Original Article

Comparison of Ketamine and Fentanyl with Propofol for Procedural Sedation and Analgesia for Dilatation and Curettage

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Abstract

Introduction: *Dilatation and curettage (D&C) is a common procedure that generally causes considerable pain and usually done under procedural sedation and analgesia. Propofol is an ideal intravenous anaesthtic agent for short interventional procedure like D&C but lack of analgesia remains it's main shortcoming therefore it is always combined with an analgesic. Ketamine and fentanyl are the popular analgesic in this context.*

Objectives: *This prospective clinical study was designed to evaluate to compare propofol ketamine combination versus propofol fentanyl combination in respect of hemodynamics and recovery time for procedural sedation and analgesia in patients undergoing D&C.*

Methods: *This prospective randomized study was performed on 100 patients who underwent elective D&C procedure. Patients were randomly allocated into two groups of fifty each: group PK received propofol 2mg/kg + ketamine 1mg/kg for induction and propofol 4mg/kg/hr + ketamine 1 mg/kg/hr for maintenance anesthesia, group PF received propofol 2 mg/kg + fentanyl 2 ìg/kg for induction and propofol 4 mg/kg/hr + fentanyl 1ìg/kg/hr for maintenance of anesthesia. The pulse rate, systolic and diastolic arterial blood pressures and peripheral oxygen saturation were recorded. Recovery times, side effects of sedation were also recorded.*

Results: *Demographic data were found similar in two groups. There were no significant differences in heart rate, systolic and diastolic arterial blood pressure in all time intervals among groups except there was statistically significant fall in systolic blood pressure after induction in PF group (P=0.005). Recovery time was statistically significant increase in Group PK compared to Group PF (p=0.004). There were no significant differences among groups in regard to side effects.*

Conclusion: Propofol ketamine and propofol fentanyl had similar hemodynamic stability without any important side effects for procedural sedation and analgesia in patients underwent D&C but propofol ketamine had longer recovery time.

Key words*: Dilatation and curettage, procedural sedation and analgesia, propofol, ketamine, fentanyl .*

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Introduction

Dilatation and curettage (D&C) is a short invasive procedure that causes significant pain due to introduction of cervical dilators and tissue extraction. D&C usually done under sedation and analgesia, general anaesthesia and neuroaxial blockade are alternatives and less used anaesthetic choices.[1] Sedation and analgesia both needed for theses types of painful interventional procedures.[2] With the introduction of shorter acting sedatives for sedation and opioids for analgesia, specific reversal agents for both opioids and sedatives and availability of noninvasive monitoring equipments, procedural sedation and analgesia can be safely administered in many health care settings.[3] The goals of procedural sedation and analgesia include

a rapid and smooth induction, effective anaesthesia and analgesia, smooth and prompt recovery with minimal or no post procedure side effects so that an early discharge is possible.[4]

Of all intravenous anaesthetic agents that are available, propofol's pharmacokinetic profiles favour its administration by continuous intravenous infusion.[5,6] As propofol has no nociceptive effect, it is generally combined with an analgesic, the popular combination being either propofol with fentanyl or propofol with ketamine. Ketamine is a potent anaesthetic that provides analgesia, sedation and amnesia and it might be appropriate option for short procedures.[7,8,9] Its main disadvantages are that it produces hypertension and precipitates emergence phenomena, propofol seems to eliminate ketamine induced emergence phenomena.[10] Fentanyl is a potent analgesic and most frequently used opioid in clinical anaesthesia today. Its disadvantages are respiratory depression and postoperative nausea and vomiting.[11]

The current study was designed to evaluate propofol ketamine combination versus propofol fentanyl combination in respect of hemodynamics and recovery time for procedural sedation and analgesia in patients undergoing D&C.

