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Original Research Article

To compare the efficacy of dexmedetomidine and esmolol in attenuation of pressor response to laryngoscopy and intubation in patients undergoing general anaesthesia for elective laparoscopic cholecystectomy

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ABSTRACT

Aims: Assessment of the degree of attenuation of pressor response to tracheal manipulation, with Esmolol and Dexmedetomidine as premedication, in patients posted for elective laparoscopic cholecystectomy.
Settings and Design: The current randomised prospective study was designed and sixty patients of American Society of Anaesthesiologist class I and II undergoing laparoscopic cholecystectomy were included in the study.
Methods and Materials: Sixty patients were randomised into two groups, Group E and Group D. Patients of group E (n=30) received Inj. Esmolol (0.50 mg/kg) in 10 ml normal saline two minutes before intubation and patients of group D (n = 30) received Inj. Dexmedetomidine (0.5μg/kg) in 10 ml normal saline over 10 minutes prior to intubation. In both the groups, at baseline and at various time intervals after study drug administration, hemodynamic parameters were recorded.
Statistical analysis: SPSS software version 15.0 is used for statistical analysis. The values were represented as Mean $\pm$ SD. Student's t-test was used for analysis of various parameters.
Results: The demographic data and initial baseline hemodynamics were statistically similar. The sympathetic response to tracheal manipulation was significantly attenuated ($p<0.05$) in the two groups but dexmedetomidine blunts the pressor response more effectively.
Conclusion: Among dexmedetomidine and esmolol, dexmedetomidine seem to be a promising drug to control the pressor response to tracheal manipulation.

1. Introduction

Now-a-days laparoscopic cholecystectomy is the treatment of choice for symptomatic gall stone disease in elective settings. Tracheal manipulation for intubation leads to a surge in the catecholamine levels leading to increase in HR and blood pressure.[1,2]

Prevention of detrimental physiological response to tracheal manipulation is indispensible. No pharmacological agent till date has been proved to be an ideal agent.[1]

Esmolol (β-blocker), is an effective drug for maintenance of hemodynamic stability following tracheal manipulation for intubation with adequate safety.[1] However, esmolol has shown a good control for heart rate but a dose-dependent response as far as blood pressure was concerned.[1–3]

α -Agonists have also been used to block the hemodynamic effects. Dexmedetomidine has greater affinity for α 2 receptor over α 1 (1620:1).[1] Dexmedetomidine decreases sympathetic and cardiovascular response to tracheal manipulation when used as premedication.

A constant search is going on for a drug which could maximally attenuate the pressor response for tracheal intubation, with maximum safety profile. In continuation to the search we have designed the present study.

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2. Materials and Methods

After clearance from Ethical Committee, the study was conducted at Department of Anaesthesiology, Shri Guru Ram Rai Institute of Medical & Health Sciences, Dehradun.

After written and informed consent sixty ASA class I & II adults (20 -50 years) posted for laparoscopic cholecystectomy under general anaesthesia, were included in the study.

2.1. Exclusion criteria would be

1. Patients with Mallampati grade III & IV,
2. Any other comorbidities (COPD, IHD, HTN, DM, Renal/ Hepatic dysfunction, etc.),
3. morbid obesity,
4. Patients who could not be intubated within 2 minutes of administration of study drugs.
5. Patients who did not consent.

A night before surgery the patients were visited for pre-anaesthetic review and standard institutional preoperative advice was given.

When the patients arrive in the operating room baseline hemodynamic parameters were recorded.

The patients were randomly divided into two groups (n=30) group E (Esmolol) and group D (Dexmedetomidine). The randomization was done using computer generated system of randomization.

Group E : The patients received Inj. esmolol (0.50 mg/kg) two minutes before intubation.

Group D: The patients received Inj. Dexmedetomidine (0.50 μg /kg) in 10 ml normal saline over 10 minutes prior to intubation.

Inj. Fentanyl (2 μg/kg) was administered for analgesia in all the patients. Preoxygenation was done for 3 minutes with 100% oxygen. All 60 patients received the study drug before tracheal manipulation, according to the respective division of two groups, Group E and Group D. Inj. Propofol (1.5mg/kg) was used as inducing agent. Patients were intubated following the administration of paralyzing dose of Inj. Succinylcholine (1.5 mg/kg). Anaesthesia was maintained with mixture of Oxygen and nitrous oxide with Isoflurane as inhalational agent delivered through closed circuit. Muscle relaxation was maintained with Inj. Vecuronium (0.1mg/kg) followed by incremental doses of Inj. Vecuronium (0.02 mg/kg).

After the completion of the surgery, patients were extubated following the reversal of residual muscle paralysis with the combination of Inj. Glycopyrrolate (10μg/kg) and Inj. Neostigmine (50μg/kg).

