Section: Anaesthesia

Original Research Article

COMPARATIVE EVALUATION OF DEXMEDETOMIDINE VERSUS PROPOFOL FOR SEDATION IN ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY (ERCP) PATIENTS WITH IMPAIRED LIVER FUNCTION

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ABSTRACT

Background: The indications for endoscopy have increased enormously as it has matured from a purely diagnostic procedure to a therapeutic subspecialty. Number of studies has been done to compare propofol and dexmedetomidine for sedation for outdoor endoscopy procedure in patients with impaired liver function. In recent years, dexmedetomidine has been used as an alternative to propofol in providing sedation. **Study Design:** Open-label Randomised Controlled Trial. **Aims:** In this study we aim to compare haemodynamic, respiratory and safety profile of dexmedetomidine with propofol for ERCP in patients with impaired liver function.

Materials and Methods: A total of 50 patients of American Society of Anaesthesiologists grade II aged 18 to 60 years were divided into two groups (25 each) depending upon the use of the drug under investigation in accordance with randomized, open label, controlled trial. In patients receiving propofol a bolus of 1mg /kg were given then propofol infusion was started at 1mg/kg/hr for maintenance of sedation whereas in patients receiving dexmedetomidine a loading dose of 1mcg /kg was given over 10 mins then infusion was started at 0.5mcg/kg/hr. The changes in the heart rate (HR), systolic blood pressure (SBP) diastolic blood pressure (DBP) and mean arterial blood pressure (MAP), respiratory rate and oxygen saturation(SpO2) were noted before during and after recovery from sedation during ERCP and analysed statistically.

Results: Our study showed no significant difference in Heart rate, systolic blood pleasure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), respiratory rate (RR) and oxygen saturation (SpO2) in the dexmedetomidine group when compared with propofol group. But incidences of complications are less in Propofol group when compared with dexmedetomidine group.

Conclusion: No significant difference found in sedation with Propofol and dexmedetomidine during ERCP in haemodynamic and respiratory parameters but safety profile of Propofol is better than dexmedetomidine in impaired liver function.

Keywords: Haemodynamic, Respiratory, Safety Profile, Sedation, Dexmedetomidine, Propofol.

INTRODUCTION

In current scenario endoscopy is the most important diagnostic modality, in fact right now it is also frequently used as a therapeutic modality. There has been much amount of change in recent years regarding practice of sedation and analgesia during endoscopic procedures. Sedation is mainly required to minimize patient anxiety, discomfort and pain to patient and also enhance patient cooperation and facilitate the performance of the procedure by Endoscopists.[1]

There are various agents available to provide sedation. Current drugs include midazolam,[2] propofol,[3,4] etc. Newer agents such as dexmedetomidine,[5,6] is also being used now a days.

In recent years propofol has been extensively used for purpose of sedation and analgesia in gastrointestinal endoscopy procedures but it has some serious side effects like dose dependent respiratory depression and hypotension which is a limiting factor for its extensive use.

Now a days dexmedetomidine is extensively used instead of propofol because it causes less respiratory depression even with accidental overdosage.

A large number of studies has been done to compare propofol and dexmedetomidine for sedation in outdoor endoscopy procedures in healthy adults. But no study have been done to compare propofol and dexmedetomidine for sedation for ERCP in subjects with impaired liver function.

MATERIALS AND METHODS

The study was done at endoscopy unit of Indira Gandhi Institute of Medical Sciences, Patna from august 2014 to June 2015 after approval by Institutional Ethical Committee.

A total of 50 patients of ASA grade II aged 18 to 60 years were divided into two groups (25 each) group P (used propofol) and group D (used dexmedetomidine) in accordance with randomized, open label , controlled trial.

It was made sure that a working anaesthesia machine was available, complete with a method of ventilating the patient with oxygen, suction, intubation equipment , and standard anaesthetic and resuscitation drugs prior to performing ERCP.

Inclusion Criteria

- Patients undergoing elective ERCP with impaired liver function.
- Normal prothrombin time (PT) and international normalized ratio (INR).
- ASA (American Society of Anaesthelogist) grade II
- Aged between 18 and 60 years.
- Those who are willing to give written informed consent.

Exclusion Criteria

- ASA grade III or more.
- Patients with comorbid conditions such as HTN, DM or renal insufficiency.
- Patients with history of operative intervention in the past 72 hrs.
- Patients with the known allergy to these drugs and with a history of sulphite, egg or soyabean allergy.
- Pregnant patients.

Written informed consent is taken from all these patients. A detailed pre-anesthetic examination including history, general physical examination, systemic examination of cardiovascular, respiratory, central nervous system was performed.

