# Effect of Dexmedetomidine on Intracranial Pressure in Gynecological Laparoscopic Surgeries: Ultrasonographic Evaluation of Optic Nerve Sheath Diameter

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## Abstract

Laparoscopy is a minimally invasive surgical procedure used in gynecology for both diagnostic and treatment purposes. During gynaecologic laparoscopy, the patient is placed in the Trendelenburg position to optimise visualization and access to the pelvis, so this study was done to investigate the effect of dexmedetomidine on changes in intracranial pressure reflected as optic nerve sheath diameter (ONSD) during gynecological laparoscopic surgery in the Trendelenburg position by ultrasonographic evaluation. This study included 76 female patients who underwent elective therapeutic gynecological laparoscopic surgeries. Patients were randomly divided into two groups: group D (dexmedetomidine group, n=38) received dexmedetomidine loading (one mcg/kg) for ten minutes (min) and infusion (0.4 mcg/kg/h for one hour), and group P (placebo group, n=38) received 0.9% normal saline loading (2.5 ml/10 kg) and infusion (one ml/10 kg/h for one hour), started 10 min before induction of anesthesia and continued for one hour. Optic nerve sheath diameter was taken after application of a high-frequency linear probe on closed eyelids and measured at three mm behind the acoustic shadow of the vitreous body. Results showed that during follow-up periods (15 minutes to 3 hours), group D showed a significant reduction in heart rates compared to group P at all-time points ($p<0.05$). Group D showed significantly lower blood pressure (BP) compared to group P at 45 minutes, one hour, 1.5 hours, two hours, and 2.5 hours. There were significantly lower values of ONSD in group D after the Trendelenburg position. So, dexmedetomidine in the studied doses effectively reduces ONSD in cases undergoing gynecological laparoscopic surgery in the Trendelenburg position, which may reflect a reduction in intracranial pressure (ICP) elevation and was associated with notable hemodynamic stability.

**Keywords**: Dexmedetomidine, Intracranial Pressure, Gynecological Laparoscopic Surgeries

## Introduction

Laparoscopic surgeries have gained much more popularity worldwide. They have several recorded advantages; in contrast, a single adverse event is the increased ICP following pneumoperitoneum and Trendelenburg position **[1]**.

In the context of laparoscopic surgeries, the mechanism of increased ICP is distinctive, as an increase in intra-abdominal pressure causes increased venous pressures and a stasis of intracranial blood outflow. This causes an abrupt and extensive increase in ICP, which might be worsened by an increase in arterial carbon dioxide ($CO_2$) due to carboperitoneum **[2]**.

The Trendelenburg position is used during gynecologic laparoscopy to maximize pelvic vision and access. Literature concerning impaired cognition following laparoscopy conducted in the steep Trendelenburg position among cases without an intracranial lesion is still rare **[3]**.

The central nervous system's (CNS) dura mater continues as the optic nerve sheath. Any alteration in the intracranial cavity pressure could affect the ONSD. Sonographic measurement of ONSD has been recommended as a valid, reproducible, non-invasive monitor for ICP **[4, 5]**.

Dexmedetomidine is a potent and selective alpha-2 adrenoceptor agonist with sympatholytic, sedative, and analgesic characteristics. It is a helpful and safe adjunct in several clinical contexts. In addition, it has analgesic effects best defined as opioid-sparing and decreases CNS sympathetic outflow in a dose-dependent manner. **[6]**.

The rationale of this study based on dexmedetomidine. It was used in previous studies to mitigate ICP increases. Its exact effects on ICP remain debated **[7, 8]**, but dexmedetomidine's mechanisms such as reducing norepinephrine release, constricting cerebral blood vessels via α2B receptor activation, and decreasing metabolic oxygen consumption likely are contributed to lowering ICP without compromising cerebral perfusion **[9, 10]**. So, we aimed to assess the effect of dexmedetomidine on changes in ICP reflected as ONSD during gynecological laparoscopic surgery in Trendelenburg position by ultrasonographic evaluation of ONSD.

## Patients and methods

This study was a prospective randomised placebo controlled double blinded study that has been conducted in Mansoura University Hospital over one year from June 2023 to May 2024. This study included 76 female patients underwent elective therapeutic gynecological laparoscopic surgeries (suspected duration more than one hour). Patients were interviewed and a written informed consent was taken from all the patients participated in this study.

