Original Research Article

A study to evaluate the effect of subcutaneous infiltration of ketamine at incisional site on post operative analgesia in patients undergoing abdominal hysterectomy under spinal anaesthesia

Savita Patil[1], Vandana Hebballi[2], Sudha Shree P[3*], R. S. Raghavendra Rao[4]

[1]Senior Resident, Department of Anaesthesia, Belagavi Institute of Medical Sciences, Belgaum, Karnataka, India

[2]Senior Resident, Department of Anaesthesia, Shimoga Institute of Medical Sciences, Shimoga, Karnataka, India

[3]Senior Resident, Department of Anaesthesia, Hassan Institute of Medical Sciences, Hassan, Karnataka, India

[4]Senoir Consultant and DNB Faculty, General Hospital, Jayanagar, Bangalore, India

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Abstract

Background: Postoperative pain is often perceived by patient as natural consequences of surgery. If poorly treated it triggers neuroendocrine stress response which may increase morbidity and mortality. Ketamine acts as non-competitive antagonist at NMDA receptors having local analgesic effect. If given subcutaneously the side effects are significantly lower. **Aims and Objectives:** To evaluate the analgesic effects of subcutaneous infiltration of ketamine at incisional site in elective abdominal hysterectomy under spinal anaesthesia. **Materials and Methods:** Fifty patients of ASA physical status 1 & 2 aged 35-60 years undergoing abdominal hysterectomy were allocated into two groups as group K and group C, using computer generated random number list each consisting 25 patients (n=25), group K received ketamine 0.5mg/kg subcutaneously and group C 0.9% normal saline subcutaneously in surgical wound site post operatively. Patients were monitored at 0 minutes, 30 minutes,1,2,4,6,8,12,16,20,24 hours interval for changes in HR, BP, SPO2,VAS. Also side effects if any are noted. Time for the first request for analgesia and total amount of rescue analgesic consumed in 24 hours noted and compared between both groups statistically. **Results:** The time for first request for analgesia in group C was 149.60$\pm$7.27 minutes whereas it was longer in group K 245.80$\pm$15.27minutes ($P<0.001$), the mean VAS scores in group K at 2,4,6,8, and 12 hours was less compared to group C recorded during same time interval, which is statistically significant and the total amount of rescue analgesia consumed during 24 hours in group C was 86.0$\pm$30.69 whereas in group K it was 46$\pm$24.66.significantly lower in group K compared to group C($P<0.001$). **Conclusion:** Patient who were given ketamine subcutaneously at incision site postoperatively had lower pain intensity and less analgesic consumption than patients who were given placebo without increase in the risk of complications.

Key Words: Ketamine, Abdominal hysterectomy, Postoperative, Subcutaneous, Tramadol.

Introduction

Post-operative pain remains an important problem, that is usually masked by patient's attitude towards pain as a natural consequence of surgery[1]. After surgery 80% of patients experience acute pain, of these 86% having moderate to severe pain[2]. This pain stimuli from periphery when transmitted to central nervous system trigger neuro-endocrine stress which may adversely increase morbidity and mortality. Poorly controlled acute post-operative pain leads to development of chronic postsurgical pain in 10%-65% patients[3]. Suboptimal postoperative pain management may be related to inadequate or improper use of available analgesic therapies.

*Correspondence
Dr. Sudha Shree P
Senior Resident, Department of Anaesthesia, Hassan Institute of Medical Sciences, Hassan, Karnataka, India.
E-mail: sudha.shree250@gmail.com

Optimization of post-operative analgesia may facilitate recovery during the immediate post-operative period and after discharge from hospital hence decreasing morbidity and mortality.

Ketamine is a non-competitive antagonist of n-methyl-d-aspartate (NMDA) used in low dose facilitate post-operative analgesia[3]. Research have shown that ketamine has a local analgesic effect[4]. Infiltration of this drug in the surgical site delays the request for additional opioid analgesia and leads to significantly less consumption of opioid analgesics post operatively[5]. this drug can be administered orally,intravenously, subcutaneously or intramuscularly. Studies have proven that subcutaneous administration of ketamine is accompanied by a significantly lower side effects[6].Very few studies have been conducted to evaluate the subcutaneous infiltration of ketamine for post-operative analgesia. As this method is easy, less expensive, if proved effective it may help in achieving better postoperative analgesia. Hence this study is selected to evaluate the analgesic effect of subcutaneous infiltration of ketamine at incision site in patients undergoing elective abdominal hysterectomy under spinal anesthesia.

Aims and objectives

To evaluate the analgesic effects of subcutaneous infiltration of ketamine at incisional site in elective abdominal hysterectomy under spinal anaesthesia

To evaluate the safety profile of ketamine.

Materials and methods

Source of data

The study was conducted on inpatients of hospitals attached to Bangalore Medical College and Research Institute. Bangalore.

Method of collection of data

Study design

Randomized double blind prospective study

Study period

November 2017 – May 2019.

Place of study

Inpatients at hospitals attached to Bangalore Medical College and Research Institute, Bangalore.

