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A comparative study of efficacy of three different proportions of ketamine and propofol in minor gynaecological procedures

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Abstract

Background: An ideal intravenous anaesthetic agent to be considered for day-care surgery should provide rapid recovery with very less side effects and available at a reasonable cost. Both ketamine & propofol has all these characteristics but however cause significantly opposing hemodynamic effects which can be detrimental in patients with high risk, if used as sole induction agent.

Aim: To assess and compare the efficacy of three different proportions of intravenous propofol-ketamine combination in minor gynaecological procedures.

Materials and methods: A prospective comparative study was done on 120 patients at Vinayaka Missions Medical College Hospital by the anaesthesia department among the females who had been posted for minor gynaecological procedures. The study subjects were classified into 3 groups of 40 each. The anaesthetic drug administered for each group is as follows Group I – Propofol 1.5mg/kg + Ketamine 0.5mg/kg; Group II - Propofol 1.5mg/kg + Ketamine 1.0mg/kg and Group III - Propofol 1.5mg/kg + Ketamine 1.5mg/kg. The vital parameters were measured immediately(1 min.) after the drug (Propofol-Ketamine combination) administration and then after every 5 minutes upto half an hour. Adequacy of depth of anesthesia will be analysed by using EVANs(1987) scoring system. Requirement of airway intervention by means of bag and mask ventilation were recorded. Untoward events like vomiting or emergence phenomena during recovery were carefully watched and recorded.

Results: The systolic BP and the mean heart rate was much lower in group 1 and it was highest among group 3. The mean time of maintaining the adequate depth of anaesthesia without giving supplement dosage, which was assessed by using EVANS scoring had shown that among the group I patients it was much lower when compared with group II and III and the difference was found to be statistically significant (P<.05). The air way intervention in the form of bag and mask ventilation was required by 82.7% of the patients in group III when compared to 7.5% in group I and the difference was found to be statistically significant. The recovery from anaesthesia by taking into consideration of the supplemental dose, was found to be very high in group III patients than that of group I and II and the difference was found to be statistically significant.

Conclusion: Of the three different doses of ketamine with a fixed dose of propofol (1.5mg/kg), ketamine 1mg/kg was found to be a better dose when compared to 0.5mg/kg and 1.5mg/kg for day care gynaecological procedures.

Keywords: Ketamine, Propofol, Day-care, Gynaecological procedures.

Introduction

Ketamine which was developed in 1960s was found to be a safer and more predictable anesthetic than its precursor phencyclidine (PCP). The unique character of this agent is its procedural sedation and analgesia (PSA) which functions by blocking communication between the thalamic and limbic regions of the brain and thereby prevents the brain from processing any other external stimuli.[1] It also provides excellent amnesia and analgesia, and it helps in preserving the muscle tone and maintains the airway reflexes and also the spontaneous respiration.[2,3] One of the major disadvantage of ketamine that warrants many anaesthetist in using ketamine is the nature of causing frightening and emergent reactions.[4] Addition to this it also causes sympathomimetic effects and vomiting when it is administered in sedating doses.[5]

Propofol is a non-barbiturate sedative hypnotic which was developed in Europe in 1970s and it slowly gained the interest of anaesthesiologist over the next two decades and recently its use has spread into the Emergency Department (ED) as a part of procedural sedation.[6] It also has additional properties like antiemetic, anticonvulsant, and amnestic.[7] Although extremely effective its use had been limited because of its effect in blood pressure causing dose-dependent hypotension and in respiratory system it causes respiratory depression.[8]

An ideal intravenous anaesthetic agent to be considered for day-care surgery should provide rapid recovery with very less side effects and available at a reasonable cost. Propofol recently has emerged as the gold standard in day-care surgeries. Thiopentone and ketamine were the time tested agents but the disadvantages like prolonged recovery, emergence delirium, and postoperative nausea and vomiting were reported to be very high. Therefore, a combination of propofol with ketamine may be a better alternative. Both Ketamine and Propofol have rapid and smooth onset in action with a significant opposing hemodynamic effects.[9,10]

Ketamine and propofol administered in combination have offered effective sedation for day care surgeries in gynecological, ophthalmological, and

cardiovascular procedures in all age groups.[11] The opposing hemodynamic and respiratory effects of each drug enhances its utility of the combination drug which helps in increasing both the safety and efficacy and also allowing to reduce the dose of propofolwhen required. Few investigators have used various combinations of propofol and ketamine with an aim to offset the hemodynamic effects and their adverse effects.[12,13] But as of today very few studies had been conducted in India in assessing the hemodynamic responses of propofol and ketamine used in various combinations, so the present study was undertaken to assess the hemodynamic response of these two drugs used in various combinations.

