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Original Article

Propranolol is effective in decreasing stress response due to airway manipulation and CO_2 pneumoperitoneum in patients undergoing laparoscopic cholecystectomy.

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Abstract

Purpose: to study the effect of Propranolol on hemodynamic response due to airway manipulation and carbon dioxide pneumoperitoneum on laparoscopic cholecystectomy cases. **Methods:** 63 patients undergoing laparoscopic cholecystectomy under general anaesthesia were randomly divided into 3 groups; group 1 received 1.0 mg of Propranolol, group 2 received 0.5 mg of Propranolol and group 3 received 1 ml saline 5 minutes before induction of anaesthesia. Haemodynamic parameters were recorded for every 5 minutes from basal to 5 minutes after extubation and analyzed. **Results:** Balanced anaesthesia used in our set up is effective in decreasing stress response due to airway manipulation (laryngoscopy and endotracheal intubation) but not effective in that due to CO_2 pneumoperitoneum. Propranolol 1 mg 5 minutes before anaesthesia is effective in decreasing stress response due to airway manipulation and CO_2 pneumoperitoneum in these groups of patients. **Conclusion:** Propranolol effectively blunts the stress response due to CO_2 pneumoperitoneum during laparoscopic cholecystectomy.

Key words: Propranolol, laparoscopy, stress response, CO_2 pneumoperitoneum

Laryngoscopy and intubation cause a marked increase in adrenergic activity due to great stress response. The resulting tachycardia, hypertension and arrhythmia may cause hemodynamic instability in patients with cardiovascular disease. Laparoscopy for diagnostic and operative procedures offers specific advantage to the patient, mainly aesthetic, less pain and shorter hospital stay due to less morbidity. Carbon dioxide pneumoperitoneum causes similar hemodynamic changes as in airway manipulation. The pattern may be due to increased abdominal pressure, neurohumeral responses and absorbed CO_2 (5,7).

Much of the initiation of the stress response relies on the outflow of the sympathetic neuronal pathway. Some success has been achieved in suppressing this response with the use of a and ß receptor blockade. Cortisol release and hepatic glycogenolysis have both been reduced by the use of such agents. Many pharmacological techniques using adrenoceptor blockers, ca channel blockers, opoids and vasodilators have been used to attenuate these responses, which indicate the lack of an ideal drug for this purpose(6).

Thus, in a prospective randomized trial, we investigated and compared the hemodynamic stress response in patients after airway manipulation and CO_2 pneumoperitoneum after giving Propranolol. On intravenous administration, highly lipid soluble drugs like Propranolol has peak onset within 10 minutes(onset within 2 minutes with IV and 30 minutes with oral administration) , elimination half life of 3- 4 hours and extensively metabolized in liver and excreted in urine.

Patients and methods:

63 patients (19-72 yr, ASA physical status I and II) undergoing laparoscopic cholecystectomy were taken for study. Exclusion criteria were patients with hypertension; coronary artery disease, chronic obstructive airway diseases and more than one attempt of intubation. All patients were premedicated with diazepam 5 mg, ranitidine 150 mg and metoclopramide 10 mg in the night before surgery. They were randomly divided into three groups and were given following medicines five minutes before induction of anaesthesia:

Group 1: 1.0 mg of Propranolol
Group 2: 0.5 mg of Propranolol
Group 3: 1.0 ml of saline

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General anaesthesia with pethidine, sodium Thiopentone, Succinylcholine and endotracheal intubation and anaesthesia maintained with oxygen, Pancuronium and 1.0±0.5% halothane. Neostigmine and atropine was used for Pancuronium reversal. Heart rate and blood pressure was recorded in following intervals:

1. Basal
2. 5 minutes after drug
3. before intubation
4. after intubation
5. before pneumoperitoneum
6. 15 minutes after pneumoperitoneum
7. before extubation
8. after extubation

Haemodynamic changes after airway manipulation and CO_2 pneumoperitoneum was monitored and analyzed in saline group and comparative study was done between saline and two Propranolol groups. Intergroup and intragroup significance was tested with independent samples t test and the p value less than 0.05 was taken as significant difference between the two groups.