The hemodynamic parameters were obtained at various time intervals:

Immediately before study drug was administered as base line - T0

At 1 min after administration of drug but prior to intubation - T1

At 1 minute post intubation - T2

At 3 minutes post intubation - T3

At 5 minutes post intubation but prior to surgical incision - T4

Any complication (bradycardia, hypotension, sedation) was noted and managed appropriately. Bradycardia (HR<50/min.) was proposed to be treated with intravenous Inj. Atropine (0.6mg). Hypotension (MAP<20% of baseline or SBP<90 mm Hg) was planned to be treated with 200ml crystalloid bolus and Inj. Phenylepherine in 100 μg increments upto maximum of 500 μg, if required.

The observations were made by another person during the study and were subjected to statistical analysis.

SPSS software version 15.0 is used for statistical analysis. The values were represented as Mean $\pm$ SD and Number (%). Student's t-test was used for inter group comparison of various parameters.

3. Results

The mean systolic blood pressure of Group E and Group D were statistically comparable at T0.

The mean systolic blood pressure of Group D was found to be lower than that of Group E at T1, T2, T3, T4.

At T2 and T3, difference was found to be statistically significant (p value <0.05) but at T4 this difference was statistically highly significant (p value <0.001)

The difference in diastolic blood pressure of the two groups was found to be statistically insignificant ($p>0.05$) at T0 and T1.

The diastolic blood pressure of Group D was found to be lower than that of Group E and the difference was found to be statistically significant ($p<0.05$) at T2, T3 and T4.

The mean arterial pressure of Group D patients was found to be higher than that of Group E but the difference was statistically insignificant ($p>0.05$) at T0.

The mean arterial pressure of Group D patients was found to be lower than that of Group E patients and this difference was found to be statistically significant ($p<0.05$) at T1, T2, T3 and T4.

Hence Dexmedetomidine controls blood pressure more effectively than Esmolol.

The difference in heart rate of Group D and Group E was found to be statistically insignificant ($p>0.05$) at T0.

Heart rate of patients in Group E patients was found to be higher than that of patients in Group D and this was statistically highly significant ($p<0.001$) at T1.

The heart rate of patients in Group D was found to be lower than that of patients in Group E and this difference was found to be statistically significant ($p<0.05$) at T2, T3 and T4.

Hence Dexmedetomidine decreases heart rate more than Esmolol.

Table 1: Patient age height and weight in the two groups

	Group E (n=30)	**Group D (n=30)**	**p-value**
Age (years)	37.07±4.43	37.27±4.4	0.86
Height (cm)	159.53±4.31	158.33±4.98	0.32
Body weight (kg)	76.93±7.72	78.9±8.51	0.35

Table 2: Systolic blood pressure of two groups at different time intervals

	Group D (n=30)		**Group E (n=30)**		**Statistical significance (Student 't' test)**	
	Mean	SD	Mean	SD	't'	'p'
Baseline (T0)	128.00	9.16	126.86	10.71	0.440	0.662
At 1 min prior to intubation (T1)	121.69	5.90	124.59	8.22	-1.567	0.123
At 1 min post intubation (T2)	135.69	4.98	140.09	7.43	-2.690	0.009
At 3 min post intubation (T3)	132.00	5.96	137.36	6.11	-3.437	0.001
At 5 min post intubation (T4)	126.92	4.97	133.59	7.01	-4.244	<0.001

Table 3: Diastolic blood pressure of two groups at different time intervals

	Group D (n=30)		**Group E (n=30)**		**Statistical significance (Student 't' test)**	
	Mean	SD	Mean	SD	't'	'p'
Baseline (T0)	83.06	7.88	81.62	6.20	0.782	0.438
At 1 min prior to intubation (T1)	76.26	7.92	79.76	8.69	-1.629	0.109
At 1 min post intubation (T2)	87.29	7.95	91.22	7.16	-2.012	**0.049**
At 3 min post intubation (T3)	84.72	9.01	89.26	7.08	-2.164	**0.035**
At 5 min post intubation (T4)	79.86	6.51	87.29	8.05	-3.929	**<0.001**

Table 4: Mean arterial pressure of two groups at different time intervals

	Group D (n=30)		**Group E (n=30)**		**Statistical significance (Student 't' test)**	
	Mean	SD	Mean	SD	't'	'p'
Baseline (T0)	98.03	7.15	96.99	4.79	0.675	0.502
At 1 min prior to intubation (T1)	91.40	5.25	94.70	6.67	-2.133	**0.037**
At 1 min post intubation (T2)	103.42	5.66	107.51	4.69	-3.045	**0.003**
At 3 min post intubation (T3)	100.48	6.61	105.29	4.79	-3.225	**0.002**
At 5 min post intubation (T4)	95.54	4.72	102.72	6.46	-4.910	**<0.001**

Table 5: Heart rate at different time intervals in the two groups

	Group D (n=30)		**Group E (n=30)**		**Statistical significance (Student 't' test)**	
	Mean	SD	Mean	SD	't'	'p'
Baseline (T0)	83.46	4.54	84.82	6.08	-0.985	0.329
At 1 min prior to intubation (T1)	78.22	4.86	89.86	5.97	-8.262	**<0.001**
At 1 min post intubation (T2)	90.89	6.43	110.56	7.70	-10.724	**<0.001**
At 3 min post intubation (T3)	85.06	5.81	106.39	7.37	-12.434	**<0.001**
At 5 min post intubation (T4)	80.52	5.49	100.12	7.90	-11.145	**<0.001**