Inclusion criteria included female patients undergoing gynecological laparoscopic surgeries (suspected duration more than one hour), with age between 18 to 60 years, with body Mass Index (BMI) <30 kg/m$^2$ and with American Society of Anesthesiologists type I or II. Exclusion criteria included patients with history of intracranial, cardiac pathology, intraocular or ophthalmic pathology, history of hepatic or renal derangement, history of allergy to alpha 2 agonist, on beta blocker, calcium channel blocker, and pregnant or lactating women,

## Randomization and blindness

By using computer-generated random number tables, we performed the randomization process. As a result, the number slips were placed in opaque sealed envelopes. The final group allocation was conducted just prior to the approach by opening the envelope by the staff nurse present, the anesthesiologists who assessed and recorded the study parameters were blinded to group allocation as the studied and solution was prepared by an anesthesiologist not involved in peri-operative assessment.

## Methods

All cases were subjected to pre-operative comprehensive history taking, clinical examination, and laboratory investigations, including complete blood count, coagulation profile, blood sugar level, liver function tests, and electrocardiography (ECG).

At the pre-anesthetic room, baseline monitors, which include a noninvasive blood pressure monitor (NIBP), a peripheral oxygen saturation monitor (SpO2), and an ECG monitor, were connected, and basal ONSD and all readings were recorded. An eye scan was performed by using portable US (Mindray Diagnostic Ultrasound System model Z60 Expert) and a high-frequency linear probe after closing and covering eyelids with sterile transparent dressing.

After complete assessment, two intravenous (I.V.) lines were established: one for maintenance crystalloid infusion and the other for dexmedetomidine (Precedex™ , Pfizer USA, dexmedetomidine hydrochloride injection 200 μg / 2 ml) or normal saline infusion (placebo) in the intra-operative period. All cases were pre-medicated with midazolam (0.02 mg/kg) and Metoclopramide 10 mg intravenously.

Patients were divided into two groups, group D (dexmedetomidine group, n=38) received dexmedetomidine loading (1mcg/kg) (2.5ml/10kg) for 10 minutes and infusion (0.4mcg/kg/h for one hour) (1ml/10kg/h for one hour) and group P (placebo group, n=38) received 0.9% normal saline loading (2.5ml/10 kg ) and infusion (1ml/10kg/h for one hour), started ten minutes prior to induction of anesthesia and continued for one hour.

The dexmedetomidine dose for group D was prepared by adding 200μg (2 ml) of drug dexmedetomidine hydrochloride to 48ml of 0.9% normal saline to a total volume of 50 ml (drug concentration was 4 μg/ml). Group P received a 50 ml syringe filled with normal saline given at the same rate.

Induction of anesthesia was achieved by fentanyl (1 mcg/kg), propofol (2 mg/ kg), atracurium (0.5 mg/kg). Patients were intubated ventilated on volume control mode, anesthesia was maintained by isoflurane at concentration 1-2%, incremental atracurium (0.1mg/kg) every 20 minutes. As regarding analgesia, Patient received paracetamol 1gm IV infusion. When the heart rate (HR) decreased less than 50 beat per minute, patients received atropine 0.02 mg/kg. When blood pressure decreased by more than 20% from baseline, the patient received IV ephedrine in 5 mg increments as needed. When heart rate increased more than 20% of basal heart rate, patient received 0.5 mcg /kg fentanyl, when no response, increasing depth of anesthesia was done by increasing concentration of inhalational anesthetic (isoflurane). At termination of the surgery, residual neuromuscular block was reversed by neostigmine 0.04mg/kg and atropine0.01mg/kg intravenously.

## Documentation of data

Patients' demographic data such as age, BMI, ASA status, co-morbidity, type and duration of the surgery, intraoperative data (HR, BP and end tidal CO2), hemodynamic parameters (measured every 15 minutes in first hour then every 30 min till the termination of the surgery), and ONSD were documented.

ONSD was taken after application of high frequency linear probe on closed eyelid and measured at 3 mm behind acoustic shadow of vitreous body at, T0: in the pre-anesthetic room, T1: following induction of anesthesia, T2: after pneumoperitoneum, T3: after Trendelenburg position and every 15 minutes till de-sufflation, T4: after De-sufflation, return to normal position and T5: 2-hours postoperatively after recovery from anesthesia.

**Ethical considerations**

The study was conducted in agreement with the Declaration of Helsinki, following approval by Institutional Research Board of the Faculty of Medicine, Mansoura University (code number: MS.22.12.2228). An informed and written consent was taken from each patient. All patients were informed about the study design and were informed about how the surgery is conducted. All data was collected by the researcher himself.