Results

All three groups were comparable in respect to age, weight, gender, duration of anaesthesia and duration of surgery (table 1 and 2 below).

Table 1. Age, weight and gender distribution:

Study groups	Age years, Mean ± SD	M:F ratio	Weight kg, Mean ± SD
Group 1	24-66, 43.6 ± 14.96	5:16	50- 79, 58.7 ± 9.27
Group 2	24-72, 46.2 ± 16.84	3:18	45-70, 55.1± 8.43
placebo	19-57, 35.76 ± 11.03	3:18	41-75, 60.90 ± 9.92

Table 2. Duration of anaesthesia and surgery:

Study groups	Duration of anaesthesia, minutes, mean ± SD	Duration of surgery, minutes, mean ± SD
Group 1	50-125, 76.5 ± 21.80	45-115, 67.5 ± 20.03
Group 2	45-150, 83.4 ± 36.83	40-150, 77.8 5± 41.7
placebo	55-135, 91.4 ± 22.25	45-120, 80.47 ± 19.16

Age range of patients was 19 to72 years and weight was 41 to 79 kg, females were more in all groups, probably symptomatic cholelithiasis is more common in them. Duration of anaesthesia was 45 minutes to maximum of 150 minutes and duration of surgery was 40 minutes to maximum of 150 minutes and three groups were comparable in duration of anaesthesia and surgery.

Table 3. Haemodynamic parameters in saline (placebo) group of patients:

Haemodynamics	Heart rate	MAP
basal	96.10 ± 12.34	106.61 ± 12.76
After intubation	101.76 ± 12.06	106.85 ± 10.23
Test of significance	***P =0.146***	***P=0.144***
After pneumoperitoneum	107.42 ± 17.39	119.52 ± 18.06
Test of significance	***P = 0.021***	***P = 0.011***

Haemodynamic changes in saline group, i.e. basal heart rate and mean arterial pressure was compared with that after intubation and after CO_2 pneumoperitoneum. Statistical test showed depth of anaesthesia was adequate for minimizing stress response after laryngoscopy and intubation (minimal change in heart rate and MAP, $p<0.05$) and inadequate for stress response due to pneumoperitoneum (significant change in Heart Rate and MAP, $p< 0.05$). Heart rate and mean arterial pressure of Propranolol groups at different time interval was compared with that of saline group. There was highly significant difference in heart rate between Propranolol 1 mg and saline group ($p=0.00$) and significant difference between Propranolol 0.5 mg and saline group ($p <0.05$), table IV below.

Table 4. Haemodynamic parameters, heart rate, per minute (mean± SD):

Study group	Saline group	Group 1	significance (p value	Group 2	Significance (p value)
basal	95.57±12.27	84.71±21.25		94.12±25.07	
After drug	97.47±19.20	83.57±10.66	0.00 ?	93.57±22.34	0.04 ?
Before intubation	100.44±18.32	77.85±7.81	0.00 ?	89.57±21.78	0.05 ?
After intubation	101.76±12.06	84.71±13.91	0.00 ?	98.00±20.36	0.017 ?
Before pneumoperitoneum	102.33±8.07	86.47±13.65	0.00 ?	96.42±20.34	0.039 ?
After pneumoperitoneum	107.42±17.39	82.71±11.80	0.00 ?	92.20±17.03	0.023 ?
Before extubation	103.28±12.05	79.04±15.09	0.00 ?	90.42±16.96	0.011 ?
After extubation	104.04±13.24	78.90±9.14	0.00 ?	84.71±21.26	0.16 ?

