

A prospective comparative evaluation of effect of dexmedetomidine and pregabalin on hemodynamic parameters during laparoscopic surgery

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Abstract

Background: Various pharmacological agents are used to attenuate the hemodynamic response of pneumoperitoneum by controlling sympathetic over activity. Present study has been designed to with primary objective to evaluate the efficacy of premedication with dexmedetomidine, pregabalin on hemodynamic parameters and secondary objective to know the analgesic requirement and adverse drug reaction. **Method:** 100 patients satisfying selection criteria were enrolled for this study and randomly divided in to two groups Group D, and Group P each having 50 patients. All patients were explained about visual analogue score. All patients were given same premedication. Various hemodynamic parameter, VAS and Ramsay sedation, analgesic requirement and adverse drug reaction was monitored. **Result:** There is significant difference between heart rate, systolic blood pressure, diastolic blood pressure and mean arterial blood pressure between dexmedetomidine group and pregabalin group. In the preoperative period and 30 and 45 min after end of pneumoperitoneum hemodynamic parameters were comparable to each other but in between that subject hemodynamic parameters in dexmedetomidine group was significantly lower. **Conclusion:** From our study we can conclude that dexmedetomidine produce better hemodynamic stability then pregabalin but it can produce bradycardia also in some patients. The mean of visual analogue score was significantly lower in dexmedetomidine group and mean of Ramsey sedation score was significantly higher in dexmedetomidine group. In present study fentanyl requirement was significantly higher in pregabalin group the dexmedetomidine.

Key words: dexmedetomidine, pregabalin, hemodynamic parameters

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INTRODUCTION

Hans Christian Jacobaeus of Sweden in 1910 performed first laparoscopic surgery and since last more than one century it become more popular and promoted as gentle surgery and many complicated procedure are performed. It is associated with less trauma, reduced post-operative complications and decreases duration of stay in hospital. To visualize the area of interest pneumoperitoneum is created which is a complex pathophysiological state with significant hemodynamic effect.^{1,2} These changes include increase in hypertension and tachycardia, increase in mean arterial pressure, increase in systemic and pulmonary

vascular resistance and increase in cardiac index.^{3,4} Hemodynamic consequences of increased intra-abdominal pressure are secondary to mechanical and neurohormonal responses. Sympathetic over activity also play important role.⁵ So appropriate control of sympathetic over activity is essential for hemodynamic stability during laparoscopic surgery.

Various pharmacological agents are used to attenuate the hemodynamic response of pneumoperitoneum by controlling sympathetic over activity. Dexmedetomidine is α_2 -AR receptor agonist used in various clinical conditions based on its analgesic, sedative, anxiolytic, cardiovascular stabilizing and reduced anaesthetic requirement without respiratory depression. Pregabalin is a GABA analogue act on $\alpha_2\delta$ subunit of voltage gated calcium channels on dorsal horn neurons. It possesses analgesic, anxiolytic, anti convalescent and sleep modulating effect. Both drugs are used to attenuate hemodynamic and stress response in laparoscopic surgery.^{5,6} After going through literature we have found that there are very few study is available regarding comparison of these drugs regarding their comparative efficacy in attenuating the undesired response of pneumoperitoneum in laparoscopic surgery. Jain A, Sinha R, Pandey S, Sahu V *et al.* has concluded that Intravenous dexmedetomidine is more effective than oral pregabalin in attenuating perioperative stress response. Vijayan NK, Talwar V, Dayal M *et al.* has concluded that Dexmedetomidine is a valuable adjunct to the technique of balanced anaesthesia for maintaining hemodynamic stability.^{7,8} Based on result of above literature present study has been designed to with primary objective to evaluate the efficacy of premedication with dexmedetomidine, pregabalin on hemodynamic parameters and secondary objective to know the analgesic requirement and adverse drug reaction.

MATERIAL AND METHOD

Place of study: Department of anaesthesia Konaseema institute of medical science and research Amalapuram'

Period of study: From January 2019 to January 2021

Study design: This study was conducted as a prospective comparative clinical study.

Ethics: Before start of this study an approval from institutional ethics committee was taken. A written informed consent was obtained from all patients before enrolling them for study.

Selection of patients: Patients posted for elective patients admitted in the department of general surgery for laparoscopic surgery under general anaesthesia were included for this study as per following inclusion and exclusion criteria.

Inclusion criteria: Age 18 to 60 years. American Society of Anaesthesiologists (ASA) Classes I and II.