Aim

To assess and compare the efficacy of three different proportions of intravenous propofol-ketamine combination in minor gynaecological procedures.

Methodology

A prospective comparative study was done on 120 patients at Vinayaka Missions Medical College Hospital by the anaesthesia department among the females who had been posted for minor gynaecological procedures. The study was done over a period of 6 months. The study subjects were randomly divided into 3 groups of 40 each. The anaesthetic drug administered for each group is as follows

1. Group 1 – Propofol 1.5mg/kg + Ketamine 0.5mg/kg
2. Group 2 - Propofol 1.5mg/kg + Ketamine 1.0mg/kg
3. Group 3 - Propofol 1.5mg/kg + Ketamine 1.5mg/kg

Patients who were allergic to ketamine or propofol and having some cardiac, respiratory and renal disorders were excluded from the study.

All the patients were premedicated with Inj.glycopyrrolate in the pre-operative room. Patients after shifted to the operation theatre were sedated with Inj.midazolam intravenously. Basal parameters like Heart rate, blood pressure and peripheral oxygen saturation(SPO2) were recorded after 3 minutes of midazolam administration. Then the patients were administered with drug (Propofol-Ketamine combination) as per the group allotment.

The vital parameters were measured immediately(1 min.) after the drug (Propofol-Ketamine combination) administration and then after every 5 minutes upto half an hour. Adequacy of depth of anesthesia was analysed by using EVANs(1987) scoring system. It includes changes in systolic Blood pressure, Heart rate, Sweating and Tear production.

Total score of 3 and below was considered as good plane(depth) of anaesthesia and the procedure was allowed. In case of more drug requirement for achieving the depth of anaesthesia (score more than 3), then propofol was administered in incremental doses(0.5mg/kg). Requirement of airway intervention by means of oxygen supplementation by assisted ventilation by bag and mask were recorded. Untoward events like vomiting or emergence phenomena during recovery were carefully watched and recorded.

The recovery time was calculated from the time of loading dose till the patient scores 9 out of 10 based on Aldrette Modified Recovery Score**,** which includes oxygen saturation, respiration, circulation, consciousness and activity score. All the data were entered in the SPSS version 18 and the statistical inference was derived by using ANOVA and Mann-whitney U tests.

Results

The age wise distribution of the study subjects was shown in Table 1. It is seen from the table that there was almost equal number of study subjects in all the age groups among the three groups. The minimum age was 19 years and the maximum was 50 years. The hemodynamic response among the study subjects was assessed by measuring their systolic blood pressure and the heart rate. The basal readings and at the end of 1st, 5th and 10th minute systolic BP and heart rate were measured. Table 2 shows that there was no difference in the basal measurements between the three groups, whereas there was a statistically significant difference noted at the end of 1st, 5th and 10th minute readings. The systolic BP and the mean heart rate was much lower in group I and it was highest among group III. The mean time of maintaining the adequate depth of anaesthesia without giving supplement dosage, which was assessed by using EVANS scoring had shown that among the group I patients it was much lower when compared with group II and III and the difference was found to be statistically significant (P<.05) (Table 3).

