in both Dex 0.3 and Dex 0.6 as compared to Control and was found to be statistically significantly (p<0.01). However, the mean time of eye opening in Dex 0.3 and Dex 0.6 did not differed significantly (p>0.05). The mean time to follow verbal commands in Control, Dex 0.3 and Dex 0.6 group was 3.32 ± 0.70 min, 4.84 ± 0.68 min and 5.29 ± 0.69 min respectively. The mean time to follow verbal commands in both Dex 0.3 and Dex 0.6 was found to be significantly (p<0.01) higher than control. The mean time to follow verbal commands of Dex 0.6 was also found to be significantly (p<0.05) higher than that of Dex 0.3. The mean time to extubate was maximum (5.94 ± 0.66 min) in Dex 0.6 group as compare to control (3.87 ± 0.62 min) and Dex 0.3 (5.25 ± 0.73 min). The mean time to extubate of Dex 0.6 was also found to be significantly (p<0.05) higher than the Dex 0.3. The mean time to extubate in both Dex 0.3 and Dex 0.6 was found to be significantly (p<0.01) higher than control.

**Table 4:** The usage of antiemetic and anlgesic in three groups

| Drug | | Control (n=20) | Dex 0.3 (n=20) | Dex 0.6 (n=20) |
|---|---|---|---|---|
| **antiemetic** | | 14 (70%) | 6 (30%) | 5 (25 %) |
| Analgesic | Voveran | 15 (75%) | 7 (35%) | 5 (25 %) |
| | Tramadol | 13 (65%) | 9 (45%) | 4 (20 %) |

The use of antiemetic was highest in Control (70%) followed by Dex 0.3 (30%) and least in Dex 0.6 (25%). On comparing, the usage of antiemetic in Dex 0.3 ($z=2.21$, $p<0.05$) and Dex 0.6 ($z=2.53$, $p<0.01$) was found to be significantly lower as compared to Control while it was not differed in Dex 0.3 and Dex 0.6 ($Z=0.00$, $p>0.05$). The usage of Voveran was highest in Control (70%) as compared to Dex 0.3 (35%) and least in Dex 0.6 group (25%) and the difference was also statistically significant. However the difference in use of voveran in Dex 0.3 and Dex 0.6 was not statically significant. ($Z=0.35$, $p>0.05$). Similarly, the usage of Tramadol was highest in Control (65%) followed by Dex 0.3 (45%) and least in Dex 0.6 (20%). On comparing, the usage of Tramadol in Dex 0.6 ($z=2.56$, $p<0.05$) was found to be significantly lower as compared to Control group. While the difference was not significant in Control and Dex 0.3 ($Z=0.95$, $p>0.05$) (Fig. 21) and Dex 0.3 and Dex 0.6 ($Z=1.35$, $p>0.05$).

## DISCUSSION

In the present study, we observed the efficacy of continuous perioperative infusion of dexmedetomidine in two different doses of 0.3µg/kg/hr and 0.6µg/kg/hr in patients undergoing laparoscopic surgeries. The 3 groups (control, dex 0.3 and dex 0.6) were similar to each other on age, sex, weight, ASA grade) and baseline hemodynamic parameters (SBP, DBP, MAP, HR) ($p>0.05$). It was observed that duration of surgery, duration of infusion and use of Fentanyl (µg) was statistically insignificant in all the three groups. During the post operative period patients were sedated more in DEX group as compared to control group, with more time needed for spontaneous eye opening. The mean time of eye opening in both Dex 0.3 and Dex 0.6 was found to be significantly ($p<0.01$) higher as compared to control. However, the mean time of eye opening in Dex 0.3 and Dex 0.6 did not differed significantly ($p>0.05$) i.e. found to be statistically the same. The mean time to follow verbal commands was comparatively higher in both Dex 0.3 and Dex 0.6 as compared to Control and was evident higher in Dex 0.6 than Dex 0.3. Further, the mean time to follow verbal commands of Dex 0.6 was also found to be significantly ($p<0.05$) higher than that of Dex 0.3. The mean time to extubate was comparatively higher in both Dex 0.3 and Dex 0.6 than Control and was found to be higher in Dex 0.6 than Dex 0.3 and was also statistically significant. The mean time to extubate of Dex 0.6 was also significantly ($p<0.05$) higher than the Dex 0.3. In our study we did not used any inhalational agent for maintenance of anesthesia therefore the DEX group patients were sedated more than the control group, or in other words patients were more calm and sound after the surgery in DEX group as compared to control group. It was observed that there was a reduced requirement of pain medication in two dex group (DEX0.3 andDEX0.6) as compared to control group. On comparing, the usage of Voveran in Dex 0.3 ($z=2.23$, $p<0.05$) and Dex 0.6 ($z=2.85$, $p<0.01$) was found to be significantly lower as compared to Control while it was not significant in Dex 0.3 and Dex 0.6 ($Z=0.35$, $p>0.05$). On comparing, the usage of Tramadol, Dex 0.6 ($z=2.56$, $p<0.05$) was found to be significantly lower as compared to Control while it did not differed in Control and Dex 0.3 ($Z=0.95$, $p>0.05$) and Dex 0.3 and Dex 0.6 ($Z=1.35$, $p>0.05$). Aho *et al*[5] also observed that after laparoscopic tubal ligation, dexmedetomidine relieved pain and reduced opioid requirements. In our study we gave fentanyl to all 3 three groups in a dose of 1 µg/kg at the time of induction; therefore for post operative pain we used either tramadol or voveran. During post operative period it was observed that use of antiemetic was significantly reduced in DEX 0.3 (30%) and DEX 0.6 (25%) as compared to control group (70%). Tufanogullari *et al*[6] also demonstrated reduced requirements of antiemetics in dexmedetomidine group as compared to placebo. Gurbet *et al*[7] also reported less nausea in dexmedetomidine group as compared to the placebo group. Dyck *et al*[8] stated that $\alpha_2$-adrenergic agonists have a marked anti-sialogogue effect which is useful in preanesthetic medication. However, a major dexmedetomidine effect is xerostomia (dry mouth), which is highly uncomfortable. In addition, there is an 11% incidence of nausea in patients sedated with dexmedetomidine. Badner *et al*[9] observed that Shivering, nausea and vomiting had a lower incidence in the dexmedetomidine group as compared to placebo group. Chaves *et al*[10] also observed that less analgesics and anti-emetics consumption in dexmedetomidine group.

## CONCLUSION

Thus we conclude that the perioperative infusion of dexmedetomidine has good efficacy during laparoscopic surgery as it, offered decreased postoperative pain level and better sedation scores, decreased the total amount of analgesic and antiemetics requirements as compared with control. Continuous infusion at 0.3µg/kg/hour is recommended over the 0.6µg/kg/hour.

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