Materials and Methods

It was as prospective comparative study of randomly selected one hundred patients (fifty patients in each group) age between 18-45 years, ASA physical status I and II scheduled for elective D&C in Border Guard Hospital, Pilkhana, Dhaka from July 2015 to June 2016. Permission was taken from departmental review board before starting the study. Patients with psychiatric illness, hypertension, ischaemic heart disease, raised intracranial pressure and emergency procedure were excluded from the study. Pre-anaesthetic check up was done 24 hours prior to surgery and the procedure was explained to the patient and written consent was obtained from each patient. All patients received oral diazepam 5 mg at night before D&C. On arrival to the operation theatre, intravenous access was established. The patients were randomly allocated into two groups as follows:

Group PK (n = 50) received propofol 2mg/kg + ketamine 1mg/kg for induction and propofol 4 mg/kg/hr + ketamine 1 mg/kg/hr for maintenance of anesthesia.

Group PF (n = 50) received propofol 2mg/kg + fentanyl 2ìg/kg for induction and propofol 4mg/kg/hr + fentanyl 1ìg/kg/hr for maintenance of anesthesia.

Blood pressure, heart rate, ECG and SpO2 (oxygen saturation) were monitored at pre induction, after induction and in perioperative period after starting infusion every 5 minutes till the end of the procedure. The level of sedation was assessed at 1–3 min intervals, and the infusion rate was adjusted accordingly to achieve a Ramsay Sedation Scale (RSS) score of 5 (Table VII).[12] Any movement of the patient was treated with increase in the study drug infusion rate. A full set of resuscitation equipments including suction apparatus, oxygen, a bag valve mask, appropriate airway, resuscitation drugs and defibrillator were available throughout procedure and recovery to combat any adverse event. Any serious adverse events as well as side effects like desaturation (SpO_2 less than 93%), hypertension (systolic BP more than 30% of baseline record), and hypotension (systolic BP less than 90 mm of Hg) were observed, recorded and managed. At the end of procedure the continuous infusion of drugs was stopped and all patients were shifted to the recovery room, vital parameters were monitored. Presence of any complication like nausea, vomiting, desaturation, hypotension, bradycardia, delirium and hallucination were observed, managed and documented. Recovery status will be assessed by the Modified Aldrete Recovery Score (Table VIII).[13] Patients will be considered to be ready to discharge from recovery room when they will have stable vital signs, oriented, have no intractable nausea or vomiting, have minimum pain, and Recovery Score is persistently at least 8 or more than 8. Recovery time was calculated as the time from the last dose of medication given until discharge criteria were met.

All statistical analysis were carried out using SPSS (Statistical Package for social sciences) 17.0 for windows. All results are expressed as mean ± standard deviation (Mean ± SD) or in frequencies as applicable. Results are considered statistically significant if $p< 0.05$.

Results

Patient's demographics were shown in Table I. Data were similar and fairly comparable in both groups and differences were statistically not significant. Changes of pulse rate in PK and PF group were shown in Table II. The mean pulse rate was 76±5 (Mean + SD) per minute and 72±7 (Mean + SD) per minute in PK and PF group respectively at pre induction level and the difference was statistically not significant. There was slight increase in pulse rate after induction in both the groups which was statistically not significant. After starting the infusion pulse rate did not show any significant difference. Changes of systolic pressure in PK and PF group were shown in Table III. The mean systolic blood pressure was 116±6 (Mean + SD) mm of Hg and 119±5 (Mean + SD) mm of Hg in PK and PF groups respectively at pre induction level and the difference was statistically not significant. There was statistically significant fall in systolic blood pressure after induction in PF group (P=0.005). After starting the infusion systolic blood pressure did not show any significant difference. Changes of diastolic pressure in PK and PF group were shown in table IV. The mean diastolic blood pressure were 76±7 (Mean+SD) mm of Hg and 74±6 (Mean+SD) mm of Hg in PK and PF group respectively at basal level and the difference is statistically not significant. After induction there was statistically no significant difference in both the groups. After starting the infusion diastolic blood pressure did not show any significant difference. Side effects were shown in Table V. There were no significant differences among groups in regard to side effects. Anaesthesia related data were shown in Table VI. Procedure time and anaesthesia time were similar in both groups and differences were statistically not significant. Recovery time was less in PF group than PK group and difference was statistically significant (P=0.004).

