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Review Article,

Effect of Ketamine in Reducing Pain after Intravenous Injection of Propofol

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Abstract

Background: Propofol is frequently associated with pain during intravenous injection ;which reported to occurs in 28-90% of patients , usage of ketamine as a pre-treatment with rubber tourniquet for one minute before propofol intravenous administration, significantly reduce the severity and incidence of propofol induced pain. **Aims:** first to evaluate the effect of pre-treatment with small dose of ketamine with venous occlusion on reducing the pain of propofol injection in adult patients, and second to find alternative to lidocaine pretreatment. **Patients and methods:** Informed consents were taken from ninety unpremeditated adult patients aged 20-60 years with ASA physical status classes 1 and 2; who were scheduled for elective surgery. Patients were assigned in to three equal groups each of 30 (1st Group -received intravenously 2mls normal saline, 2nd - 2mls of 1% I.V. lignocaine, 3rd - 2mls of ketamine 10 mg (i .v). **Results**: there was no significant differences in age ,sex or weight .The incidence of pain was 33.3% in the ketamine group as compared to 30% in the lidocaine group and 63.3% in the normal saline group , The difference between the two proportions is :63.3 - 30= 33.3 is significant because the difference is more than twice the SE (P). (b)Saline Vs Ketamine: S E (P) = √ (63.3× 36.6)/30+ (33, 3× 66, 6)/30=12.3. The difference between two proportions =33.3 (Statistically significant) c) lidocaine Vs ketamine: S E (P) = √ (30× 70)/30+ (33, 3× 66, 6)/30 =12.00 Difference = 3.3 (no significant difference) There was no significant difference in pain score among lidocaine and ketamine groups. Although there was significant difference between group of normal saline other two groups The overall incidence and severity of pain during injection of propofol in the various groups .The incidence of pain in saline group was 63.3% as compared to 30% and 33.3% in the lidocaine group and ketamine groups respectively. None of patients had any side effects like erythema, itching, and bradycardia. There is no significant difference in the incidence of pain between the lidocaine (30%) and ketamine (33.3%) groups. Severe pain occurred in two patients (6%) in the saline group as compared to (0 %) in both lidocaine and ketamine groups. No pain was 36.63% in the saline group, 70% in the lidocaine group and 66.6 % in the ketamine group**. Conclusion:** the current study confirmed that pretreatment with intravenous 10mg ketamine with one minute venous occlusion by tourniquet reduced the incidence and severity of propofol (i.v) injection pain, and this can be an alternative for lidocaine.

Introduction

Propofol is frequently associated with pain during intravenous injection; this pain occurs in 28-90% of patients as reported by Picard P and Tramer MR 2000(1). However Briggs LP et al 1981(2) showed that pain on injection of propofol can be immediate or delayed. Immediate pain probably results from a direct irritant effect whereas delayed pain has latency of between 10 and 20 seconds probably results from an indirect effect via the kinine cascade. Mattila MAK and Koski E M Z 1985(3) described the sensation produced is usually described as tingling, cold, numbing, or at its worst a severe burning pain proximal to the site of injection, this sensation tends to last only for the duration of injection and despite this

discomfort, the incidence of venous squalae such as phlebitis is less than 1%. Different methods have been used to decrease this discomfort, including cooling, adding lignocaine, applying nitroglycerine ointment to the venepuncture site, injecting cold saline prior to the injection of propofol, diluting the propofol with 5% dextrose or intralipid, and Intravenous lignocaine which is the most commonly used pretreatment but has a failure rate of 13% to 32% as reported by Scot RPF et al 1988 (4). Tan CH et al 1998 (5); suggest that prior administration of ketamine 10mg over 30sconds before propofol without temporary venous occlusion reduced the propofol associated pain. Recently Batra YK et al 2005 (6) used ketamine pre-treatment with rubber tourniquet for one minute before intravenous propofol administration, which significantly reduced the incidence and severity of propofol pain, and they found that it was as effective as lidocaine in reducing this pain. Hand, is a subjective emotional state of excessive anxiety, uncertainty, irrational fear where it is caused by a threat whose source is either of unknown etiology or has minimal intensity compared to the intensity of normal and emotional (psychological) reaction it causes. Fear leads to specific activities such as running away or attacking while stress has the ability to detune and disorganize the sufferer. Fear brings about changes both on a psychological level (subjective feeling of fear) as well as at a normal level (acceleration of the heart rhythm, acceleration of respiration, redistribution of blood from the skin and viscera to the large muscles). These changes prepare the body for muscle activity (fight or flight), which may be necessary in response to the threat (Mohan, 2017). When the stress exceeds the normal degree, and prevails for a long time period then is a morbid manifestation, and is considered pathological resulting in impaired adaptive capacity of man. Pathological stress is defined as disproportionate reaction to a situation or reaction resulting from conflicts belonging to the

Aims of the Study

These are two: first to evaluate the effect of pre-treatment with small dose of ketamine with venous occlusion on reducing the pain of propofol injection in adult patients ,and second to find alternative to lidocaine pretreatment .