Routine investigations and investigations recommended by the ASA guidelines for the age and co-morbid illness if any were carried out.

On the arrival of patient in Endoscopy Room, all vital parameters such as heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP),mean arterial pressure (MAP) , respiratory rate and oxygen saturation (SpO2 %) was recorded and thereafter readings were taken following the loading dose and every 5 min until the completion of the procedure.

The intervention was in the form that both group patients were given Injection fortwin 0.3 to 0.5mg/kg i.v. for analgesia at the beginning of the procedure.

Group P: Patients receiving propofol. A bolus of 1mg /kg were given then propofol infusion was started at 1mg/kg/hr for maintenance of sedation until Ramsay Sedation Score reached 3-4.

Group D: Patients receiving dexmedetomidine. A loading dose of 1mcg /kg was given over 10 mins then infusion was started at 0.5mcg/kg/hr for maintenance of sedation until Ramsay Sedation Score reached 3-4.

All patients received respective drugs i.v during ERCP procedure and the infusions were stopped at the completion of procedure.

Parameters Monitored

1. Heart Rate
2. Systolic Blood Pressure
3. Diastolic Blood Pressure
4. Mean Arterial Pressure
5. Respiratory Rate
6. Oxygen Saturation
7. Side effects of dexmedetomidine and propofol.

Statistical Analysis

Dichotomous outcomes were compared by Fisher's exact test as applicable. Numerical data were expressed as mean and standard deviation. Qualitative data were expressed as frequency and percentage. Chi-square test (Fisher's exact test) was used to examine the relation between qualitative variables. For quantitative data, comparison between two groups was done using independent sample t-test Comparison of repeated measures was done

using ANOVA test for repeated measures. A p-value<0.05 was considered significant.
Analysis was performed using SPSS version 20.0.

RESULTS

In group D there were 11 (44 %) female and 14 (56%) male ; group P had 13(52%)female and 12 (48%) male .However the male to female ratio in all three groups was comparable. [Table 1]
The patients in the group –D and group –P were statistically comparable (p >0.05) with regard to their age and body weight. [Table 2]
The mean baseline heart rate was 89.08±10.91 and 86.24±8.77 in group D and group P respectively. Similarly mean baseline systolic and diastolic Blood Pressure was 123.00±10.09, 77.80 ± 6.98 and 127.68±9.65, 73.02 ±9.09 in group D and group P respectively. Statistically these baseline parameters were comparable ,p> 0.05- Not significant. [Table 3]
The heart rate was measured after infusion of loading dose, at 5, 10, 15 and 20 min during ERCP and during recovery in both the groups. However it was found to be statistically not significant ,p >0.05. [Table 4]
Similarly systolic blood pressure measured prior to and after loading as well as at 5mins ,10 mins,15 mins and at recovery in both the groups was not statistically significant , p>0.05. [Table 5]
The diastolic blood pressure measurements at different point of time during the procedure and after recovery also came out to be statistically not significant, >0.05 – Not significant. [Table 6]
The mean ± standard deviation of mean arterial pressure at above point of time in both the groups also showed statistically not significant observation, p> 0.05. [Table 7]
The respiratory rate after infusion of loading dose, at 5, 10, 15 and 20 min during ERCP and during recovery in both the groups was comparable , p>0.05, Not significant. [Table 8]
The oxygen saturation in terms of mean ± standard deviation also came out to be statistically not significant , p>0.05 in both the groups at above point of observations. [Table 9]
In Group D patients had significantly more incidences of vomiting (16%), gagging (4%) and restlessness (24%) during the procedure compared with the Group P (8% ,0 and 4% respectively) while more patients had Respiratory depression in group P (12%) than group D(4%). However there is no incidence of shivering in both the groups. [Table 10]

Table 1: Demographic Data

Gender	Group D		Group P	
	Cases	%	Cases	%
Male	14	56.0	12	48.0
Female	11	44.0	13	52.0

Table 2: Comparison of mean age and mean weight of patients

Variable	Group		p value	Significance
	D	P		
Age (years)	**44.40±13.0**	**47.52 ± 13.03**	**>0.05**	**NS**
Weight(kgs)	**52.60±6.63**	**48.40 ± 4.94**	**>0.05**	**NS**

Table 3: Mean Baseline Hemodynamic and Respiratory Parameters

Parameter	Group		P value	Significance
	D	P		
Heart Rate	89.08±10.91	86.24 ±8.77	>0.05	NS
Systolic Blood Pressure	123.00±10.09	127.68±9.65	>0.05	NS
Diastolic Blood Pressure	77.80 6.98	73.02 9.09	>0.05	NS
Mean arterial blood pressure	88.23± 8.98	86.00 ± 7.09	>0.05	NS
respiratory rate	12.67± 2.99	14.08 ± 3.57	>0.05	NS
oxygen saturation(spO2)	98.96 ± 1.14	98.56 ± 1.64	>0.05	NS