**Statistical analysis**

Data was analysed by the SPSS for Windows version 26 (SPSS Inc., Chicago, IL, USA). Numbers and percentages were utilized to represent qualitative data. After assessing for normality using the Kolmogrov-Smirnov test, quantitative data were presented using mean±SD for normally distributed data and median for non-normally distributed data. The results were evaluated for significance (*p-value*) at the ($\leq 0.05$) level. The Chi-Square test was utilized to compare qualitative data between groups. For normally distributed data, two independent groups were compared using the Student t test.

**Results**

Table **(1)** displays non-significant difference between the two studied groups as regarding age, weight, height, BMI, and ASA. Non-significant differences in surgical procedures and duration between both studied groups were detected. The results suggested that the two groups are demographically and clinically comparable, indicating well-matched cohorts for further analysis.

Heart rate changes between both studied groups showed non-significant difference at baseline (0 minutes). But during Follow-up periods (15 minutes to 3 hours), group D showed significantly lower heart rates compared to Group P at all time points ($p<0.05$).

Mean arterial pressure (MAP) changes showed no significant difference in MAP between the two studied groups at baseline (zero minutes), 15 minutes, 30 minutes, and 3 hours. But group D showed significantly lower BP compared to group P at 45 minutes, one hour, 1.5 hours, two hours and 2.5 hours with p values 0.014, 0.001, 0.001, 0.006 and 0.02 consequentially. Mean $EtCO_2$ Changes showed no significant differences in EtCO2 levels between both studied groups at any time point. EtCO2 levels remained relatively stable in both groups throughout the follow-up period.

**Table 1. Comparison of demographic characters, Intraoperative heart rate changes, mean arterial blood pressure, ETCo2 changes among studied groups**

| | **Group P n=38** | **Group D n=38** | ***P value*** |
|---|---|---|---|
| **Age/years** | 36.51±9.37 | 37.51±8.76 | 0.611 |
| **Weight b** | 72.67±6.65 | 74.7±5.37 | 0.124 |
| **Height** (cm) | 167.33±2.45 | 166.91±2.71 | 0.475 |
| **BMI** (Kg/m$^2$) | 25.95±2.78 | 26.61±2.17 | 0.255 |
| **ASA** | | | 0.634 |
| I | 25 (65.8%) | 23 (60.5%) | |
| II | 13 (34.2%) | 15 (39.5%) | |
| **Duration of operation** (min) | 125.63±37.6 | 124.82±44.62 | 0.932 |
| **Laparoscopic Myomectomy** | 3 (7.9%) | 8 (21.1%) | 0.320 |
| **Laparoscopic hysterectomy** | 9 (23.7%) | 8 (21.1%) | |
| **Diagnostic laparoscopy** | 20 (52.6%) | 16 (42.1%) | |
| **Tubal dissection** | 5 (10.5%) | 6 (15.8%) | |
| **Extra uterine removal of IUD** | 2 (5.3%) | 0 | |
| **Heart rate** (b/minute) | | | |
| 0 | 80.13±8.01 | 78.79±7.87 | 0.464 |
| 15 minutes | 77.63±7.19 | 68.87±6.93 | 0.001* |
| 30 minutes | 75.45±8.22 | 64.53±4.78 | 0.001* |
| 45 minutes | 78.47±5.46 | 64.95±5.38 | 0.001* |
| 1h | 81.13±8.08 | 66.32±4.07 | 0.001* |
| 1.5 h | 79.71±8.99 | 70.50±6.08 | 0.001* |
| 2 h | 80.26±8.26 | 72.26±5.24 | 0.001* |
| 2.5 h | 82.59±6.75 | 72.89±5.31 | 0.001* |
| 3 h | 83.33±8.96 | 73.0±4.57 | 0.028* |
| **Mean Arterial Blood Pressure** | | | |
| 0 | 84.89±11.91 | 83.68±10.17 | 0.635 |
| 15 minutes | 81.66±10.47 | 80.50±8.69 | 0.602 |
| 30 minutes | 83.82±11.37 | 82.50±10.02 | 0.594 |
| 45 minutes | 86.47±12.08 | 80.37±8.94 | 0.014* |
| 1h | 86.28±11.87 | 76.0±6.97 | 0.001* |
| 1.5 h | 85.16±10.50 | 74.18±6.85 | 0.001* |
| 2 h | 79.81±8.31 | 74.09±7.48 | 0.006* |
| 2.5 h | 78.77±9.04 | 72.89±6.75 | 0.02* |
| 3 h | 69.33±5.51 | 68.38±5.47 | 0.802 |
| **End Tidal Co2 (ETCo2)** | | | |
| 15 minutes | 29.87±0.77 | 30±0.77 | 0.461 |

