ROLE OF KETAMINE IN SUBANESTHETIC DOSE TO ALLEVIATE PROPOFOL INJECTION PAIN IN PATIENTS UNDERGOING CESAREAN SECTION SURGERY

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ABSTRACT

Objective: To evaluate the role of sub anesthetic dose of ketamine when given 5 minutes prior to Propofol injection in alleviating pain of injection during cesarean section surgery.

Study Design: Randomized controlled trial.

Place and Duration of Study: Department of anesthesia and critical care, Nishtar Hospital Multan, from Aug 2016 to Feb 2017.

Material and Methods: A total number of 130 (100%) patients were included in the study. Data was analyzed using SPSS (v 23.2), mean and SD calculated for continuous data (age, BMI) and in continuous data was presented as frequency and percentages (ASA status, pain of propofol injection). Effect modification seen by applying chi square test and *p*-value ≤0.05 considered as significant.

Results: A total number of 100% (n=130) patients were included in this study, all were females. The main outcome variable of this study was pain of propofol injection. It was observed that, in control group, 87.7% (n=57) patients complaints about pain after propofol injection and 12.13% (n=8) remain normal. But, in ketamine group only 16.9% (n=11) patients complaint about pain of propofol injection and 83.1% (n=54) were remained pain free.

Conclusion: Administration of ketamine 0.25µg/kg five minutes before propofol injection is a safe and effective method in preventing propofol injection pain.

Keywords: Anesthesia, Ketamine, Pain, Propofol.

INTRODUCTION

Propofol is a commonly used induction drug mostly used in short duration surgeries and cases in which rapid induction is needed[1]. A common complaint of this agent is pain on injection site that occurs in 28-90% of cases and intensity of this pain is mostly very severe[2]. Many techniques have been applied to treat this pain. Metaclopramide, local injection of lignocain, alfantanyl were tried in this aspect[3]. Other techniques include administration of propofol in large vein, chilling of drug before use and dilution of propofol in other medicines like intralipid[4,5]. Ketamine is a drug of choice used in this aspect of pain relief, and thus is in use for more than thirty years. Although it has some side effects like hallucination and emergence reactions[6]. It is observed that Ketamine also have less cardiac and respiratory depression like side effects[7], and it is a good anesthetic and analgesic effect. Due to its good analgesic efficacy, Ketamine was also tried to relieve pain due to propofol injection[8]. Our assessment method of direct questioning about pain is a more effective and accurate than any other technique[9]. Ketamine is a local anesthetic on intravenous use and analgesic properties when administered intra-thecaly, we use low doses of Ketamine 0.25 mg/kg, this dose is much lower than dose required for central analgesia. Mechanism of this pain control is peripheral action on afferent pain pathway. Ketamine acts on NMDA receptors in central nervous system or in vascular system and is a NMDA antagonist[10]. In 2009 Zahedi *et al* conducted a study on Prevention of propofol injection pain with small-dose ketamine[11]. He reported 88% pain relief in ketamine group and 65% in placebo group. There is no regional study available on this topic before our study, a limited knowledge available. So this study is planned to

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evaluate the role of sub anaesthetic dose of ketamine when given 5 minutes prior to Propofol injection in alleviating pain of injection during cesarean section surgery. In near future this study will be used as local references in further research.

MATERIAL AND METHODS

This randomized controlled trial was conducted in the department of anesthesia and critical care Nishtar Hospital Multan, from August 2016 to February 2017. After approval from the institutional ethics committee informed consent was obtained from the patients. Patients were also informed about their inclusion in the study and purpose of research. A total number of 130 (100%) patients were included in the study, Sample size was calculated from an online source openepi.com with following values; confidence interval 95%, power of test 80%, percentage in group Ketamine (P1) 65% and in control group (P2) 88%[11]. Non probability consecutive sampling technique was used to select the patients. Patients who were taking any type of sedatives or pain killers before 1 day of operation, patients having allergic reaction to propofol and ketamine were excluded from the study. Two I/V lines of 18 gauges were inserted on large veins of both hands and patients were loaded with 10 ml/kg ringer lactate solution. Patients were equally divided into two equal groups (65 patients in each group) by lottery method. In ketamine group patients were given 0.25 mg/kg ketamine before propofol injection and in control group normal saline 0.25 mg/kg was given before propofol injection. After these medication propofol 1% 2.5 mg/kg was injected over 30 seconds. After 5 seconds of propofol injection a new anesthetist was asked to label the pain score by observing the patient about intensity of pain. Pain score was labeled as grade 0=no pain, grade 1 = mild pain (pain full facial expressions), grade 2 = moderate pain(verbal expression of pain by patient), grade 3=severe pain (withdrawal of limb due to pain). All the information was recorded on a predesigned proforma. Data was entered and analyzed by using SPSS (version 23.2) was expressed as mean and SD for numerical values

Table-I: Demographics in both groups.

Groups		**Mean**
Control Group	Age in years	28.01 ± 4.44
	BMI	28.49 ± 2.24
Ketamine Group	Age in years	27.49 ± 4.99
	BMI	27.78 ± 2.23

Table- II: Frequencies and percentages.