Table 4: Comparison of heart rate between the two groups at different point of observation (N=25)

Time	Group		p value	Significance
	D	P		
Preloading	89.08± 10.91	86.24 ±8.77	>0.05	NS
Postloading	82.92 ± 8.57	82.64 ± 9.92	>0.05	NS
At 5 mins	88.40± 12.89	88.08± 10.57	>0.05	NS
At 10 mins	94.28 ±9.82	94.40± 11.34	>0.05	NS
At 15 mins	91.28 ± 10.86	92.56 ± 11.61	>0.05	NS
Recovery	90.48 ± 10.49	91.92 ± 10.38	>0.05	NS

Table 5: Comparison of systolic blood pressure between the two groups at different point of observation (N=25)

Time	Group		P value	Significance
	D	P		
Preloading	123.00 ± 10.09	127.68 ±9.65	>0.05	NS
Postloading	113.28 ± 11.21	114.08 ± 9.10	>0.05	NS

At 5 mins	116.24 ±9.71	111.6 ± 12.50	>0.05	NS
At 10 mins	116.08 ± 8.02	116.64± 13.10	>0.05	NS
At 15 mins	116.08 ± 14.60	116.16± 10.39	>0.05	NS
Recovery	124.08 ± 9.25	121.12 ±9.71	>0.05	NS

Table 6: Comparison of diastolic blood pressure between the two groups at different point of observation (N=25)

Time	Group		P value	Significance
	D	P		
Preloading	77.80 6.98	73.02 9.09	>0.05	NS
Post loading	74.66 8.55	70.56 10.00	>0.05	NS
At 5 mins	75.92± 8.89	75.28± 10.50	>0.05	NS
At 10 mins	74.80± 9.31	74.48 ± 11.18	>0.05	NS
At 15 mins	76.24± 7.38	80.08± 7.22	>0.05	NS
Recovery	81.36± 6.68	86.72 ± 6.37	>0.05	NS

Table 7: Comparison of mean arterial blood pressure between the two groups at different point of observation (N=25)

Time	Group		P value	Significance
	D	P		
Preloading	88.23± 8.98	86.00 ± 7.09	>0.05	NS
Postloading	90.54±10.09	88.94± 11.00	>0.05	NS
At 5 mins	89.34± 8.54	87.39± 10.78	>0.05	NS
At 10 mins	88.54± 8.14	88.50± 11.41	>0.05	NS
At 15 mins	82.30± 7.09	80.08 ± 8.00	>0.05	NS
Recovery	84.00± 6.90	80.60± 11.00	>0.05	NS

Table 8: Comparison of respiratory rate between the two groups at different point of observation (N=25)

Time	Group		P value	Significance
	D	P		
Preloading	12.67± 2.99	14.08 ± 3.57	>0.05	NS
Postloading	15.76 ± 3.65	13.00± 5.09	>0.05	NS
At 5 mins	12.96 ± 4.04	13.2± 4.31	>0.05	NS
At 10 mins	12.16± 4.67	13.52± 4.19	>0.05	NS
At 15 mins	15.20 ± 4.58	13.24± 5.01	>0.05	NS
Recovery	20.12 ± 3.50	19.92 ± 3.33	>0.05	NS

Table 9: Comparison of oxygen saturation (spO2) between the two groups at different point of observation (N=25)

Time	Group		p value	Significance
	D	P		
Preloading	98.96 ± 1.14	98.56 ± 1.64	>0.05	NS
Postloading	99.04± 1.02	98.52±1.56	>0.05	NS
At 5 mins	99.00 ± 1.08	98.40 ±1.71	>0.05	NS
At 10 mins	99.12 ± 1.05	98.28 ± 1.93	>0.05	NS
At 15 mins	99.04±1.06	98.56 ±1.58	>0.05	NS
Recovery	99.24± 0.78	98.72± 1.51	>0.05	NS

Table 10: Complications during ERCP in two groups

Complication	N (%)	
	D	P
Vomiting	4(16)	2(8)
Respiratory depression	1(4)	3(12)
Shivering	0	0
Gagging	1(4)	0
Restlessness	6(24)	1(4)
Other complications	5(20)	2(8)

DISCUSSION

Endoscopy can be successfully performed by applying moderate sedation which relieve patient anxiety and pain, and patients' cooperation is achieved. Thus many complications like intestinal perforation and pancreatitis can be avoided by increasing patients cooperation using good sedation.