Table I *Demographic data*

Characteristics	Group PK (n=50)	Group PF (n=50)	P Value	Result
Age	29.03+5.98	28.63+6.69	0.897	NS(student 't' test , unpaired)
Weight	56.83+8.45	56.83+8.45	0.775	NS(student 't' test , unpaired)
ASA physical status				
I	43(86%)	44(88%)	0.767	NS(chi square test)
II	7(14%)	6(12%)	0.974	NS(chi square test)

Values are expressed in Mean + SD and Percentage NS– Not significant

Table II *Comparison of changes in pulse rate (rate/min)*

Time	Group PK (n=50)	Group PF (n=50)	P Value	Result (student 't' test, unpaired)
Pre induction	76+5	72+7	0.181	NS
After induction	81+4	83+5	0.068	NS
5 minutes	80+4	83+7	0.061	NS
10 minutes	81+5	81+6	0.921	NS
15 minutes	81+5	78+6	0.093	NS
20 minutes	80+6	78+5	0.064	NS
25 minutes	79+5	77+6	0.128	NS
30 minutes	79+6	78+5	0.327	NS

Values are expressed in Mean + SD
NS– Not significant

Table III *Comparison of changes in systolic blood pressure (mm of Hg)*

Time	Group PK (n=50)	Group PF (n=50)	P value	Result (student 't' test, unpaired)
Pre induction	116+6	119+5	0.161	NS
After induction	115+13	109+8	0.005	Sig
5 minutes	116+8	118+10	0.640	NS
10 minutes	118+8	116+11	0.273	NS
15 minutes	117+7	114+10	0.218	NS
20 minutes	117+7	114+9	0.019	NS
25 minutes	116+6	114+9	0.230	NS
30 minutes	117+7	114+10	0.075	NS

Values are expressed in Mean + SD
NS- Not significant
Sig- Significant

Table IV *Comparison of changes in diastolic blood pressure (mm of Hg)*

Time	Group PK (n=50)	Group PF (n=50)	P value	Result (student 't' test, unpaired)
Pre induction	76+7	74+6	0.171	NS
After induction	74+5	73+6	0.542	NS
5 minutes	76+4	75+6	0.153	NS
10 minutes	78+7	76+5	0.072	NS
15 minutes	77+6	74+6	0.081	NS
20 minutes	76+7	75+7	0.443	NS
25 minutes	77+6	75+6	0.250	NS
30 minutes	76+5	74+6	0.125	NS

Values are expressed in Mean + SD
NS– Not significant

Table V *Side effects*

Side effect	Group PK (n=50)	Group PF (n=50)	P value	Result (student 't' test, unpaired)
Nausea	3(6%)	4(8%)	0.718	NS
Vomiting	3(6%)	2(4%)	0.532	NS
Desaturation	4(8%)	3(6%)	0.682	NS
Hypotension	3(6%)	4(8%)	0.718	NS
Bradycardia	2(4%)	3(6%)	0.587	NS
Delirium	5(10%)	4(8%)	0.813	NS
Hallucination	3(6%)	2(4%)	0.532	NS

Values are expressed in Percentage
NS– Not significant

Table VI Anaesthesia related data

Time	Group PK (n=50)	Group PF (n=50)	P value	Result (student 't' test, unpaired)
Procedure time (minutes)	14.71+ 5.59	15.23+ 6.13	0.697	NS
Anaesthesia time (minutes)	20.12+ 5.87	19.32+ 6.11	0.752	NS
Recovery time (minutes)	11.17+ 2.65	8.34+ 1.26	0.004	Sig

Values are expressed in Mean + SD
NS- Not significant Sig- Significant

Table VII *Ramsey Sedation Scale*

Sedation level	Description
1	Patient is anxious, agitated or restless, or both
2	Patient is cooperative, oriented, and tranquil
3	Patient responds only to commands
4	Patient responds to light glabellar tap or loud auditory stimulus
5	Patient has a sluggish response to light glabellar tap or loud auditory stimulus
6	No response

Table VII The Modified Aldrete Recovery Score

Parameter	Number
Activity	
Voluntary movement of all limbs to command	2
Voluntary movement of two extremities to command	1
Unable to move	0
Respiration	
Breathe deeply and cough	2
Dyspnea, hypoventilation	1
Apneic	0
Circulation	
BP +/- 20 mm Hg of pre-anaesthesia level	2
BP > 20-50 mm Hg of pre-anaesthesia level	1
BP > 50 mm Hg of pre-anesthesia level	0
Consciousness	
Fully awake	2
Arousable	1
Unresponsive	0
Colour	
Pink	2
Pale, blotch	1
Cyanotic	0

Total score must be > 8 at conclusion of monitoring.