Exclusion criteria: Diabetes mellitus, spinal deformities, bleeding or clotting disorders, Cardiopulmonary, renal and hepatic abnormality, peripheral neuropathy, hypersensitivity to drug and CNS disorder, chronic alcoholic

Sample size calculation: Based on true mean difference between treatment and control group and Expected population standard deviation, SD from previous study, type 1 error 0.5 and power of study 0.8 sample sizes was calculated to be 50 in each group.⁹

Method

So 100 patients satisfying selection criteria were enrolled for this study and randomly divided in to two groups Group D, and Group P each having 50 patients. All patients were explained about visual analogue score. All patients were given same premedication.

Group D: 50 patients of this group were received one vitamin B complex tablet 90 min before surgery and IV dexmedetomidine (1 μ g /kg) prepared in 100 ml of 0.9% normal saline were given 10 min before induction

Group P: 50 patients of this group were received 150 mg pregabalin in the form of two capsules each having 75 mg strength 90 min before surgery and 100 ml of 0.9% normal saline were given 10 min before induction. After induction heart rate, systolic blood pressure, diastolic blood pressure and SpO₂, and Ramsay's sedation scale were monitored at 10, 20, 30, 40, 45, 50, 55, and 60 min. In the operation theatre intravenous line was secured with 18G cannula. Monitor was attached and baseline parameters like heart rate (HR), systolic blood pressure (SBP), systolic blood pressure (SBP), respiratory rate, SpO₂, and electrocardiography (ECG) tracing was recorded. All patients included in this study have received same general anaesthesia protocol was followed. In the intraoperative period duration of pneumoperitoneum and duration surgery was recorded. Any change in vital parameters 20% from preoperative value were treated appropriately. Hemodynamic parameters were recorded before induction T₀ and first, second and 3rd min after induction was taken as T₁, T₂, and T₃ after that first, third, fifth and tenth min of intubation that was noted as T₄, T₅, T₆ and T₇, then before, after creation of pneumoperitoneum and end of pneumoperitoneum that was notes as T₈, T₉ and T₁₀ and then after every 15 min that was T₁₁, T₁₂, T₁₃ and so on.⁷ Visual analogue score and Ramsey sedation score was recorded preoperative period, after extubation then after 1 hr, 2hr 4 hr, 6 hr and 12 hour. Mean requirement of analgesic and adverse drug reaction was recorded. If VAS score was more than 4 then Fentanyl was administrated iv and requirement of bolus doses of fentanyl was also quantified.

RESULT

As per selection criteria 100 patients were included in this study as per selection criteria.

Table 1: Demographic profile of three groups under study

Variable	Group D	group P	P value
Age (mean yrs)	46.67±8.13	44.03±12.81	.22
sex			
M	26	30	.42
F	24	20	
BMI(kg/m ²)	23.12±1.98	23.94±2.01	.37
Duration of laparoscopy(minutes)	62.24±4.52	64.23±5.41	.07
ASA			
I	44	42	.54
II	6	8	
Duration of pneumoperitoneum	52.45±2.12	54.87±3.01	.17

As per table 2 regarding demographic profile of subjects in two groups are comparable to each other with respect to age (46.67±8.13 vs 44.03±12.81) (P=.22) and sex. There is no significant difference between two groups regarding BMI (23.12±1.98 vs 23.94±2.01) and ASA class. Both groups are comparable to each other regarding duration of laparoscopy (62.24±4.52 vs 64.23±5.41) (P=.07) and duration of pneumoperitoneum (52.45±2.12 vs 54.87±3.01) (P =.17).

Table 2: Comparison of heart rate between two groups

Variable	Group D	group P	P value
T ₀	81.54±4.70	80.26±7.21	.07
T ₁	77.45±4.85	82.36±3.89	.001
T ₂	78.22±3.84	84.56±6.47	.001
T ₃	76.21±5.86	86.87±7.86	.001
T ₄	79.41±4.45	88.21±6.89	.001
T ₅	78.48±3.46	91.01±4.87	.0001
T ₆	77.21±5.41	90.11±5.64	.0001
T ₇	78.48±4.56	89.45±4.54	.001
T ₈	74.62±4.10	86.02±3.98	.001
T ₉	76.45±4.85	86.44±6.47	.001
T ₁₀	78.41±3.84	87.24±5.45	.001
T ₁₁	79.42±5.42	84.78±6.01	.002
T ₁₂	78.54±4.52	79.45±3.12	0.87
T ₁₃	76.41±5.23	74.52±4.51	0.57

Regarding comparison of heart rate between two groups, there is significant difference between heart rate of dexmedetomidine group and pregabalin group. In the preoperative period and 30 and 45 min after end of pneumoperitoneum heart rate was comparable to each other but in between that heart rate of subject in dexmedetomidine group was significantly lower.