Sample size

Based on the previous study by **Behaeen K et al**[12], it is observed that total duration of analgesia was 97.8 minute in control group. To detect a minimum of 10 min difference in duration of analgesia between control and test group, assuming normal distribution of values.

The sample size calculation was

$$N=\frac{2(SD)2(Z\alpha+Z\beta)2}{d2}$$

N=Sample size

Zα=1.96Zβ=0.84

d=10 min

SD=standard deviation= 10 min

N=16, sample size was taken as 25 in each group. Total = 50.

Inclusion Criteria

- All patients who gave written informed consent.
- All patients posted for abdominal hysterectomy.
- Age group- 35-60 years.
- American Society of Anesthesiologists (ASA) grade 1 and 2.
- Weight 45-65 kg.
- Height 150cm to 170 cm.

Exclusion Criteria

- Patients who did not give written informed consent.
- Allergy to ketamine.
- Cardio vascular disease.
- Diabetes mellitus
- Hepatic/Renal insufficiency
- Pregnancy.
- Duration of surgery more than 120 minutes.
- Absolute/relative contraindications to spinal anesthesia.
- Narcotic drug abuse/Alcohol abuse in past 6 months.
- Refusal for spinal anesthesia/ketamine infiltration.
- Minimum block lower than T6 dermatome level.
- Any supplementations are excluded.

Methodology

50 female patients aged between 35 to 60 years of physical status American society of Anesthesiologists (ASA) grade 1, and grade 2, undergoing abdominal hysterectomy, fulfilling inclusion criteria were included in the study after ethical clearance and informed written consent by patient. Using computer generated random list in https://www.random.org/, patients were randomly allocated to two groups of 25 each. An anaesthetist who was not involved in the study prepared the study medication.

Group K- Was scheduled to receive Inj. Ketamine 0.5mg/kg diluted with 0.9% normal saline to 15 ml Subcutaneously.

Group C- Was scheduled to receive inj.0.9% normal saline 15 ml, subcutaneously.

A routine pre-anaesthetic examination was conducted on the evening before the scheduled day of surgery, assessing:

- History and general condition of the patient
- Airway assessment by Mallampatti grading
- Nutritional status, height and weight of the patient
- A detailed examination of the systems like Cardiovascular system, Respiratory system and Central nervous system.
- Examination of the Spine

The following investigations were done in all patients

- Complete blood count
- Random blood sugar
- Serum electrolytes, Renal Function Tests
- Urine Routine Examination
- Standard 12-lead Electrocardiogram
- Chest X ray
- Other investigation as indicated

All patients were kept fasting for 8 hours on the previous day of surgery. Patients were pre medicated with tab Alprazolam 0.25 mg and tab Ranitidine 150 mg on the night before the day of surgery. On the day of surgery, in preoperative room, intravenous line was secured with 18 G IV cannula and were preloaded with 10 ml/kg of Ringer Lactate. Injection Ranitidine 50 mg was given intravenously half an hour preoperatively.

On arrival to the operating room, non invasive blood pressure, pulse oxymeter and three lead ECG were connected. The baseline systolic, diastolic blood pressure, Mean arterial pressure (SBP, DBP, MAP), heart rate (HR) Respiratory rate(RR) and oxygen saturation (SpO2) were recorded.

After explaining the procedure, steps and drugs, an informed written consent was obtained by an anesthestist, who was available to answer the questions regarding the study procedure and drug. And the patients were counselled that they were free to opt out from the study whenever they decided.

In left lateral position under aseptic precautions a 25 Gauge Quincke‘s needle was introduced into the subarachnoid space at L3-4 intervertebral level. With the needle bevel turned cephalad and after confirmation of free flow of CSF, 3.0 ml of 0.5% heavy bupivacaine was injected through the spinal needle, and the patient was then turned supine, and the table was kept flat. All patients were given supplementary oxygen through a face mask at 6L/min.

Sensory testing was assessed by loss of pinprick sensation to 23 G sterile hypodermic needle for the onset and dermatomal levels were tested every 2 minutes until the highest level had been achieved and stabilized for four consecutive tests. Motor block was assessed by using Bromage Scale. Surgery was allowed toproceed after sensory block of level of T6 and motor block to the level of Bromage scale of 4 was achieved.

Intra operatively, vital parameters like heart rate, non-invasive blood pressure, oxygen saturation (SPO2), was recorded till the end of surgery. Alteration in the hemodynamic parameters like fall in the systolic blood pressure more than 20% from baseline, patients received Injection ephedrine 6 mg intravenously. If heart rate went below 60/minute., Injection atropine 0.6 mg was administered intravenously, doses were repeated if needed.

Under asepsis patient received one of the following depending on group allocation after the incision closure and before dressing.

Just before the infiltration the drug syringe was handed over to the surgeon performing the infiltration in presence of anesthesiologist who was also observer .The patients were not aware of the drug being

administered to them. Thus both the observer and the patient were blinded.

