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COMPARATIVE EVALUATION OF HEMODYNAMIC STABILITY AND RECOVERY DURING CONSCIOUS SEDATION BY DEXMEDETOMIDINE WITH FENTANYL V/S KETAMINE WITH FENTANYL IN DILATATION AND CURETTAGE

[1]*Dr. Virendra Sharma MBBS., M.D, [2]Dr. Smita Barya M.B.B.S, M.S, [3]Dr. Prakash Chandra Audichya M.B.B.S, M.D, [4]Dr. Sameer Goyal MBBS., M.D, [5]Dr. Vijay Kumar MBBS., M.D. and [6]Dr. Jyoti Petkar MBBS., MD

[1]*Assistant Professor, Department of Anaesthesiology, PMCH, Udaipur, Raj., India.
[2]Assistant Professor, Department of Obs. And Gynae., A.I.M.S, Rajsamand, Udaipur, Raj.
[3]Professor and Head, Department of Anesthesiology, PMCH, Udaipur, Raj., India.
[4]Assistant Professor, Department of Anaesthesiology, PMCH, Udaipur, Raj., India.
[5]Senior Resident, Department of Anaesthesiology, PMCH, Udaipur, Raj., India.
[6]Assistant Professor, Department of Anaesthesiology, PMCH, Udaipur, Raj., India.

***Corresponding Author: Dr. Virendra Sharma**

Assistant Professor, Department of Anaesthesiology, PMCH, Udaipur, Raj., India.

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ABSTRACT

Background: The aims of present study are to compare the adequacy of sedation, hemodynamic and respiratory stability, time to achieve "street fitness" status by Dexmedetomidine with Fentanyl v/s Ketamine with Fentanyl in Dilatation and Curettage. **Material And Method:** This prospective randomized controlled study was conducted in department of anaesthesiology, Pacific Medical College and hospital. In this study 60 healthy patients of age between 18-65 years and ASA Grade I & II scheduled for Dilatation and Curettage were taken. After taking valid consent they were divided into two groups, each group comprising of 30 patients **Group D+F-** In this group randomly selected 30 patients were given injection Dexmedetomidine along with inj. Fentany. **Group K+F-** In this group randomly selected 30 patients were given injection ketamine, along with inj. Fentanyl. The scales used during the study were Aldrete's score for post-operative recovery and Ramsay's score for sedation. **Results and Conclusion:** Our study concluded that Dexmedetomidine in 1 mcg/kg with Fentanyl 1 mcg/kg has a superior hemodynamic stability in comparison to ketamine0.5mg/kg with Fentanyl 1 mcg/kg. Dexmedetomidine and Fentanyl combination is an effective modality to provide analgesia and anaesthesia for D & C procedure without significant side effects apart from bradycardia which was transient in duration and no patient required any pharmacological intervention. Dexmedetomidine is a new invention in daycare surgery with advantage of early discharge and reasonable cost.

KEYWORDS: Conscious sedation, Dexmedetomidine, Fentanyl, Ketamine, Dilatation and Curettage.

INTRODUCTION

Conscious sedation is administered with the dual goals of rapidly and safely establishing satisfactory procedural condition for the performance of therapeutic or diagnostic procedures while ensuring rapid, predictable recovery with minimal post operative sequels.

Careful titration of short-acting drugs permits safe transfer of patients directly from the operating room suite to a less labor intensive recovery area; some patients can be discharged home within 1 hour after surgery. Conscious sedation provides greater flexibility in scheduling operations so we can go with higher volume of patients. Early recovery and early ambulation decreases morbidity and mortality rates. It also reduces overall procedural costs. Patients are able to observe the procedure and can communicate with surgeon during the procedure; therefore patients and surgeon satisfaction are high. Dilatation and curettage is the most frequently performed minor surgery in obstetrics and gynecology and usually performed as a day care surgical procedure.