? : $p<0.01$, highly significant, ?: $P < 0.05$, significant test

Mean arterial pressure (MAP) was compared among the three groups in different stages of Intra-anaesthetic period. The rise in MAP is there in saline group in all stages of anaesthesia in comparison to Propranolol groups. The rise in MAP is maximum after CO_2 pneumoperitoneum, which shows the stress response is more after pneumoperitoneum compared to that after endotracheal intubation. In Propranolol groups, the rise in MAP is minimal, highly significant difference between Propranolol 1 mg and saline group and significant difference between saline and 0.5 mg Propranolol group, table V below.

Propranolol may cause bradicardia in post operative period, so that we monitored the patients with pulse oximeter and there was no heart rate less than 55 in any patients up to 6 hours of drug use.

Table 5. Haemodynamic parameters mean arterial pressure (MAP), mmHg (mean ±SD):

Study group	Saline group	Group 1	significance (p value)	Group 2	Significance (p value)
Basal	106.61±12.76	102.42±12.42	0.287	102.50±8.53	0.234
After drug	109.57±11.88	102.0±13.11	0.057	101.57±11.56	0.040
Before intubation	101.19±12.16	96.95±8.95	0.206	100.28±12.25	0.927
After intubation	101.14±15.06	92.61±11.20	0.041	97.14±18.68	0.051
Before pneumoperitoneum	103.47±13.35	94.95±19.30	0.105	94.57±11.85	0.051
After pneumoperitoneum	119.52±18.07	93.42±15.39	0.000	95.14±11.27	0.01
Before extubation	106.76±16.10	103.90±14.78	0.553	103.57±14.10	0.420
After extubation	110.61±11.93	103.52±12.55	0.040	105.85±16.51	0.130

Discussion

Propranolol is non selective ß blocker, which may be effective in decreasing stress response due to laryngoscopy as well as CO_2 pneumoperitoneum, which are due to adrenergic over activity secondary to catecholamine release. $ß_1$ effect decreases heart rate and $ß_2$ effect on skeletal muscle vascular bed may help in decreasing after load of heart. We hypothesized that these effects may be useful during laparoscopic surgery done under General Anaesthesia. It may cause bradicardia, AV dissociation and hypoglycaemia. Bronchospasm, congestive heart failure and drowsiness can occur with low doses.

In our study, balanced anaesthesia technique used was adequate to decrease the stress response due to laryngoscopy and endotracheal intubation but was inadequate for that due to CO_2 pneumoperitoneum. We used 0.5 and 1.0 mg of Propranolol to decrease that response in patients with laparoscopic surgery. Propranolol 1 mg decreased the heart rate and pressure response after intubation and after CO_2 pneumoperitoneum significantly. 0.5 mg Propranolol was effective in tachycardia but pressure response was not as good as 1 mg of drug.

In a double blind study, esmolol an ultra short acting beta 1 receptor antagonist was compared to physiological saline under 1 MAC isoflurane anaesthesia. Esmolol effectively prevented the pressure response to induction and maintenance of CO2 pneumoperitoneum (1).

The cardiovascular changes follow a pattern of linear increases of SVR following induction of GA, insufflations of the abdomen with CO2 and reverse trendelenberg position and this increase in after load could lead to both an increase in myocardial O_2 consumption and to the potential risk of myocardial ischemia in congestive heart failure in susceptible patients. Laparoscopic surgery of the upper abdomen has become a frequently performed surgery due to the perception that is a smaller operation than the open surgery and that postoperative recovery is faster, nevertheless, the procedure results in considerable alterations of Intraoperative cardiopulmonary function. (8)

The pneumoperitoneum created for laparoscopy increased pulmonary capillary wedge pressure by 32%, central venous pressure by 58% and mean arterial pressure by 39% in horizontal position (3,4). Intra abdominal insufflation of CO_2 is associated with Haemodynamic and hormonal changes. Investigating CO_2 and argon insufflated pigs and using a vasopressin antagonist ,it is found that CO_2 insufflation released vasopressin, which in turn , induced Haemodynamic changes(2).

Conclusion

1 mg Propranolol is superior to 0.5 mg in decreasing pressure response due to CO2 pneumoperitoneum in laparoscopic surgery in ASA I and II patients without significant bradicardia in post operative period .

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