Group K- Ketamine 0.5mg/kg diluted with 0.9% normal saline to 15 ml, was injected subcutaneously with equal intervals and volumes at the end of the surgery and after skin closure along the incision line on both sides. **Preservative free Ketamine 50 mg/ ml used. Brand name-Aneket, Neon laboratories**.

Group C- 0.9% normal saline 15 ml, was injected subcutaneously with equal intervals and volumes at the end of the surgery and after skin closure along the incision line on both sides.

Postoperative pain scores and analgesic requirement were recorded along with hemodynamic parameters. Immediately after shifting to postoperative recovery room at 0 min, 30 mins, 1, 2, ,4, 6, 8, 12, 16, 20, and 24 hours, respectively.

Any patient with VAS greater than or equal to 4 or complained of pain, was administered 75 mg intravenous injection of Diclofenac, which is the first dose of analgesic &duration noted from the time of administration of subarachnoid block as First Request for Analgesia(FRA). If the patient still reported VAS ≥4 after 15 minutes of receiving Diclofenac; or thereafter- intravenous injection of tramadol 50mg in 100 ml saline infusion as Rescue Analgesic(RA) was given. The total rescue analgesic consumption for the 24 hours after surgery was recorded.

Any adverse events like nausea, vomiting, pruritus, sedation, delirium, hallucinations, was noted and treated accordingly.

Statistical analysis: Data was entered into Microsoft excel data sheet and was analyzed using SPSS 20 version software. Categorical data was represented in the form of Frequencies and proportions. **Chi-square test** was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation. MS Excel**,** SPSS version 22 **(**IBM SPSS Statistics, Somers NY, USA) was used to analyze data.

Results

Demographics data

Table 1:Comparison of age distribution between control and ketamine groups

	GROUP*				
ATTRIBUTE	**CONTROL**		**KETAMINE**		**P VALUE#**
Age(Years)					
36-49	4	(16%)	2	(8%)	0.121
39-42	11	(44%)	6	(24%)	
42-45	8	(32%)	6	(24%)	
45-48	2	(8%)	4	(16%)	
48-56	-		3	(12%)	
51-54	-		2	(8%)	
54-57	-		2	(8%)	

Table 2: Comparison of Height, Weight between control and ketamine groups

	Group			
	Control	**Ketamine**		**P value**
	Mean	**Mean**		
Weight (Kg)	55.48(5.94)	54.72(5.61)		0.644
Height (M)	1.58(0.05)	1.58(0.05)		0.809

**The values depict mean; and SD in parentheses.
student's t test to compare the means. P < 0.05 is significant.

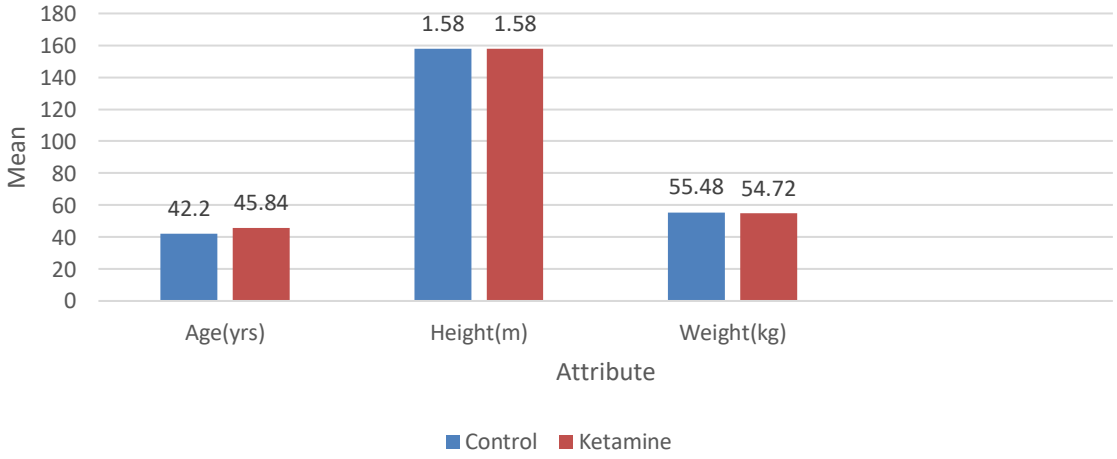

Figure.1 Bar diagram showing comparison of mean age, height, weight of study patients between group C and group K

In Group C, majority of subjects were in the age group 39-42 years (44%), in Group K, majority of subjects were in the age group 39 to 45 years (48%). There was no significant difference in age distribution between two groups. The mean height and weight were comparable between control group and ketamine group.