Dexmedetomidine, a selective alpha-2 agonist with analgesic and sedative properties is the "star" or welcome drug in the armamentarium of anesthetic practice.[1-3] Dexmedetomidine has been successfully tried for conscious sedation purpose in ICU setup, for sedation during dental surgery, for conscious sedation in endoscopies, for decreasing the dose as well as potentiating the analgesic effect of local anesthetics intrathecally for vaginal hysterectomy and lower abdominal surgeries.[4-7]

Ketamine has a wide range of effects in humans including analgesia, anaesthesia, hallucinations, elevated blood pressure and bronchodilation. Ketamine induces a state referred to as "dissociative anaesthesia**".**[9]

We find very few studies comparing Dexmedetomidine & ketamine and both drugs are used in conscious sedation in different combinations. Present study was done with aim to evaluate the safety and efficacy of Dexmedetomidine and ketamine in Dilatation & Curettage procedures along with Fentanyl. The study will evaluate the hemodynamic changes, requirement of supplementary anesthetic agent, the recovery profile and any side effects related to drug administration. The aims of present study are to compare the adequacy of sedation, hemodynamic and respiratory stability, Time to achieve "street fitness" status, Requirement of supplementary anesthetic agent.

MATERIALS AND METHODS

This prospective randomized controlled study was carried out at Pacific medical college and hospital, Udaipur, Rajasthan, India. Standard Performa was prepared and thorough preoperative evaluation including complete present and past history, complete general, systemic and local examination with relevant investigation was carried out as per outlined in Performa. Ethical approval is taken from the institution and written informed consent was taken from the participants.

In this study 60 healthy patients of age between 18-65 years and ASA Grade I & II scheduled for Dilatation and Curettage were taken. After taking valid consent they were divided into two groups, each group comprising of 30 patients.

a) **Group D+F-** In this group randomly selected 30 patients were given injection Dexmedetomidine along with inj. Fentanyl.
b) **Group K+F-** In this group randomly selected 30 patients were given injection ketamine, along with inj. Fentanyl.

Exclusion Criterias were Renal and Hepatic insufficiency, Diabetes, Hypertension, Cardiac disease & Heart blocks, Chronic use of sedatives, narcotics, alcohol or illicit drugs, Allergy to either Dexmedetomidine or Ketamine, Pregnancy or inability to tolerate technique of the study drugs.

On entering the OT, standard monitoring including NIBP, Pulse oximetry and ECG leads were attached to the patient. After establishing intravenous access using an 18/20 G cannula, Inj.ringer lactate 500 ml was given during the entire procedure. Pre –operative vitals were recorded. Inj. Fentanyl 1 µg/kg was given 5minutes prior to surgery.

Group D+F: Inj. Dexmedetomidine 100µg was added to 100ml of normal saline and made to a concentration of 1 µg/ml. This solution was administered at a constant rate to make a total dose of 1 µg/kg of dexmedetomidine over 10 min and followed by 0.5µg /kg/hr infusion of dexmedetomidine till the completion of surgery. After loading dose of dexmedetomidine surgical procedure was allowed to be conducted when Ramsay sedation score 3 is achieved. If not achieved than propofol was given as incremental dose of 10mg every 30 sec till Ramsay sedation score 3 is achieved.

Group K+F: ketamine was given 0.5mg/kg slow intravenous bolus and wait for Ramsay sedation score 3 is achieved than start surgery .If Ramsay sedation score 3 is not achieved than propofol was given as incremental dose of 10mg every 30 sec till RSS score 3 is achieved.

Intra-operative vitals and Ramsay's sedation score were recorded at 2min, 5min and 8min. Any incidence of adverse effects like nausea, vomiting, bradycardia, hypotension, hypoxia, and hypertension was recorded. For nausea & vomiting injection Ondensetron (0.1mg/kg), for bradycardia injection Atropine (.01mg/kg) and for hypotension injection Ephedrine (0.1mg/kg) were used. Total duration of the procedure and total dose of Propofol required during the surgery were also recorded.

After completion of procedure patients vitals were once again recorded and patients were shifted to recovery room. Patients were kept under close observation and shifted to post operative ward if found to be fully conscious and oriented with stable vital parameters ie Aldrete score 8-10. The scales used during the study were Aldrete's score for post-operative recovery and Ramsay's score for sedation.