Propofol is increasingly being used for sedation in endoscopy in many countries because the satisfaction of endoscopists with propofol sedation is greater compared with their satisfaction with conventional sedation. Moreover, the use of propofol is currently preferred for the endoscopic sedation of patients with advanced liver disease due to its short biologic half-life and, consequently, its low risk of inducing hepatic encephalopathy.

In some areas dexmedetomidine is preferred our propofol because it causes less dose dependent respiratory depression.

Our study showed no significant differences between propofol and dexmedetomidine in

hemodynamic parameters i.e. heart rate, systolic blood pressure, diastolic blood pressure and mean arterial blood pressure just after loading, after 5 minutes, 10 minutes, 15 minutes and after recovery.
Similarly respiratory parameters i.e. respiratory rate and oxygen saturation also show no significant difference between Dexmedetomidine and Propofol sedation.
When we consider complications during sedation, our study concluded that, in subject on which dexmedetomidine is used for sedation more incidence of vomiting, restlessness , gagging and other complications occur but subject on which propofol is used more incidence of respiratory depression found. But overall Dexmedetomidine group shown more incidence of complications than Propofol group.
Above findings are in accordance with the study by Sethi et al,[7] Hassan et.al,[8] and Nishizawa et al,[9] they also find statistically insignificant difference in hemodynamic parameters (heart rate, systolic, diastolic and mean blood pressure) between propofol (group P) and dexmedetomidine(group D). Hypotension and bradycardia are recognized as two major adverse effects associated with α2-agonist agents. It has been suggested that these effects are mediated by activation of α2-adrenoceptors, imidazoline preferring receptors or both in the ventrolateral medulla and especially in the solitarius nucleus tract.[10] However in our study the heart rate in both the groups at post loading, 5 mins, 10 mins, 15 mins and after recovery indicated no significant difference.
Susanne Ebert et al (2013) conducted a study involving 64 patients for esophageal endoscopy to compare safety and effectiveness of dexmedetomidine versus propofol for sedation.[11] Patient monitoring included time adapted heart rate, SPO2, ECG , Sedation, Aldrete score etc. It was a questionnaire based study for both patients and gastroenterologists. It is concluded that acceptance level among patients after propofol sedation is high.
Similar study done by Anchalee Techanivate (2012) involving 70 patients for colonoscopy. Patients were divided into two groups.[12] Group P received Propofol for sedation and group D received Dexmedetomidine for sedation. The incidence of hypotension was greater in group P (50%) than in group D (20%) (P=0.015). Thus conclusion of this study is not in accordance with our study.
Another study not showing similar results as our study is of C.S Tsai (2009) et al. In this study subjects chosen for tracheal intubation were divided in to two groups. In one group dexmedetomidine was used for sedation and in other group propofol used. The median comfort score was higher in the dexmedetomidine group than the propofol group ($p = 0.027$), favouring the former. The dexmedetomidine group experienced fewer airway events and less heart rate response to intubation than the propofol group ($p < 0.003$ and $p = 0.007$, respectively).[13]
Study done by Kaygusuz K (2007) found respiratory rate during sedation with Dexmedetomidine was significantly slower than sedation with Propofol but SpO2 was significantly higher than with Propofol ($P < 0.05$). Other clinical variables were similar ($P > 0.05$). As our study shown similar respiratory parameter (respiratory rate and Spo2) in both Dexmedetomidine and Propofol group, this study differs from our study in this regards.[1]
Thus from above discussion it can be said that if we consider hemodynamic parameters (heart rate, systolic blood pressure, diastolic blood pressure and mean blood pressure) and respiratory parameters (respiratory rate and Oxygen saturation), no significant difference between sedation with Propofol and dexmedetomidine during ERCP is found.
But when we consider safety profile of two drugs, propofol show better safety profile than dexmedetomidine. However incidence of respiratory depression is more with propofol than dexmedetomidine.
As we have recruited only subjects with abnormal liver function test. We can say in subjects with abnormal liver function test Propofol can be more safely used than Dexmedetomidine.
Limitations And Future Suggestions: In this study we have considered only hemodynamic, respiratory parameters and incidence of complications for comparison between sedation with Propofol and Dexmedetomidine. A study can be planned with consideration of more parameters for comparison like facial pain score (FPS), endocrinologist satisfaction score and patient satisfaction score with a larger sample size.

CONCLUSION

Propofol have better safety profile than Dexmedetomidine when used for sedation during ERCP procedure, specially in subjects with deranged liver function test.
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