Patients and methods

Informed consents were taken from ninety unpremeditated adult patients aged 20-60 years with ASA physical status classes 1 and 2; who were scheduled for elective surgery for the period between July 2017 to August 2018 at Albasrah general hospital. Those with history of allergy to Propofol, lignocaine, anticipated difficult venous access, were excluded from the study.

Patients were assigned in to three equal groups each of 30.

Group 1 -received 2mls normal saline intravenously (i. v).

Group 2 - received 2mls of 1% lignocaine (i .v).

Group 3 - received 2mls of ketamine 10 mg (i .v)

On arrival to the operation theater routine monitoring was applied for pulse oximetry, blood pressure, and electrocardiogram.

Intravenous cannula size 20 gauge, was placed without the use of local anesthesia; in the largest vein on the dorsum of non-dominant hand.

Venous occlusion was performed for one minute using a rubber tourniquet placed on the upper arm after elevating the arm for 30 seconds for gravity drainage of venous blood as described by Lia WJ et al 1999 (6),and the study drug was injected over 10 seconds and thereafter the occlusion was released and propofol 2mg/kg was delivered .During the 10 seconds after the first 25% of the calculated propofol dose was given, the intensity of pain was graded using a verbal rating scale and the patients were informed of the possibility of burning sensation in the forearm during induction of anesthesia and were requested to grade the severity of pain as none, mild ,moderate or severe after 10 seconds interval after injection. Limb withdrawal ,tears and grimacing were taken to be signs of severe pain table 1 ;Batra YK et al 2005 (6) .

Thereafter, the induction of anesthesia was continued as planned with the remainder of the calculated propofol dose delivered. Anesthesia

was maintained with halothane 0.5- 2% and oxygen 100% with spontaneous or controlled ventilation.

Statistical analysis: the standard error of the difference between two proportions was used as follows

SE (P) = √ (p1× q1) /n1+ (p2× q2)/n2

Where p1 and q1 are the percentage in one sample which have and do not have the characteristic, and p2 and q2 are the corresponding percentage in the second sample.

Table 1: Assessment of Pain Intensity

Pain Score	Severity Of Pain
Non	No Pain
Mild	Complaint OF Pain Only When Asked
Moderate	Spontaneous Complaint OF Pain
Severe	**Spontaneous Complaint OF Pain Associated With Grimacing And\Or Withdrawal of Hand During Injection**

RESULTS

Table l l: Characteristics of Patients in All groups.

Character	Group l normal saline (30)	Group ll lidocaine **(30)**	Group lll ketamine **(30)**
Age in years Mean(SEM)	34.066 (11.62)	33.86 (10.15)	**36.866 (13.405)**
Gender Males / females	22 / 8	23 / 7	**22 / 8**
Weight in kg. Mean(SEM)	76.06 (16.61)	76.46 (15.54)	**72.96 (16.44)**
Height in cm. Mean(SEM)	165 (10.611)	163.93 (13.24)	**163.32 (13.88)**

The demography of the patients in three groups are shown in table II with no significant differences in age ,sex or weight .The incidence of pain was 33.3% in the ketamine group as compared to 30% in the lidocaine group and 63.3% in the normal saline group as shown in (Table lII).

Table lII: Incidence Of Pain Due To Intravenous Admistration of Propofol

Pain Score	Saline %	Lidocaine %	Ketamine%
Non	11 (36.6%)	21 (70%)	20 (66.6%)
Mild	11 (36.6%)	7 (23.3%)	8 (26.6%)
Moderate	6 (20%)	2 (6.6%)	2(6.6%)
Severe	2 (6.6%)	0 (0%)	0 (0%)
Total In Pain	**19 (63.3%)**	**9 (30%)**	**10(33.3%)**

(a)Saline Vs lidocaine : p1=63.3 , p2=30 , q1=36.6 , q2=70 ,n1=30 ,n2=30.

SE (P) = √ (36.6×63.3) /30+ (30×70)/30 =12.133

The difference between the two proportions is: 63.3 - 30= 33.3 significant difference because the difference is more than twice the SE (P).

(b)Saline Vs Ketamine:

S E (P) = √ (63.3× 36.6)/30+ (33, 3× 66, 6)/30=12.3

The difference between two proportions =33.3 (Statistically significant)

(c) Lidocaine Vs. ketamine:

S E (P) = √ (30× 70)/30+ (33, 3× 66, 6)/30 =12.00

Difference = 3.3

(No significant difference)

*If two means or two proportions differ by more than twice the value of the standard error of the difference, the deference is said to be significant. I.e. more than is likely to have arisen by chance.