Characteristics	**Frequency (n=130)**	**Percentage**
ASA		
II	91	70
III	39	30
Stratified Age		
18-25 years	45	34.6
26-36 years	85	65.4
Stratified BMI		
25-27 BMI	54	41.5
28-32 BMI	76	58.5
Descriptive Statistics		
	Mean	**SD**
Age in years	27.75	4.71
BMI	28.13	2.25

and frequencies and percentages for categorical variables. Statistical test chi square was applied to see the effect modification. A *p*-value of ≤0.05 was taken as significant.

RESULTS

A total number of (n=130) patients were included in this study, all were females. The mean age and BMI of the patients was 27.75 ± 4.71 years and 28.13 ± 2.25 BMI respectively (table-I). Out of 100% (n=130), majority of the patients i.e. 70% (n=91) were ASAII and 30% (n=39) were ASAIII. These 100% (n=130) patients were divided into 2 groups, 65 in each, i.e. control and ketamine. The mean age and BMI of the patients in control group were 28.01 ± 4.44 and 28.49 ± 2.24 respectively, in ketamine group the mean age and BMI were 27.49 ± 4.99 and 27.78 ± 2.23 respectively (table-II). The main outcome variable of this study was pain of propofol injection. It was observed that, in control group, 87.7% (n=57) patients complaints about pain after propofol injection and 12.13% (n=8) remain normal. But, in ketamine group only 16.9% (n=11) patients complaint about pain of propofol injection and 83.1% (n=54) remain normal (table-III). When patients were categorized into different age and BMI categories, it was noted that majority of patients i.e. 65.4% (n=76) having age from 28 to 32 years and 34.6% (n=45) having age from 18 to 25 years. 41.5% (n=54) patients having BMI from 25 to 27 and 58.5% (n=76) patients have BMI from 26 to 32 respectively (table-IV). When chi-Square was applied to check the effect modification, it was noted that pain of propofol injection was significantly associated with ASA and groups with *p*-values 0.000 and 0.000 respectively. Pain of propofol injection was not significantly associated with stratified age and BMI with *p*-values 0.349 and 0.247 respectively.

Table-III: Pain of propofol injection in both groups.

Groups		Frequency	Percentage
Control	Yes	57	87.7
	No	8	12.3
	Total	65	100.0
Ketamine	Yes	11	16.9
	No	54	83.1
	Total	65	100.0
p-value		0.000	

Table-IV: Association of pain of propofol injection with effect modifiers (n=130).

Effect Modifiers		Pain of Propofol Injection		Total	*p*-value
		Yes	No		
Stratified age	18-25 years	21	24	45	0.349
	26-36 years	47	38	85	
Total		68	62	130	
Stratified BMI	24-27 BMI	25	29	54	0.247
	28-32 BMI	43	33	76	
Total		68	62	130	
ASA	II	68	23	91	0.001
	III	0	39	39	
Total		68	62	130	

DISCUSSION

In a study cremopher *et al* reported 30-80% of frequency of pain due to propofol injection[12]. Many methods have been evolved to reduce its pain as it is diluted in soya been oil emulsion. Intensity of pain was reported more in dorsal

hand vein and 0-30% in large veins[13]. This pain is due to the release of pain mediators but change in osmolarity, PH and irritation in endothelial cells also contributing factors. To reduce propofol injection induced pain many techniques have been described such as mixing of lignocain with propofol is widely used in this time but its failure rate is much more about 13-44%[14]. But protein is not complete yet its failure rate is 44%. Reported in some studies that cooling the propofol injection at 4^0C is also a useful method to reduce pain at propofol injection site. This technique reduces the pain by delaying the release of pain mediators. Avoiding the direct contact of endothelium and drug is also helpful. For this purpose propofol injection should be introduced in large vein of forearm. Pain due to propofol injection was reported 26% to 84% when administered in large veins[15, 16]. Local application of analgesic creams before injection and dilution of injection in itralipids remain a useful method for few decades. Metaclopramide injection also reduced pain of propofol injection because of structural similarity with lignocain. It is also weak anesthetic agent. It's properties to reduce pain is same as lignocain injectable[15,17]. The use of opiod analgesic is also a suggested technique and it is successful in 84% cases, most widely used opiod is alfantanyl. In our study we assessed the use of Ketamine and it confirmes the success of Ketamine as reported 26% to 84 %. In a study Tan *et al*[18] reported that 10mg of Ketamine diluted in 1 ml normal salin and given before injection of propofol significantly reduces the pain after propofol injection. This method decreases the incidence about 80% of cases. Doses of Ketamine for this purpose varies between 0.1 mg/kg to 1 mg/kg[19]. In two previous studies the dose of one. 1 mg/kg was supported but meanwhile there are two more studies supported the higher dose 0.3 mg/kg was recommended. In a study Saadawey *et al*[20] reported 0.4 mg/kg Ketamine is more effective than thi open tone, lignocain and meri dine when administered before propofol injection. In another study Kobachi *et al*[21] compare with premixed lignocain, ketamine and suggested that lignocain is more effective agent for POPI when used in pediatric population. It's role may be due to local anesthetic property of Ketamine.

LIMITATION OF STUDY

We conducted our trial in obstetrical group of patients in only female gander. Further trials are required to make proper guide lines on this subject.

CONCLUSION

Administration of ketamine 100 microg x kg (-1) five minutes before propofol injection is a safe and effective method in preventing propofol injection pain.

RECOMMENDATIONS

On the observations of our study results , we recommend that ketamine in a dose of 0.25mg/kg is a reasonable option to prevent Propofol injection pain in patients undergoing ceasearn section surgery.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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