Table 3: Comparison of clinical attributes between control and ketamine group					
	GROUP				
ATTRIBUTE	Control		Ketamine		P Value#
DIAGNOSIS*					
AUB	6	(24.00%)	8	(32.00%)	0.529
FIBROID UTERUS	19	(76.00%)	17	(68.00%)	
COMORBIDITIES*					
ANEMIA	4	(16.00%)	3	(12.00%)	0.627
ARTHIRITIS	0	(0.00%)	1	(4.00%)	
HTN	8	(32.00%)	7	(28.00%)	
HYPOTHYROIDISM	2	(8.00%)	2	(8.00%)	
ASA GRADE*					
1	11	(44.00%)	12	(48.00%)	0.777
2	14	(56.00%)	13	(52.00%)	
*The values depict numbers; and percentage in parentheses. **The values depict mean; and SD in parentheses. #The Chi Square test was used to compare the proportions and student's t test to compare the means. P < 0.05 is significant.					

In group C 76% of the patients had fibroid uterus,whereas in group K 68% of the study patients had fibroid uterus.In group C 14% of patients were ASA-2,16% had anemia,32% had systemic hypertension and 8% had hypothyroidism.Where as in group K 13% patients were ASA-2 amongst them 12% had anemia,4% had arthritis, 28% had systemic hypertension and 4% had hypothyroidism respectively. There was no significant difference in distribution of diagnosis or comorbidities between two group.

Table 4: Comparison of characteristics of surgery and subarachnoid block between control and ketamine group					
	GROUP*				
Characteristics	Control		Ketamine		P Value
Maximum height of sensory block*					
T4	2	(8.00%)	1	(4.00%)	0.836
T5	4	(16.0%)	4	(16.0%)	
T6	19	(76.0%)	20	(80.0%)	
Two segment Regression time (mins) **	98.32	(4.93)	98.64	(4.34)	0.809
Duration of motor block (mins) **	246.44	(5.74)	247.24	(5.97)	0.631
Duration of surgery(min)**	90.88	(9.95)	90.76	(10.49)	0.967
*The values depict numbers; and percentage in parentheses. **The values depict mean; and SD in parentheses. #The Chi Square test was used to compare the proportions and student's t test to compare the means. P < 0.05 is significant.					

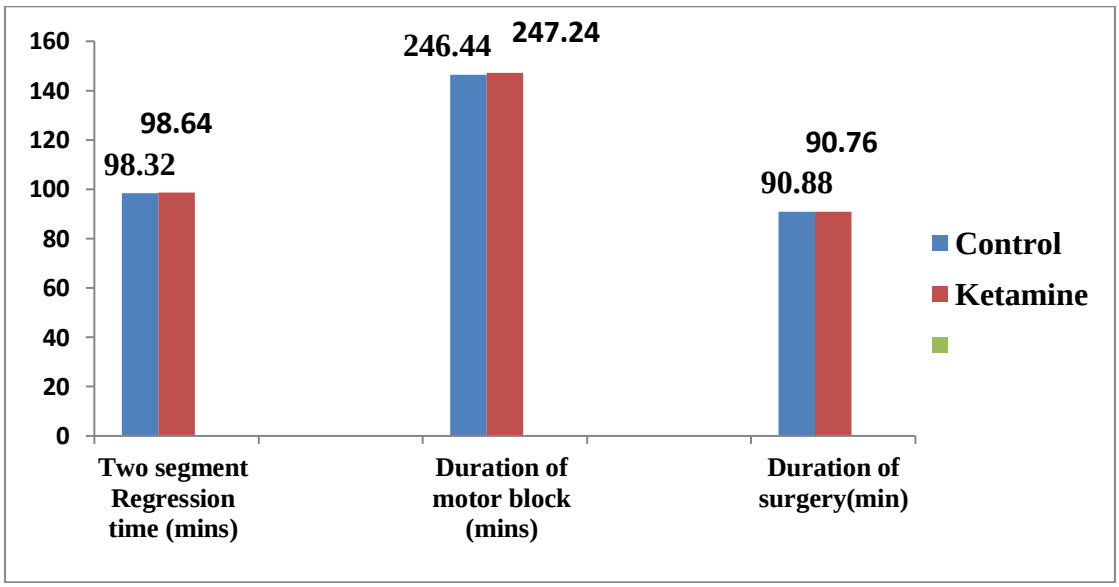

Fig 2: Graph showing the characteristics of surgery and subarachnoid block across control and ketamine group

In Group C, majority of subjects had maximum height of sensory block at T6(76.0%) and in Group K, majority of subjects had maximum height of sensory block at T6 (80%). There was no significant difference in maximum height of sensory block between two groups.(p>0.631).

In Group C mean duration of motor block was 246.44±5.74 minutes, and in Group K it was 247.74±5.97 minutes. There was no significant difference in duration of motor block between two groups.(p>0.836).

In Group C mean duration of surgery was 90.88±9.95, and in Group K it was 90.74±10.49. There was no significant difference in duration of motor block between two groups.(p>0.967)

Intraoperative parameters
Intraoperative HR, SBP, DBP, MAP, RR, SPO2 were comparable in both groups. (p>0.05)

Post operative parameters
Group K- Ketamine 0.5mg/kg diluted with 0.9% normal saline to 15 ml Group C- 0.9% normal saline 15 ml.