| | | | |
|---|---|---|---|
| 30 minutes | 31.63±1.55 | 31.42±1.46 | 0.544 |
| 45 minutes | 36.42±1.0 | 36.50±0.952 | 0.726 |
| 1h | 36.42±1.41 | 35.95±1.09 | 0.105 |
| 1.5 h | 34.84±1.60 | 35.16±1.92 | 0.440 |
| 2 h | 33.11±1.98 | 33.26±2.02 | 0.732 |
| 2.5 h | 33.27±2.07 | 33.37±1.64 | 0.872 |
| 3 h | 31.33±1.52 | 33.0±1.77 | 0.186 |

*statistically significant, P value <0.05. Data were expressed as mean ± SD or number (percentage)

Table **(2)** shows significant lower values of ONSD in group D than group P after pneumoperitoneum with p value 0.002, immediately ,15, 30, 45 after Trendelenburg position with P value 0.001 and 60, 105, 120 minutes after Trendelenburg position with *P values* 0.017, 0.001,0.019 indicating potential variations in the ICP.

**Table 2. Mean ONSD changes among studied groups**

| **ONSD** | **Group P (n=38)** | **Group D (n=38)** | ***P value*** |
|---|---|---|---|
| **T0** | 4.66±0.16 | 4.68±0.14 | 0.373 |
| **T1** | 4.89±0.25 | 4.84±0.25 | 0.338 |
| **T2** | 5.26±0.24 | 5.07±0.28 | 0.002* |
| **T3** | | | |
| • immediately | 5.32±0.19 | 5.09±0.27 | 0.001* |
| • 15 min | 5.35±0.19 | 5.14±0.31 | 0.001* |
| • 30 min | 5.26±0.23 | 4.97±0.26 | 0.001* |
| • 45 min | 5.35±0.19 | 5.02±0.31 | 0.001* |
| • 60 min | 5.27±0.26 | 5.11±0.32 | 0.017* |
| • 75 min | 4.79±027 | 4.82±0.21 | 0.705 |
| • 90 min | 4.57±0.45 | 4.62±0.36 | 0.631 |
| • 105 min | 5.31±0.23 | 5.06±0.31 | 0.001* |
| • 120 min | 5.29±0.26 | 5.12±0.33 | 0.019* |
| • 135 min | 5.02±0.41 | 4.99±0.27 | 0.778 |
| **T4** | 5.12±0.27 | 4.99±0.30 | 0.059 |
| **T5** | 4.76±0.17 | 4.68±0.17 | 0.052 |

T0: in the pre-anesthetic room
T1: after induction of anesthesia
T2: after pneumoperitoneum
T3: after trendelenburg position and every 15 minutes till desufflation
T4: after Desufflation, return to normal position
T5: 2-hours postoperatively after recovery from anesthesia
*Statistically significant
Data were expressed as mean ± SD

Table **(3)** displays that there were non-significant differences in metoclopramide, granisetron, dexamethasone, or ketorolac doses observed between both studied groups. However, paracetamol dose differed significantly (*p < 0.001*).

**Table 3. Total dose antiemetics among studied groups**

| **Total Dose Antiemetics** | **Group P n=38** | **Group D n=38** | ***P value*** |
|---|---|---|---|
| Metoclopramide | 8.42±2.35 | 7.88±2.51 | 0.351 |
| Granisteron | 1.0±0.0 | 1.0±0.0 | 1.0 |
| Dexamethasone | 8.0±0.0 | 8.0±0.0 | 1.0 |
| Ketorolac dose | 30±0.0 | 30.0±0.0 | 1.0 |
| Paracetamol | 1000±0.0 | 0.0±0.0 | P<0.01 |

## Discussion

In the current study, dexmedetomidine in a dose of one mcg/kg for ten minutes followed by 0.4mcg/kg/h for an hour had a successful effect in reduction of ONSD in cases undergoing gynecological laparoscopic surgery in Trendelenburg position and this may reflect the attenuation of ICP elevation. Moreover, it was associated with a notable hemodynamic stability and insignificant changes in the adverse effects. Achieving an optimal surgical field in gynecological laparoscopic surgery often requires a combination of pneumoperitoneum and trendelenburg position. While necessary for visualization, this positioning and insufflation can raise ICP, as reported in previous studies **[3, 8]**.