Table 3: Comparison of SBP between two groups

Variable	Group D	group P	P value
T ₀	121.23±8.48	120.86±9.87	.48
T ₁	118.64±10.12	122.41±10.65	.04
T ₂	116.54±9.98	118.47±11.54	.08
T ₃	119.47±10.44	123.45±10.88	.021
T ₄	120.44±9.87	128.23±8.45	.014
T ₅	121.75±10.01	126.47±9.41	.04
T ₆	122.87±8.47	128.01±7.47	.016
T ₇	123.09±9.44	127.89±8.87	.03
T ₈	121.65±8.74	128.42±9.45	.01
T ₉	121.22±9.45	127.86±10.27	.006
T ₁₀	117.87±10.12	124.33±9.46	.02
T ₁₁	118.24±9.45	124.21±8.44	.019
T ₁₂	110.21±11.25	118.35±14.25	.04
T ₁₃	116.45±14.68	118.47±12.41	.07

As per table 3 systolic blood pressures was within normal range in both groups. In the preoperative period and during induction SBP was comparable in both group but during the laparoscopic surgery SBP was lower in group D then group P which was significant statistically.

Table 4: Comparison of DBP between two groups

Variable	Group D	group P	P value
T ₀	77.98±6.45	79.44±7.01	.7
T ₁	76.23±8.42	82.14±10.12	.02
T ₂	74.44±10.12	84.25±12.02	.01
T ₃	77.41±9.47	86.88±10.47	.02
T ₄	76.56±11.23	89.41±10.84	.001
T ₅	77.14±10.23	91.21±10.44	.0001
T ₆	78.98±9.12	94.10±10.77	.0001
T ₇	74.56±10.12	91.23±9.98	.0001
T ₈	78.21±9.89	90.11±11.14	.001
T ₉	77.32±10.47	88.47±9.42	.01
T ₁₀	76.44±9.45	82.41±10.33	.001
T ₁₁	77.89±10.65	81.47±9.45	.016
T ₁₂	76.41±11.02	78.24±26.11	.04
T ₁₃	74.21±9.24	75.48±10.19	.7

As per table 4, diastolic blood pressure was significantly lower in group D then group P during surgical procedure but in preoperative period and 45 min after end of pneumoperitoneum DBP was comparable in both groups.

Table 5: Comparison of MAP between two groups

Variable	Group D	group P	P value
T ₀	91.24±9.45	92.22±9.22	.87
T ₁	88.89±10.18	98.44±10.86	.001
T ₂	86.35±8.25	101.21±8.56	.0001
T ₃	91.12±10.48	104.12±11.14	.001
T ₄	92.22±11.35	101.48±8.84	.001
T ₅	89.21±10.4	99.47±11.48	.002
T ₆	92.44±8.42	104.68±8.41	.0001
T ₇	93.23±10.75	99.14±9.87	.042
T ₈	88.38±11.22	100.47±6.41	.0001
T ₉	90.11±9.12	98.23±7.68	.0024
T ₁₀	68.21±32.12	72.11±29.41	.041
T ₁₁	76.22±10.23	77.24±23.25	.064
T ₁₂	78.14±20.14	79.12±28.22	.09
T ₁₃	84.22±12.47	86.78±9.47	.78

As per table 5, mean arterial pressure was significantly lower in group D then group P during surgical procedure but in preoperative period and 15 min, 30 min and 45 min after end of pneumoperitoneum mean arterial pressure was comparable in both group as P value was more than .05.

Table 6: Comparison of VAS score of two groups

Variable	Group D	group P	P value
Pre op	1.64±.41	1.66±.58	.84
After extubation	1.92±.44	2.01±.64	.06
1hr	2.47±.49	3.21±.74	.02
2hr	3.44±.89	4.98±.96	.001
3hr	3.88±.96	5.85±1.01	.001
4hr	3.65±.86	4.21±.98	.02
6hr	2.88±.12	2.68±.56	.09

The mean of visual analogue score was significantly lower in dexmedetomidine group then pregabalin group except in preoperative and 6 hour after extubation.