Tables 5: Comparison of Postoperative HR between control and ketamine group

Time	Control	Ketamine	p value
Immediate Postop	87.32(11.64)	88.08(11.59)	0.818
30m	88(12.4)	96.08(7.38)	0.007*
1h	90.72(14.16)	98.2(9.59)	0.034*
2h	90.36(13.83)	97.96(11.52)	0.04*
4h	90.44(12.84)	93.72(20.76)	0.505
6h	90.6(13.01)	96.72(10.11)	0.069
8h	88.28(12.07)	92.52(7.93)	0.149
12h	90.6(13)	96.72(10.11)	0.069
16h	91.48(11.18)	94.76(9.53)	0.27
20h	91.28(11.29)	95.84(9.05)	0.122
24h	91.36(11.35)	96.52(10.04)	0.095

In group K there was statistically significant increase in mean HR at 30 minutes,1,2 hours compared to control group postoperatively. But clinically the change in HR lies well within the normal HR range. At other intervals there was no significant difference in mean HR between two groups.

Tables 6: Comparison of Postoperative SBP between control and ketamine group

Time	Control	Ketamine	p value
Immediate Postop	102.2(8.6)	104.72(8.36)	0.299
30m	103(6.97)	117.72(8.29)	0*
1h	112.88(8.55)	117.6(9.85)	0.077
2h	114.96(7.55)	122.16(7.25)	0.001*
4h	118.88(9.15)	118.64(8.44)	0.924
6h	119.6(10)	121.36(8.88)	0.514
8h	118.88(8.31)	121.76(5.7)	0.159
12h	119.52(7.83)	118.96(7.39)	0.796
16h	115.68(10.24)	119.76(6.98)	0.106
20h	113.76(9.1)	119.76(6.98)	0.106
24h	117.28(7.76)	121.6(11.21)	0.12

In group K there was statistically significant increase in SBP at 30 minutes, 2 hours compared to control group postoperatively. But clinically the change in SBP lies well within the normal SBP range. At other intervals there was no significant difference in mean SBP between two groups.

Table 7: Comparison of postoperative DBP between control and ketamine group

Time	Control	Ketamine	p value
Immediate Postop	63.92(7.91)	63.2(7.44)	0.742
30m	66.4(3.81)	65.08(5.85)	0.349
1h	69(5.72)	69.88(4.99)	0.565
2h	67.76(4.63)	68.76(4.65)	0.45
4h	67.72(4.66)	67.88(4.48)	0.902
6h	67.84(4.79)	68.76(3.96)	0.463
8h	69.2(5)	68.16(5.77)	0.499
12h	68.24(2.11)	70.88(6.38)	0.055
16h	68.72(4.89)	70.76(6.44)	0.213
20h	70.48(6.76)	70(6.03)	0.792
24h	69.04(8.04)	69.96(7.85)	0.684

In groups K and group C there was no statistically significant change in DBP postoperatively.

Table 8: Comparison of postoperative MAP between control and ketamine group

Time	Control	Ketamine	p value
Immediate Postop	76.68(5.65)	77.04(5.33)	0.818
30m	78.6(2.99)	82.63(4.7)	0.001*
1h	83.63(4.14)	85.79(4.89)	0.098
2h	83.49(3.59)	86.56(3.39)	0.003*
4h	84.77(4.75)	84.8(3.39)	0.982
6h	85.09(4.61)	86.29(4.49)	0.356

8h	85.76(3.59)	86.03(4.2)	0.81
12h	85.33(2.98)	86.91(4.65)	0.161
16h	84.37(4.74)	87.09(4.59)	0.045*
20h	84.91(5.33)	86.59(4.39)	0.23
24h	85.12(5.39)	87.17(7.74)	0.282

There was increase in mean MAP at 30 minutes,2,16th hour in group K than group C but the mean MAP values lie in the normal range. At other intervals there was no significant difference in mean MAP between two groups.

Table 9: Comparison of postoperative RR between control and ketamine group.

Time	Control	Ketamine	p value
Immediate Postop	13.28(1.51)	13.28(1.51)	1
30m	16.84(1.82)	16.81(1.85)	0.939
1h	17.44(1.73)	17.48(1.66)	0.934
2h	16.16(1.84)	16.16(1.86)	1
4h	15.72(1.31)	15.72(1.31)	1
6h	15.8(1.29)	14.92(1.29)	0.02*
8h	14.76(1.39)	15.44(2.14)	0.19
12h	15.6(2.1)	14.83(1.93)	0.189
16h	14.84(1.93)	14.84(1.93)	1
20h	14.96(2.09)	15.12(1.67)	0.766
24h	14.92(1.78)	15.12(15.15)	0.68

There was increased mean RR at 6th hour in group C than group K but the mean RRbut values lie in the normal range. At other intervals there was no significant difference in mean RR between two groups.

Tables 10: Comparison of postoperative SPO_2 between control and ketamine group.