There was no significant difference in pain score among lidocaine and ketamine groups. Although there was significant difference between group of normal saline and other two groups The overall incidence and severity of pain during injection of propofol in the various groups was shown in table lll .The incidence of pain in saline group was 63.3% as compared to 30% and 33.3% in the lidocaine group and ketamine groups respectively. None of patients had any side effects

like erythema, itching, and bradycardia.

There is no significant difference in the incidence of pain between the lidocaine (30%) and ketamine (33.3%) groups. Severe pain occurred in two patients (6%) in the saline group as compared to (0 %) in both lidocaine and ketamine groups. No pain was 36.63% in the saline group, 70% in the lidocaine group and 66.6 % in the ketamine group.

Discussion

Ketamine pre-treatment before propofol administration; significantly reduces the incidence and severity of pain associated with intravenous injection of propofol Suzuki S et al 2002 (7). However Durrani Z et al 1989 (8) reported that > 0. 3 % ketamine(approximately10 mol/l) produced adequate regional anesthesia with complete sympathetic, sensory and motor block .Ketamine in low doses is a potent noncompetitive NMDA receptors antagonist ,and the analgesic action of ketamine is linked to that action as reported by Clements JA, e t al 1981(9) . Ketamine resembles cocaine in chemical structure and shares some of its effects as described by Hess WC and Ohi A 2001 (10).

Suzuki S et al 2002(7) found in their study that 84% of the saline treated patients experienced mild or severe pain compared to 26% of those who were given ketamine (i.v) pretreatment. F Tan CH et al 1998(11) described that the incidence of pain was significantly less with prior administration of ketamine10mg (26%) as compared to saline (86%). Also Briggs L.P. et al 1981(2) administrated 1% ketamine 2 mls(i.v) prior to propofol which reduced the incidence of pain from 68% to 33%. Authors in the above three studies did not use tourniquet. Recently Batra YK et al 2005(6) in similar study but with tourniquet occluded for one minute with(i. v) ketamine or lidocaine pretreatment; found that ketamine as effective and alternative to lidocaine for reducing pain of propofol. They found pain in 80% after normal saline, 12% after ketamine and 10% after lidocaine administrations. Our results showed that pain in saline group was 63.3%,while in ketamine was 33.3% ,and lidocaine was 30% .These are in agreement with Batra YK et al 2005 .

Conclusion

The current study confirmed that pretreatment with intravenous 10mg ketamine with one minute venous occlusion by tourniquet reduced the incidence and severity of propofol (i.v) injection pain, and this can be an alternative for lidocaine.

References

1. Picard P, Tramer MR .Prevention of pain on injection with propofol:a quantitative systemic review. Anaesth Analg 2000; 90:963-992.
2. Briggs LP, Clarke RSJ, Dundee JW, Moore J, Bahar M, Wright PJ. Use of di-isopropyl phenol as main agent for short procedure. Br J Anaesth 1981; 53:1197-201.
3. Mattila MAK,and Koski EMZ . Venous squalae after intravenous propofol: a comparison with methohexitone in short anaesthesia. Postgrad med J; 1985; 61 ;(suppl.):162-164.
4. Scott RPF, Saunders DA, Norman J. Propofol: Clinical strategies for the preventing the pain of injection. Anesthesia: 1988; 43; 492-4.
5. Liaw WJ, PangWW,Chang DP, Hwang MH .Pain on injection of propofol:the mitigating influence of metoclopramide using different techniques. Acta Anaesthesiol Scand.1999; 43:24-27.
6. Batra YK, A.R. Al Qattan H.M. Marzouk HM.Smilka M, Agzamov A.Ketamine pretreatment with venous occlusion attenuates pain on injection with propofol. Eur J Anaesthesiol. 2005; 22:67-79.
7. Suzuki S, Masamune T, Nonaka A, Kumazawa T. Pre-treatment with ketamine reduces incidence and severity of pain on propofol injection. Masui 2002; 409-3898.
8. Durrani Z,Winnie AP,Zsigmond EK, Burnett M. Ketamine for intravenous regional anesthesia. Anesth Analg;1989;68:328-333

9. Clements ja, nimmo ws. Pharmacokinatics and analgesic effect of ketamine in man. Br j anaes 1981; 53:27-30.
10. Hesswc, ohe a. Dose ketamine /propofol anesthesia possess antiarrythmogenic quality? Aperioperative study in
12. 8; 53:302-305.

aortocoronary by bass patient .eur j med res2001; 6:543-550.
11. Tan CH, Onsiong MK, Kua SW..The effect of ketamine pretreatment on propofol injection pain in 100 women. Anesthesia 199