Ramsay Sedation Scale

1. Anxious and agitated
2. Cooperative, tranquil, oriented
3. Responds only to verbal command
4. Asleep with brisk response to light stimulation
5. Asleep without response to light stimulation
6. Non responsive

TABLE -1 Mean Blood Pressure during observation period

	MODIFIED ALDRETE SCORING SYSTEM	
	Criterion	**Score Maximum Score: 10**
Consciousness	Fully awake Aroused by verbal stimulus Not aroused by verbal stimulus	**2** **1** **0**
Breathing	Takes full breaths and can cough Takes only shallow breaths or has dyspnea Cannot breath without assistance (apnea)	**2** **1** **0**
Blood Pressure	Within 20 mm Hg of pre-op value 20 to 50 mm Hg different from pre-op value ≥50 mm Hg different from pre-op value	**2** **1** **0**
Oxygenation	>92% blood oxygen saturation (SpO_2) on room air Needs supplemental O_2 to maintain SpO_2 >90% SpO_2 ≤90% on supplemental O_2	**2** **1** **0**
Motor Function	Can move all 4 extremities on request Can move 2 extremities on request Cannot move any extremities on request	**2** **1** **0**

STATISTICAL EVALUATION

All results are expressed as mean ±SD. Statistical software namely SAS9.2, SPSS15.0, Stata10.1, Medcalc9.0.1 and R Enviourment ver.2.11.1 were used for analysis of data and Microsoft word and excel have been used to generate graphs and tables etc. Unpaired t test and Chi Square test were performed and two tail p value <0.05 was taken as statistically significant.

RESULTS

60 patients were allocated to participate in this study (30 in each of the study group). Both groups were comparable as regards to demographic data and preoperative hemodynamic parameters (P>0.05).

Table-1 shows the Mean Blood Pressure (mmHg) during the observation period in the both groups. Statistically significant difference was found between Group D+F and Group K+F at 2min, 5 min, 8 min and post operative period. Mean blood pressure in D+F group fall by at 2min(8.79%),5min(8.14%),8min(8.95%) and postoperative period (8.22%). The maximum fall was noted at 8min. where as in other group K+F mean BP rise at 2min(13.4%),5min(17.58%), 8min(16.21%) and post op(11.12%).so maximum rise was noted at 5min. This was statistically significant. (P value <.0001).

Table-2 shows the Heart Rate during the observation period in the both groups. Statistically significant difference was found between Group D+F and Group K+F at 2min, 5 min, 8 min and postoperative value. Heart rate in D+F group drop at 2min (19.9%), 5min (19.38%), 8min (19.02%) and postoperative (16.25%). And maximum fall was noted at 2min. where as in other group K+F heart rate rise at 2min (16.12%), 5min (25.39%), 8min (20.81%) and post operative (17.77%). so maximum rise was noted at 5min. That was statistically significant.(p value <.0001) but only 5 patients had a pulse rate below 60, which was transient and heart rate recovered without receiving Atropine.

TABLE -2 HEART RATE DURING OBSERVATION PERIOD (PER MIN)

Time	Group D+F		Group K+F		
	Range	**Mean ± SD.**	**Range**	**Mean ± SD**	**P value**
0 min	84-112	99.92±07.24	83.-110	101.57±06.64	0.2836
2 min	75-119	90.86±12.50	100-135	115.20±10.73	0.0001
5 min	72-120	91.51±11.10	99-155	119.43±11.60	0.0001
8 min	74-105	90.70±07.15	102-138	118.04±10.10	0.0001
Post- perative	75-121	91.43±08.43	100-131	112.87±08.36	0.0001

There was greater fall in SpO2 in D+F group in comparision to K+F group but this fall was not statistically significant. Similarly fall in respiratory rate was more but statistically insignificant in K+F group in comparision to D+F group.

TABLE 3 Average Dose of Propofol Supplementation

	Group D+F	Group K+F	P value
Average Dose of Propofol supplementation	12.0	2.3	.0005

Table 3 shows the Average Dose of Propofol (mg) supplementation required during the observation period in the both groups. Average Dose of Propofol (mg) supplementation was significantly high in group D+F.

TABLE 4 SEDATION SCORE

Time	Group D+F		Group K+F		
	Range	Mean ± SD.	Range	Mean ± SD	P value
2 min	2-4	3.33±0.60	2-5	3.60±0.81	0.1555
5 min	3-5	3.51±0.68	3-5	3.96±0.71	0.0170
8 min	3-5	3.34±0.62	3-6	3.73±0.82	0.0650
Post op	2-4	3.10±0.54	2-5	3.20±0.84	0.5892

Table 4 shows the Ramsay sedation score during the observation period in the both groups. Average sedation score was 3.70 in K+F group whereas 3.40 in D+F group.