Table 7: Comparison of Ramsey sedation score of two groups

Variable	Group D	group P	P value
Pre op	1.94±.46	1.98±.54	.78
After extubation	2.94±.51	2.41±.44	.028
1hr	3.52±.62	2.21±.47	.012
2hr	3.01±.62	2.35±.56	.034

3hr	2.89±.55	2.17±.57	.046
4hr	3.014±.32	1.92±.39	.001
6hr	2.51±.55	1.75±.87	.018

The mean of Ramsey sedation score was significantly higher in dexmedetomidine group then pregabalin group except in preoperative.

Table 8: Adverse drug reaction

Adverse reaction	Group P	group G
Nausea and vomiting	0	0
Headache	0	1
Somnolence	1	3
Dizziness	1	3
Bradycardia	3	0
Hypotension	1	0

Regarding adverse drug reaction Somnolence and Dizziness are common in pregabalin group but Bradycardia and Hypotension was common in dexmedetomidine group.

Table 9: Analgesic requirement

Variable	Group D	group P	P value
Fentanyl requirement	34.25±22.47	65.24±44.32	.0001

There is significantly more requirement of fentanyl in group P then group D.

DISCUSSION

Laparoscopic surgery is very popular and considered as gentle surgery with less morbidity and duration of stay in hospital but hemodynamic instability due to pneumoperitoneum is major challenge especially in patents cardio respiratory compromised patients. Various drugs have been used for hemodynamic stability in intraoperative and post operative patients undergoing laparoscopic surgery with different outcome. Present study has been designed to with primary objective to evaluate the efficacy of premedication with dexmedetomidine, pregabalin on hemodynamic parameters and adverse drug reaction associated with it. Both drugs have different mechanism of action. Subjects allotted in both premedication groups are comparable to each other with respect to age, sex BMI, ASA class duration of laparoscopy and duration of pneumoperitoneum which is similar to the study of Jain A, Sinha R, Pandey S, Sahu V *et al.* and Vijayan NK, Talwar V, Dayal M *et al.*^{7,8} Regarding comparison of hemodynamic parameters heart rate of dexmedetomidine group of subjects are significantly lower than pregabalin group ($P>.05$). There was no fluctuation in systolic blood pressure, diastolic blood pressure and mean arterial blood pressure in dexmedetomidine group and mean value of these parameters were lower in dexmedetomidine group then pregabalin group ($P>.05$). This finding corroborates with the study of Samal, S., S. K. Pattnaik, N. Swain, and S. S. Jena *et al.* and Ibrahim E, Sultan W, Helal S, Abo-Elwafa H, Abdelaziz A. *et al.*^{10,11} The mean of visual analogue score was significantly lower in dexmedetomidine group then pregabalin group except in preoperative and 6 hour after extubation. The mean of Ramsey sedation score was

significantly higher in dexmedetomidine group then pregabalin group except in preoperative. This finding is supported with the work of Lee C, Lee J, Lee G, Lee H, Koh E, Hwang *et al.* and J. Salama AK, Abdallah NM *et al.*^{12,13} Regarding adverse drug reaction Somnolence and Dizziness are common in pregabalin group but Bradycardia and Hypotension was common in dexmedetomidine group. This is supported by the work of Jain A, Sinha R, Pandey S, Sahu V *et al.*, Vijayan NK, Talwar V, Dayal M and Sambandam KG, Chandrasekran D, Dhanasekaran R, *et al.*^{7,8,14}

In present study fentanyl requirement was significantly higher in pregabalin group the dexmedetomidine. Manne GR, Upadhyay MR, Swadia V *et al.* has concluded that low dose dexmedetomidine infusion in the dose of 0.4 mcg/kg/h effectively attenuates hemodynamic stress response during laparoscopic surgery with reduction in post-operative analgesic requirements.¹⁵ This finding supports our study. Our study is also supported by the work of Bielka, K., Kuchyn, I., Babych, V. *et al.*¹⁶

CONCLUSION

From our study we can conclude that dexmedetomidine produce better hemodynamic stability then pregabalin but it can produce bradycardia also in some patients. The mean of visual analogue score was significantly lower in dexmedetomidine group and mean of Ramsey sedation score was significantly higher in dexmedetomidine group. In present study fentanyl requirement was significantly higher in pregabalin group the dexmedetomidine.

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