Table 1: Age wise distribution of the study population

Age group	Group I	Group II	Group III	Total
</=20	3 (7.5%)	2 (5%)	3 (7.5%)	8 (6.6%)
21–30	8 (20%)	8 (20%)	12 (30%)	28 (23.3%)
31–40	15 (37.5%)	15 (37.5%)	8 (20%)	38 (31.6%)
41–50	14 (35%)	15 (37.5%)	17 (42.5%)	46 (38.3%)
Mean age	36.12 (9.4)	36.72 (8.9)	36.12 (10.3)	120 (100%)

Table 2: Hemodynamic response among the three study groups

Group	Systolic Blood pressure (mmhg)		Heart rate (beats/min)	
	Mean (SD)		Mean (SD)	
Group I	Basal	124.8 (10.1)	Basal	87 (7.4)
	At 1 min	113.4 (10.6)	At 1 min	79.9 (7.4)
	At 5 min	111.1 (8.7)	At 5 min	83.3 (10.9)
	At 10 min	134.2 (12.5)	At 10 min	92.7 (10.4)
Group II	Basal	124.9 (10.5)	Basal	82 (7.4)
	At 1 min	124.9 (9.8)	At 1 min	83 (7.8)
	At 5 min	127.5 (9.4)	At 5 min	83.2 (8.4)
	At 10 min	128.4 (9.5)	At 10 min	85.2 (8.1)
Group III	Basal	126.9 (11.1)	Basal	82 (6)
	At 1 min	134.6 (11.9)	At 1 min	91.5 (6.9)
	At 5 min	133.5 (10.9)	At 5 min	90.2 (7.3)
	At 10 min	129.8 (10.2)	At 10 min	87 (6.5)
ANOVA P value (intergroup comparison)	Basal	0.638	Basal	0.817
	At 1 min	<.0001	At 1 min	<.0001
	At 5 min	<.0001	At 5 min	<.0001
	At 10 min	0.371	At 10 min	0.148

Table 3: Total mean duration of adequate depth of anaesthesia achieved by the three groups

Group	Mean (mins)	SD	95% CI	P value (ANOVA)
Group I	4.42	1.26	4.03 – 4.81	<.0001
Group II	14.27	3.00	13.34 – 15.2	
Group III	21.42	2.29	20.54 – 21.94	

Supplementation of anaesthetic drug in the form of propofol at the dose of either 0.5 mg/kg or 1mg/kg was given to the subjects for whom further adequacy in acquiring the depth of anaesthesia is required. Majority of the group I subjects were given this supplemental dose and only 12 patients in group II and 2 patients in group III had required the supplemental dose (Table 4). The air way intervention in the form of bag and mask ventilation was required by 82.7% of the patients in group III when compared to 7.5% in group I and the difference was found to be statistically significant (Table 5). The incidence of emergence in the form of patient becoming restless and shouting had occurred in 23.5% of patients in group III, whereas it was only 5% among group I and this difference was found to be statistically significant (Table 6). Adverse events like nausea and vomiting had occurred slightly more among the patients in group III but the difference was not statistically significant (Table 7). The recovery from anaesthesia by taking into consideration of the supplemental dose, was found to be very high in group III patients than that of group I and II and the difference was found to be statistically significant (Table 8).

Table 4: Total number of patients required supplementation dose of anaesthesia among the three groups

Supplementation dose given	Group I	Group II	Group III	P value (Mann Whitney U test)
No supplementation	2 (5%)	28 (70%)	38 (95%)	<.0001
0.5mg/kg propofol	23 (57.5%)	12 (30%)	2 (5%)	<.0001
1mg/kg propofol	15 (37.5%)	0	0	<.0001
Total	40 (100%)	40 (100%)	40 (100%)	

Table 5: Distribution of the patients requiring airway intervention in the form of bag and mask compression among the three groups

Air way intervention in form of bag and mask compression	Group I	Group II	Group III	P value (Mann Whitney U test)
Required	3 (7.5%)	15 (37.5%)	33 (82.5%)	<.0001
Not required	37 (92.5)	25 (62.5)	7 (17.5%)	

Total	40 (100%)	40 (100%)	40 (100%)	

Table 6: Incidence of emergence during anaesthesia among the study subjects

Emergence	Group I	Group II	Group III	P value (Mann Whitney U test)
Occurred	2 (5%)	7 (17.5%)	9 (22.5%)	0.0318
Not occurred	38 (95%)	33 (82.5%)	31 (77.5%)	
Total	40 (100%)	40 (100%)	40 (100%)	