Time	Group D+F		Group K+F		
	Range	Mean ± SD.	Range	Mean ± SD	P value
0 min	71-114	92.90±12.33	72-121	94.10±14.86	0.7340(NS)
2 min	58-113	74.4±10.04	79-150	109.27±19.30	0.0001
5 min	57-130	74.89±13.40	86-160	118.00±20.59	0.0001
8 min	58-95	75.23±09.12	78-170	113.69±22.13	0.0001
Post op	63-98	77.80±06.48	75-142	110.83±21.18	0.0001

Figure 1 shows the post operative recovery time (required to achieve Aldret's score 8 to 10) in the both groups. The post operative recovery time was significantly high in group K+F. Average recovery time in our study was 12.46 min in D+F group and 21.55 min in K+F group.

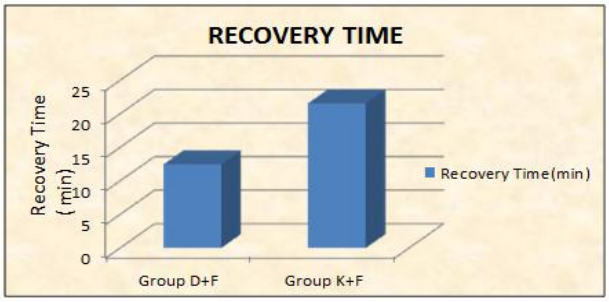

Fig. 1 POSTOPERATIVE RECOVERY TIME

Incidences of side effect bradycardia (18%), hypotension (18%) and hypoxia (20%) were less in D+F group in comparison to the K+F group 40 %.Hypertension and 3.3% hypoxia and 23% nausea & vomiting were significant problems Figure 2.

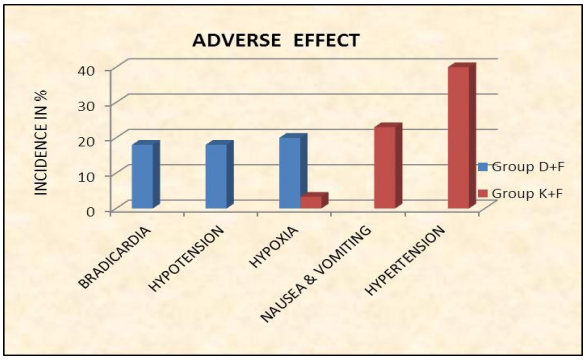

Fig. 2 Number of patients developing Adverse Effect

DISCUSSION

Conscious sedation is technique of providing analgesia, sedation and anxiolysis while ensuring rapid recovery without side effects.

Conscious sedation is administered with the dual goals of rapidly and safely establishing satisfactory procedural condition for the performance of therapeutic or diagnostic procedures while ensuring rapid, predictable recovery with minimal post operative sequels.

Conscious sedation provides greater flexibility in scheduling operations so we can go with higher volume of patients. There is lack of dependence on the availability of hospital beds. There is also lower incidence of infection, respiratory complications and cardiovascular complication. It requires less preoperative testing and postoperative medication. Early recovery and early ambulation decreases morbidity and mortality rates. Conscious sedation also reduces overall procedural costs. Patients are able to observe the procedure and can communicate with surgeon during the procedure; therefore patients and surgeon satisfaction are high. Dexmedetomidine a selective alpha-2 agonist with analgesic and sedative properties. These properties of dexmedetomidine render it suitable for sedation and analgesia during the whole perioperative period. Its applications as a premedication, as an anesthetic adjunct for general and regional anesthesia and as a postoperative sedative and analgesic are similar to those of the benzodiazepines.[8] Ketamine has a wide range of effects in humans including analgesia, anaesthesia, hallucinations, elevated blood pressure and bronchodilation. Ketamine induces a state referred to as "dissociative anaesthesia"[9] and is used as a recreational drug. In low doses typically used for conscious sedation it does not affect pharyngeal-laryngeal reflexes and, thus, allows a patent airway as well as spontaneous respiration

to maintain intact.

Cardiovascular and respiratory stimulation are observed following administration, although transient respiratory depression may occur if administered too rapidly or in high doses. The unique dissociative action and partial agonism at opiate mu-receptors permits painful procedures to be performed in a consistent state of sedation and patient comfort. Ketamine is contraindicated in patients who have underlying conditions in which increased blood pressure would pose risk of complications. An increase in oropharyngeal secretions is often triggered and diligent patient monitoring for laryngospasms needs be employed.