Time	Control	Ketamine	p value
Immediate Post OP	99.87(0.46)	99.78(0.77)	0.505
1hr	99.87(0.40)	99.84(0.42)	0.800
2hr	99.82(0.44)	99.91(0.29)	0.261
3hr	99.84(0.42)	99.82(0.49)	0.819
4hr	99.87(0.42)	99.87(0.34)	1.000
8hr	99.73(0.54)	99.76(0.53)	0.844
12hr	99.56(0.87)	99.58(0.84)	0.902
16hr	99.58(0.84)	99.64(0.77)	0.696
20hr	99.69(0.60)	99.69(0.67)	1.000
24hr	99.60(0.75)	99.64(0.71)	0.774

There was no significant difference in mean SpO2 between group K and group C postoperatively.

Tables 11: Comparison of postoperative RSS between control and ketamine group

Time	Control*	Ketamine*	P value
Immediate Postop	2.12(0.33)	2.12(0.33)	1
30m	2(0.29)	2.04(0.2)	0.572
1h	2.04(0.2)	2.04(0.2)	1
2h	1.84(0.37)	2(0)	0.038*
4h	1.8(0.41)	1.84(0.37)	0.72
6h	1.8(0.41)	1.83(0.36)	0.71
8h	1.76(0.44)	1.92(0.28)	0.128
12h	1.8(0.41)	1.84(0.38)	0.72
16h	1.84(0.37)	1.92(0.28)	0.394
20h	1.8(0.41)	1.84(0.37)	0.72
24h	1.88(0.33)	1.76(0.44)	0.279
*The values depict mean; and SD in parentheses. #The Mann Whitney U Test used to compare the means. P < 0.05 is significant.			

In group K there was higher RSS score that in group C, otherthan that there was no significant difference in mean RSS between group K and group C postoperatively.

Table-12: Comparison of postoperative VAS between control and ketamine group

Time	Control*	Ketamine*	p value#
Immediate Postop	0	0	-
30m	0.12(0.33)	0(0)	0.077
1h	1.2(0.65)	1.16(0.62)	0.825
2h	2.8(0.96)	1.6(0.5)	0*

4h	2.88(0.83)	2.32(0.56)	0.007*
6h	3.4(1.71)	2(0.77)	0.03*
8h	3.6(1.26)	2(0.87)	0*
12h	3.36(1.19)	2.2(0.65)	0*
16h	2.68(0.85)	2.4(0.76)	0.227
20h	2.76(0.83)	2.48(0.96)	0.276
24h	2.72(0.94)	2.68(0.99)	0.884
*The values depict mean; and SD in parentheses. #The Mann Whitney U Test used to compare the means since variables. P < 0.05 is significant.			

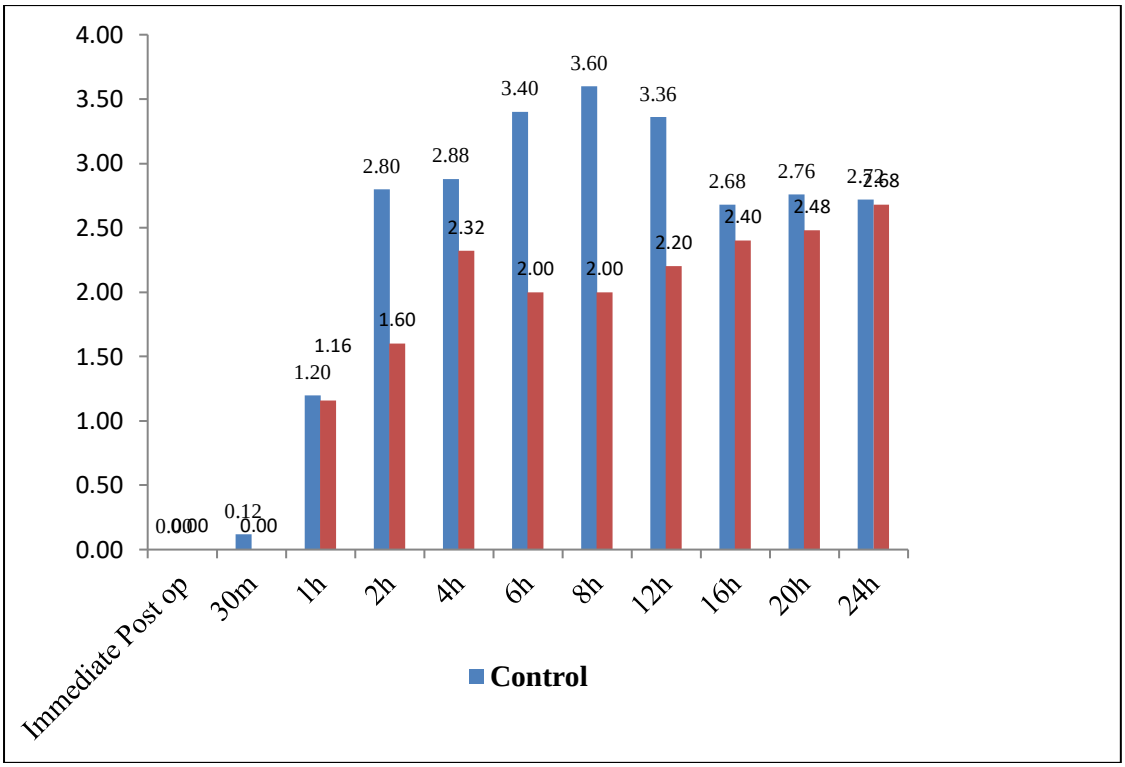

Fig 3: Comparison of postoperative VASbetween control and ketamine group

The mean VAS scores in group K at 2,4,6,8, and 12 hours was less compared to group C recorded during same time interval, which is statistically significant. (P<0.05) there was no statistically significant change recorded in other time intervals.