Discussion

Procedural sedation and analgesia is the use of sedative, analgesic, and dissociative drugs to provide anxiolysis, analgesia, sedation, and motor control during painful or unpleasant diagnostic and therapeutic procedures.[14] Goals of procedural sedation and analgesia include providing an adequate level of sedation while minimizing pain and anxiety, maximizing amnesia, minimizing the potential for adverse drug-related events, controlling behavior, and maintaining a stable cardiovascular and respiratory status.

In this present study, with the present study, we compared propofol ketamine with propofol fentanyl for procedural sedation and analgesia in D&C. We found that both groups have similar hemodynamics, similar side effect profile and shorter recovery time with propofol fentanyl. The ideal pharmacologic agent for procedural sedation and analgesia should have rapid onset and fast recovery time. However, there is still no consensus for best sedoanalgesic management for short-term procedures like D&C. Unfortunately, at this time no single agent exists that has all of the aforementioned qualities, so anaesthesiologists must use combinations of different drugs at varying does to achieve as many of the desired goals as possible.[15] Propofol is a substituted phenol anesthetic, which is associated with smooth induction, good maintenance and rapid recovery. Ketamine, a powerful analgesic has a high margin of safety. It produces no negative influence on ventilation or circulation. Its main disadvantage is emergence delirium.[16,17] Fentanyl, a phenylpeperidine derivative has analgesic potency 50-100 times that of morphine. But it is associated with respiratory depression and post operative nausea and vomiting. Different combinations like remifentanyl/propofol,[18] fentanyl/propofol,[19] alfentanyl/propofol or ketamine/propofol were shown to provide reliable and effective hypnosis and analgesia in D&C.[20] There is a limited number of studies concerning the use of propofol-ketamine for sedation in gynecological procedures.[20] Sahin et al. reported that alfentanil/propofol and ketamine/propofol combinations provide reliable and effective hypnosis and analgesia; however, the ketamine/propofol combination leads to higher consumption of propofol and results in a longer orientation time than the alfentanil/propofol combination.[20]

There was fall in systolic blood pressure in Propofol Fentanyl group after induction as compared to propofol-ketamine group. After starting of infusion the systolic blood pressure did not show any significant change in perioperative period. Guit JB et al[21] have also reported similar trend though both groups were haemodynamically stable. Ketamine stimulates cardiovascular system associated with increases in blood pressure and cardiac index respectively. Propofol decreases mean arterial pressure and cardiac index respectively. Modest doses of diazepam and midazolam attenuate haemodynamic effects when given as continuous infusion with it.[22] The haemodynamic stability of propofol ketamine combination makes it suitable for use during outpatient anaesthesia.[23]

In this study, incidences of side effects of both sedation regimens found less and almost similar. Desaturation and airway problems were found mild, transient and corrected easily with supplemental oxygen and repositioning of airway. Nausea, vomiting, delirum and hallucinations were less in both groups and manageable. It is also assumed that sedative and antiemetic effects of propofol may counterbalance the nauseant and psychomimetic effects of ketamine.[24]

Mean recovery time was more in group PK than group PF and the difference is statistically significant (P=0.004). Keatmine is safe and useful for procedural sedation agent but it delays recovery.[25] Mean recovery time was 11.17+2.65 (Mean+SD) minutes with propofol and ketamine in this study. Mean recovery time from etomidate has been reported between 12.6±10 (Mean+SD) minutes[26] and 17.0±10.1 (Mean+SD) minutes.[27] Studies of fentanyl/midazolam combination have shown recovery times from 28.5 minutes[28] to 113.7±36.9 (Mean+SD) minutes.[29] A limitation of this study was that we could not measure end tidal carbon dioxide (EtCO2). For measurement of EtCO2, require special sensor containing facemask.

Conclusion

Propofol ketamine and propofol fentanyl mixture had similar hemodynamic stability without any important side effects for procedural sedation and analgesia in patients underwent D&C but propofol ketamine had longer recovery time.

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