Opiates provide analgesia and sedation during painful procedures. Fentanyl is favored because of its prompt onset and short duration of action. Unlike morphine, fentanyl has minimal cardiovascular depressive effects and hypotension rarely occurs. Fentanyl binds with stereo specific receptors at many sites within the CNS and increases pain threshold, alters pain reception, and inhibits ascending pain pathways. In addition to analgesia, fentanyl suppresses the cough reflex and cause respiratory depression, drowsiness, and sedation. The half-life is 2-4 hours.

Dilatation and curettage is the most frequently performed minor surgery in obstetrics and gynecology and usually performed as a day care surgical procedure. Jalowiecki et al[10] observed that dexmedetomidine provide a relatively satisfactory level of analgesia and conscious sedation without clinically distinguished respiratory side effects in patients undergoing colonoscopy. However, Fentanyl supplementation (analgesic requirement(0.1-0.2mg) was required in 47% of patients in the dexmedetomidine group to achieve a satisfactory level of analgesia, and in patients given Fentanyl, vertigo (five patients), nausea and vomiting (five patients), ventricular bigeminy (one patient), and hemodynamic instability with prolonged recovery were observed. In the present study, Fentanyl was used as an analgesic; satisfaction after the procedure was considerably good in both groups. In addition, the dexmedetomidine group recovery time was not prolonged, and the numbers of other adverse events were lower than the ketamine group.

In our study, continuous infusion of dexmedetomidine was used to maintain a steady state sedation level. To quantify the level of sedation, the RSS score had been used.

It causes dose-dependent decrease in heart rate and blood pressure. Tanskanen *et al*[11] in their study showed that intraoperative infusion of dexmedetomidine at a rate of 0.4µg/kg/h maintains heart rate and blood pressure in acceptable range for a longer duration as compared to placebo group. The decrease in heart rate and blood pressure is similar to the findings by Feld *et al*[12] who compared dexmedetomidine with Fentanyl in bariatric surgery. Similar hemodynamic changes have been reported by Arain and Ebert[13], who compared dexmedetomidine with propofol for sedation during surgery under regional anaesthesia. These findings are consistent with our study results which showed a significant decrease in heart rate, systolic blood pressure and diastolic blood pressure.

Sachie Ogawa, Hiroaki Seino, Hiroshi Ito[14] used dexmedetomidine in dental surgeries. Thirteen healthy volunteers were sedated with Dexmedetomidine at a loading dose of 6 µg /kg /h for 5 minutes and a continuous infusion dose of 0.2 µg /kg/h for 25 minutes. The tidal volume decreased significantly despite no significant changes in respiratory rate, minute ventilation, oxygen saturation, and end-tidal carbon dioxide. The mean arterial pressure and heart rate also decreased significantly but within clinically acceptable levels.

In our study maximum fall in spo_2 was noted at5 min. D+F group showed greater fall (2.59%) of spo2 as compared to group K+F (1.30%) Regarding respiratory rate Dexmedetomidine showed no significant change but ketamine showed average 15.96% drop in respiratory rate at postoperative period.

A prospective randomized study by Varadarajulu et al[15] evaluated the use of ketamine for endoscopic procedures concluded that ketamine can result in better quality and depth of sedation with shorter recovery time than benzodiazepines. In our study ketamine showed greater Ramsay sedation score then Dexmedetomidine. Average sedation score in K+F group was 3.70 whereas in Dexmedetomidine group it was 3.40. Kenan Kaygusuz et al,[16] Shahbaz et al.[17] Different studies showed different sedation score yet common to all was less sedation of Dexmedetomidine then ketamine. Although different studies showed different recovery time yet all showed earlier recovery with Dexmedetomidine.

Yavuz demiraran et al, observed retching was found to be significantly lower in the dexmedetomidine group. Decreasing of retching reflex in the dexmedetomidine group may be due to its sympatholitic and vagomimetic effects. In our study no episode of nausea and vomiting found in D+F group these findings demonstrate that dexmedetomidine may be safely and effectively used in patients undergoing short surgical procedure. Where as in K+F group show 23% episode of nausea and vomiting.

CONCLUSION

Our study concluded that Dexmedetomidine in 1 mcg/kg with Fentanyl 1 mcg/kg has a superior hemodynamic stability in comparison to ketamine0.5mg/kg with Fentanyl 1 mcg/kg. Dexmedetomidine and Fentanyl combination is an effective modality to provide analgesia and anaesthesia for D & C procedure without significant side effects apart from bradycardia which was transient

in duration and no patient required any pharmacological intervention. Dexmedetomidine is a new invention in daycare surgery with advantage of early discharge and reasonable cost.

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