Table-13: Comparison of time for FRA &RA between control and ketamine group					
	GROUP*				
Monitoring values at baseline	**Control**		**Ketamine**		**P Value**
Time for first request for analgesia (minutes)	149.6	(7.27)	245.80	(15.27)	**<0.001#**
Quantity of Rescue Analgesia consumed (in mg)	86.00	(30.69)	46.00	(24.66)	**<0.001##**
*The values depict mean; and SD in parentheses. #The Student t test used to compare the means. P < 0.05 is significant. ## The Mann Whitney U Test used to compare the means. P < 0.05 is significant.					

In this studywe found that in group C the time for first request of analgesia was 149.60 ±7.27 minutes. Whereas in group K it was 245.80 ±15.27 minutes. The duration for the first request of analgesia was prolonged in ketamine group than control group which was statistically significant. The mean requirement of rescue analgesia i.e injection Tramadol was 46.00±(24.66) mg in group K, where as in group C it was 86.00± 30.69mg. The need for rescue analgesia was higher in control group compared to ketamine group and is statistically significant P<0.001.

Safety profile

Tables-14 :Comparison of postoperative RSS between control and ketamine group					
	GROUP*				
SIDE EFFECT	CONTROL		KETAMINE		P value
Nausea	2	(8.00%)	1	(4.00%)	0.837
Vomiting	2	(8.00%)	2	(8.00%)	
*The values depict numbers; and percentage in parentheses. #The Chi Square test was used to compare the proportions. P < 0.05 is significant.					

There is no statistically significant change found in side effects of group K and group C (p>0.05)

Discussion

Laparotomy performed through a Pfannenstiel incision is one of the most common operations involving the female abdomen; being a major surgical procedure, substantial postoperative discomfort and pain is always anticipated. Many new strategies continue to evolve in an effort to alleviate pain. Few of the most commonly used postoperative analgesic methods in our hospitals are-

1. **Opioids**- Opioid drugs have been used to treat pain for centuries now. The fears of opioid side effects, such as respiratory depression, sedation, and addiction, have apparently led to administration of inadequate analgesics.
2. **NSAIDS** and other adjuncts (e.g., gabapentin) routinely used in developed countries are used much less in Low and medium income countries (LMIC) because they are expensive or unavailable.
3. **Ultrasound**- guided regional techniques, a novel method in countering postoperative analgesia may not be feasible at all the time and place due to limitation in the availability of a ultrasound machines, and skills.

Published studies of anaesthetic care have provided the following details regarding LMIC: 1) There are few anesthesiologists 2) There are many surgical patients on the surgical wards with few nurses, especially at night (commonly only two nursing staff for a ward of 50 patients), and consequently, administration of analgesic drugs is considered low priority[18]. Subcutaneous injection has a more prolonged and less peaked pharmacokinetic concentration profile than intravenous or intramuscular injections. Furthermore, the procedure is easily taught to nursing assistants and requires only inexpensive and ubiquitous supplies.

Hence there is a need for a simple inexpensive method of postoperative pain control in LMICs.

In this study titled A study to evaluate the effect of subcutaneous infiltration of ketamine at incisional site on postoperative analgesia in patients undergoing abdominal hysterectomy under spinal anaesthesiaconducted in hospitals attached to Bangalore medical college and research institute, Bangalore, to evaluate the analgesic effect of ketamine.

Included 50 patients randomly distributed in 2 groups, Group C-received subcutaneous infiltration of saline as placebo and Group K-received subcutaneous ketamine infiltration.

In our study, low dosage of ketamine was used to control the postoperative pain. Because of the known psychomimetic complications of ketamine along with its analgesic effects with low plasma concentration of 100-200 ng/mL we paid more attention to administering low dosages of ketamine when it comes to curing clinical pain.

Hypothesis made before starting the study

We hypothesized that subcutaneous infiltration of ketamine in surgical site postoperatively in abdominal hysterectomy patients, provides better analgesia in the form of longer duration for the first request of analgesia, low VAS scores, decreased consumption of rescue analgesia compared to saline infiltration(Placebo).

Demographic data

Demographic data comparing age, gender, weight, height, ASA grade shows no statistically significant difference among both groups.