4. Discussion

Hemodynamic changes are the principal changes following tracheal manipulation because of increase in the sympathetic and sympathoadrenal reflex activity (Kovac *et al*).[4] These changes can be detrimental in some patients as in patients with hypertension, coronary artery disease, or cerebrovascular disease as they can lead to myocardial infarction, arrhythmia and cerebrovascular insult (Lev *et al.*, 1994).[5] Several drugs prevent accentuation of hemodynamic response to tracheal manipulation such as opioids, α- and ß- adrenergic blockers, vasodilator agents inhibiting sympathoadrenal response and lidocaine (Helfman *et al.*, 1991).[6]

In present study, an assessment of one of the commonly used beta-blocker esmolol for premedication against stress generated by hemodynamic reflex[7–12] was done against new drug dexmedetomidine, an α-adrenergic agent, which has been used relatively less but shown to be a promising choice against hemodynamic reflex.[13–16]

Many studies have used 0.5 0 μg/kg dose of dexmedetomidine to be efficient for controlling hemodynamic reflex following laryngoscopy and intubation.[16] Although, literature has shown a high variability in dosage selection of esmolol, with a range of 0.2 to 2.0 mg/kg. We have used 0.5 mg/kg dose of esmolol for the study.

All the patients in Group D and Group E were statistically similar with respect to height, weight and age. At T0, the hemodynamic parameters of two groups were statistically comparable.

There was statistically insignificant ($p>0.05$) fall in systolic blood pressure at T1 in both the groups. There was a sharp increase in systolic blood pressure in both the groups at T2. In both the groups a decreasing trend of systolic blood pressure was observed at T3 and T4. At T1 and T4, group D had statistically significant lower mean systolic blood pressure whereas at T2 and T3 it is significantly higher mean value when compared with the values at T0.

In Group E, at all the post-intubation intervals, the values of mean systolic blood pressure were higher than that at T0.

The increase in blood pressure and heart rate is greatest at T2 following tracheal manipulation, and this surge in SBP lasts for 5 to 10 minutes (Bruder *et al.*, 1992).[17] In present study, we found that while both the drugs were capable of controlling the blood pressure by limiting the post-intubation rise within 10-15%. Thus showing an attenuation of pressor response by almost two-third. However, with respect to heart rate only, dexmedetomidine could attenuate the response whereas β-blocker (esmolol) has failed to prevent the rise in heart rate.

Efficacy of dexmedetomidine in variable doses has been studied and significant incidence of bradycardia is seen with higher doses of the same.[18] However, the dose of 0.50 μg/kg used in our study, did not result in any such event.

In present study, although esmolol provided a good attenuating response as far as blood pressure control is concerned; however it failed to provide a good control over heart rate. One of the explanations for this could be due to selection of a lower dose of esmolol in our study. Clinical studies have shown that esmolol has shown to have a delayed reduction in heart rate which is preceded by fall in blood pressure (Cuneo *et al.*, 1994),[19] this could be the reason for selective action of esmolol on blood pressure and not on heart rate. As hemodynamic reflex is a transitory response, it is essential that the action of drug should be initiated within a short time. It also shows a dose dependent control on the heart rate and cardiac index (Cuneo *et al.*, 1994).[19]

There are limited studies available that compare esmolol and dexmedetomidine. The results obtained in our study were similar to Yavascaoglu *et al.* (2008)[20] on whose study we based our dosage selection. They also concluded that, Dexmedetomidine is more efficient than Esmolol, in attenuating the pressor reponse. They found that fall in MAP and HR was more in Group D than in Group E, both the observations are in accordance with the present study. In another study (Gogus *et al.*, 2014)[21] results were comparable to our study as for heart rate, however, for blood pressure they showed a superior control of esmolol using a dosage of 2 mg/kg against 1μg/kg dexmedetomidine. This difference could be attributed to a proportionally double dosage of esmolol as compared to dexmedetomidine in their study.

In present study, no side effects of either of two drugs were observed. Both the drugs were safe, probably due to lower dosages of the drugs used in the study, however, they provided a good attenuating response. However, dexmedetomidine no doubt had a better and superior control. The present study endorsed the findings reported in some previous works. However, as far as comparable dosage of esmolol is concerned, there are studies reporting a high variability, it is essential that an optimum dose of drugs should be determined in order to avoid probable side effects and minimize the drug use. Hence, further studies on comparison of two drugs are recommended at variable dosage to find out the exact comparability of two drugs as well as to determine the optimum dose for both the drugs.

5. Conclusion

Following tracheal manipulation, Dexmedetomidine blunts the pressor response more effectively than Esmolol. Hence, dexmedetomidine (0.5μg/kg) is a promising option for blunting the pressor response.

6. Source of Funding

None.

7. Conflict of Interest

None.

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