Table 7: Incidence of nausea and vomiting among the three study groups

Nausea and vomiting	Group I	Group II	Group III	P value (Mann Whitney U test)
Present	5 (12.5%)	4 (10%)	7 (17.5%)	0.361
Absent	35 (87.5%)	36 (90%)	33 (82.5%)	
Total	40 (100%)	40 (100%)	40 (100%)	

Table 8: Duration of recovery from anaesthesia among the study subjects

Group	Mean (mins)	SD	95% CI	P value (ANOVA)
Group I	22.8	4.0	21.6 – 24.0	<.0001
Group II	27.2	4.5	25.8 – 28.6	
Group III	38.1	3.3	37.08 – 39.12	

Discussions

Minor gynecological techniques are usually done as a out-patient procedures rather than admitting the patients. So for a day-care anesthesia we require anaesthetic agents with following characteristics like fast in onset, good anesthesia depth, rapid recovery and with very less side effects. Various induction agents such as thiopentone, propofol, midazolam, fentanyl, and ketamine have all almost satisfied all these characteristics with each one of them having its adverse events. However ketamine and propofol had received a unique role in the field of day-care anaesthesia.[14]

Many studies[14,15] had shown a strong synergistic interaction between ketamine and propofol. A recent prospective study done by Hui T W etal on one hundred and eighty female patients for whom propofol and ketamine was administered for performing minor gynaecological procedures found an additive effect at hypnotic and anaesthetic end points.[16]

In the present study most of the females were young and had had posted for surgeries like D&C and fractional curettage and demographic characteristics were almost similar in all the three groups.

In our study patients in group I showed a greater decrease in systolic BP than the patients in group II and III. Propofol has the property of decreasing myocardial contractility, peripheral vascular resistance and thereby decreasing systolic and diastolic blood pressures, as majority of the patients in group I had received the supplemental dose of propofol for maintain the depth of anaesthesia. On the other hand ketamine has a property of stimulanting the myocardium and so thereby it increases peripheral vascular resistance and invariably the systolic and diastolic blood pressures also increases and so the patients in group III had shown a significant increase in the systolic blood pressure. Hence, with the mixture of propofol and ketamine the decrease of blood pressure caused by one agent is compensated by the other.[17,18] Ketamine because of its property of stimulating the myocardium it causes tachycardia, which had proven in our study by showing the group (group III) which had received the highest concentration of ketamine had a shown an increase in the heart rate.

The additional/supplemental dose of anesthetic agent was required more with the patients in group I, as because increase dose of ketamine shows an excellent analgesic property and so the depth of anesthesia was sustained for a longer duration in group III when compared to group I and a similar type of results was also shown in a study done by Vora *et al.*, in 2005.[14] The present study had shown that the patient with increase dose of ketamine (group III) had shown respiratory depression requiring bag and mask ventilation and the same was also proven in a study done by David H et al.[19]

The incidence of emergence reactions like delirium was seen in the higher-dose ketamine group (group III). This could be a dose-dependent interaction between the excitatory effect of ketamine and the depressant effect of propofol on the central nervous system.[20,21]

Nausea and vomiting had occurred only in few patients in all the three groups which might be due to the antiemetic properties of propofol and few of the studies done with ketamine and propofol combination had also proven the same. The recovery time from anestheisa was significantly high in group III due to the high concentarion of ketamine which has the property

of prolonged anaesthetic effect which was in par with the studies done by Hemani Ahuja et al[22] and Sanjay Arora.[23]

Conclusion

So our study had proven that Ketofol mixture (ketamine and propofol) is an excellent agent for day care gynaecological procedures. Keeping a fixed propofol concentration of 1.5mg/kg in all the three groups the group with ketamine 1mg/kg had shown a better hemodynamic stability, with a moderate period of maintaining the depth of anesthesia and a moderate supplemental dose requirement of propofol. Though there were a very few patients required supplemental dose of propofol in group who had received high dose of ketamine (group III) the requirement of bag and mask type of airway intervention was very high and also the number of patients reported with emergence and nausea and vomiting were more and the recovery time was very much prolonged. We conclude the study by quoting that of the three different doses of ketamine with a fixed dose of propofol (1.5mg/kg), ketamine 1mg/kg was found to be a better dose when compared to 0.5mg/kg and 1.5mg/kg.

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