**Dip et al., [11]** and **Blecha et al., [12]** had recorded that even in patients without preexisting neurological conditions, ICP levels exceeding 20 mmHg have been observed during laparoscopic surgery which requires pneumoperitoneum and Trendelenburg position. This elevated ICP can reduce cerebral perfusion pressure, which may severely affect individuals, particularly older adults or those with compromised cerebrovascular autoregulation.

Increased ICP occurs when the volume equilibrium within the cranial cavity is disrupted. Since the subarachnoid spaces of the brain and optic nerve sheath are connected, elevated ICP is reflected in the widening of the ONSD, which can be measured using ultrasound **[13]**.

Previous studies have demonstrated a potent correlation between increased ONSD measured by ultrasound and increased ICP obtained through transcranial Doppler or invasive monitoring techniques. These studies validate the utility of ONSD as a valid, non-invasive indicator for detecting ICP increase **[10, 14, 15]**.

The effect of pneumoperitoneum and trendelenburg position on ONSD had been assessed by **Colombo et al., [16]** in 20 cases undergoing laparoscopic radical prostatectomy in 2019, Colombo found that pneumoperitoneum and trendelenburg position had increased ONSD in comparison with his control group in which 10 volunteers in recumbent flat position had been studied, which may reflect ICP elevation.

Baseline ONSD, an indirect marker of ICP, is larger in obese individuals compared to those with normal weight. Under pneumoperitoneum, this disparity becomes more pronounced, likely due to higher pleural fat and thoracic pressure, which impairs ventilation and exacerbates ventilation-perfusion imbalances. Therefore, obese patients were excluded from our study **[11].**

Mean while **Zhu *et al.*, [8]** found that dexmedetomidine infusion in a dose of 0.5 mcg/kg for 10 min followed by 0.5mcg/kg/h till the termination of the surgery in gynecological laparoscopic surgery attenuates the increase in ONSD. Our findings showed that dexmedetomidine in a dose of one mcg/kg for ten minutes followed by 0.4mcg/kg/h for an hour had a successful effect on reduction of ONSD and this may reflect the attenuation of ICP elevation.

Dexmedetomidine is a selective α2-adrenergic agonist with sedative and neuroprotective properties, such as reducing norepinephrine release, constricting cerebral blood vessels via α2B receptor activation, and decreasing metabolic oxygen consumption consistent with findings by **Xu et al., [17]** and **He *et al.*, [7]** who highlighted its role in mitigating ICP elevation.

Moreover, **Chin et al., [18]** revealed that α2 agonists are more effective venous constrictors in the cerebrovascular system than arteriolar vasoconstrictors, and the venous compartments account for the bulk of cerebral blood volume, so α2 agonists can reduce intracranial pressure without significantly increasing arteriolar cerebrovascular resistance, and this may explain the role of dexmedetomidine in attenuation of the ICP elevation **[18, 19]**.

Although HR and BP revealed a significant decrease in group D at certain time points, hemodynamic stability was observed all over the period of our study, and this is in the same line with **Zhu et al., [8]** who revealed no notable differences in MAP between the groups, though heart rates were lower in the dexmedetomidine group at certain time points.

## Study limitations

The sample size was relatively small; larger multi-center studies are warranted. The study did not evaluate ONSD changes under varying angles and pressures to avoid interfering with the surgery.

## Recommendations

Further research should incorporate tools like transcranial Doppler for precise cerebral blood flow monitoring alongside cerebral oxygen saturation measurements. Further research should investigate the correlation between dynamic changes in ONSD and transcranial Doppler parameters during ICP fluctuations. Establishing this relationship could enhance the clinical utility of non-invasive monitoring techniques. Exploring different doses of dexmedetomidine and their effects on ICP. Examining long-term postoperative outcomes could provide deeper clinical insights.

**Conclusion**

Dexmedetomidine in the studied doses effectively reduces ONSD in patients undergoing gynecological laparoscopic surgery in the Trendelenburg position which may reflect a reduction in intracranial pressure elevation and was associated with notable hemodynamic stability. Its ability to attenuate ICP increase and maintain hemodynamic stability highlights its potential benefits to improve surgical outcomes.

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