Subarachnoid block

Both Group K and Group C patients received subarachnoid block with Bupivacaine 0.5% heavy 3ml in both groups by same technique. The mean Two segment regression time of sensory block found in our study in ketamine group 98.64±4.34 and control group 98.32±4.93 (p=0.809) which are comparable. Duration of analgesia was 149.60 ±7.27 in control group.

Kubre J et al[17], found that injection Bupivacaine 0.5% hyperbaric 15 mg given in infra-umbilical surgeries had two segment regression of sensory block was at 96.67 ± 7.649 minutes, the total duration of analgesia achieved was 164.17 ± 6.170 minutes. The characteristics of subarachnoid block observed in our study are comparable with this study. And the duration of analgesia in control group which received saline as Placebo are comparable to this study.

As patients received either subcutaneous ketamine or saline infiltration post operatively, hence any change in the duration for the first demand for analgesic is due to study drug infiltration.

Intraoperative Hemodynamic parameters

Intraoperative HR, SBP, DBP, MAP, RR, SPO2 were comparable in both groups. (p>0.05)

Analgesic efficacy

First request of analgesia

In our study, in group C the time for first request of analgesia was 149.60 ±7.27 minutes. Whereas in group K it was 245.80 ±15.27 minutes. The duration for the first request of analgesia was prolonged in ketamine group than control group. There was significant difference between two groups. (p<0.05)

In a previously conducted study by **Behaeen et al**.[12]–**'**Analgesic Effect of Low Dose Subcutaneous Ketamine Administration Before and After Cesarean Section**'** it was found that first request of analgesia in patients who received subcutaneous infiltration of ketamine 0.5 mg/kg before caesarian section was 202.40 ± 15.77 minutes, after was 206.00 ± 14.49 minutes compared to control group 97.8 ± 6.59 minutes. Duration of first request for analgesia was more in postsurgical infiltration than in pre surgical infiltration, which in turn was prolonged compared to control, which is statistically significant. This is compared well with our study.

Rescue analgesia

In our study the mean requirement of rescue analgesia i.e injection Tramadol was 46.00±(24.66) mg in group K, where as in group C it was 86.00± 30.69mg. The need for rescue analgesia was higher in control group compared to ketamine group and is statistically significant P<0.001.

In a previously conducted study by **Behaeen et al[12]** the total analgesic consumed was 175 ± 100 mg of Diclofenac ,in patients who received ketamine pre or postoperatively. But in control group 275 ±00 was consumed. The analgesia consumed was more in control group than ketamine group which was statistically significant. There was no substantial difference in the rate and amount of analgesic consumed between the two groups receiving ketamine before and after surgery.

VAS score

In our study the mean VAS scores in group K at 2,4,6,8, and 12 hours postoperatively was less compared to group C recorded during same time interval, which is statistically significant. ($p<0.05$)The mean pain intensity in the both groups did not show any significant difference at 16, 20 and 24 hours post operatively ($p > 0.05$)

In **Behaeen et al** it was found that VAS scores in 2,4,6,12 hours after beginning the anesthesiawere reduced significantly in patients who received ketamine before and after surgery (duration of surgery 47.7 ± 5.59, 46.1±3.95 respectively) compared to control group(duration of surgery 46.7 ± 3.4). And it was statistically significant. The mean pain intensity in the three groups did not show any significant difference at 18 and 24 hours after the beginning of anesthesia ($p > 0.05$).

Vital parameters

In our study the mean Heart rate at 30 minutes,1, 2hours in group K is higher compared to group C, which is statistically significant but the values lie in the normal range of heart rate hence not indicating any clinical significance. The mean SBP in group K is higher at 30 minutes & 2 hours than group C, there is no significant variation between both groups in DBP any time post operatively, there is increased MAP at 30 minutes,2,16th hour in group K than group C but the values lie in the normal range hence not indicating any clinical significance.There was increased mean RR at 6^{th} hour in group C than group K but values lie in the normal range.There was no significant difference in mean SpO2 between group K and group C postoperatively.

In a previously conducted study by **Behaeen et al[12]** observed thatSpO2, HR, systolic, diastolic, and mean arterial pressure were not significantly at any time intervals throughout surgery and in the postoperative period in ketamine .

Safety profile

In our study, the incidence of nausea and vomiting is found to be comparable in both groups, and is not statistically significant. There was no patient with delirium, hallucinations, or nightmares in any of the groups.

In a previously conducted study by **Honarmand A et al**[8]-the sedation scores in groups receiving ketamine were compared with control. The median sedation values at any time postoperatively were not significantly different between the three groups. The groups who received ketamine subcutaneously and IV, when compared with control the incidence of adverse effects was not significantly different between the three groups. There was no patient with emergent delirium, hallucinations, or nightmares in any of the groups.

In a previously conducted study by **Safavi et al.[9]**which compared subcutaneous and IV ketamine with control found that the median sedation values at any postoperative period were not statistically different between groups.

Conclusion

Patient who were given ketamine subcutaneously at incision site postoperatively had lower pain intensity and less analgesic consumption than patients who were given placebo without increase in the risk of complications.

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