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COMPARATIVE STUDY OF ONDANSETRON WITH LIGNOCAINE TO ALLEVIATE PAIN DURING INJECTION OF PROPOFOL

Prashant J. Pachore¹, Sonal A. Chaudhari², Abhimanyu S. Tarkase³, Ganesh K. Nikam⁴

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ABSTRACT: Propofol is commonly used newer induction agent of choice with smooth and rapid recovery from anaesthesia. It has one adverse effect which is restricting its use i.e. pain during injection. We in present study are comparing Ondansetron with Lignocaine to alleviate pain during injection of Propofol, as ondansetron is routinely used to prevent post-operative nausea and vomiting, so it can have both effects viz prevention of pain on injection of Propofol and prevention of post-operative nausea and vomiting. The aims of study were to evaluate incidence to alleviate pain during injection of propofol, efficacy of Ondansetron & Lignocaine to alleviate pain during injection of propofol, incidence and severity of pain in Ondansetron and Lignocaine group, incidence of side effects in both groups. **MATERIAL AND METHODS:** The present study was carried out in S.R.T.R. Govt. medical college and hospital Ambajogai after ethical committee approval. 120 patients of ASA grade I and II of either sex undergoing short surgical procedures requiring general anaesthesia without endotracheal intubation were randomly allocated to three equal groups of 40 patients each; Group I: Received 0.9% Normal saline (2ml) as pretreatment, Group II: Received 2% lignocaine hydrochloride (2ml) as pretreatment, Group III: Received 4mg ondansetron (2ml) as pretreatment. **EXCLUSION CRITERIA:** patients with history of allergy to propofol, neurological disorders or altered sensorium or those on anti-psychotropic medication and patient with cardiac conduction abnormalities. It was pre decided that patients with sedation score of >3 would be excluded from study, however none of the patients in our study had sedation of >2 with 1/4th calculated dose of propofol. Assessment of pain was done using Verbal Pain score and Face pain score. **OBSERVATION:** Statistical analysis was done by ANOVA test while comparing 3 groups and by Z test while comparing group II & III. Incidence of pain was more in control group than study groups & difference was statistically significant. There was no significant difference in adverse effects. **CONCLUSION:** Pretreatment with either Lignocaine or Ondansetron can be used to alleviate incidence of pain on Propofol injection with cardiovascular stability and minimal side effects.

KEYWORDS: Ondansetron; Lignocaine; Pain during injection of Propofol.

INTRODUCTION: In early 1970s a new induction agent 2, 6 di isopropyl phenol (propofol) was introduced in practice for induction of anaesthesia. It gains popularity due to its rapid induction, good quality of course of anaesthesia and rapid recovery. Propofol has some side effects such as pain on injection (due to its chemical constituents 16% cremophore EL) [S.H.Hansen et al 1988],[¹] Yew W.S.et al 2005,[²]Nyman Y et al 2005,[³] schaub E et al 2005,[⁴] Kam E et al 2004,[⁵]Adam s et al 2004,[⁶]cardiovascular and respiratory depression, myoclonus and anaphylaxis.

Many changes in constituents of propofol are being carried out to alleviate pain on injection but failed. Various methods tried to alleviate pain on propofol injection. Here in our study we are comparing ondansetron with lignocaine to alleviate pain.

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AIMS OF STUDY:

- To evaluate incidence of pain during injection of propofol.
- To evaluate efficacy of Ondansetron to alleviate pain during injection of propofol.
- To evaluate efficacy of Lignocaine 2% to alleviate pain during injection of propofol.
- To compare the incidence and severity of pain during injection of propofol in Ondansetron and Lignocaine group.
- To evaluate incidence of side effects in both groups.

MATERIAL AND METHODS: The present study was carried out in S.R.T.R. Govt. medical college and hospital Ambajogai after ethical committee approval. 120 patients of ASA grade I and II of either sex undergoing short surgical procedures requiring general anaesthesia without endotracheal intubation were randomly allocated to three equal groups of 40 patients each:

Group I: Received 0.9% Normal saline (2ml) as pretreatment.

Group II: Received 2% lignocaine hydrochloride (2ml) as pretreatment.

Group III: Received 4mg ondansetron (2ml) as pretreatment.

Written, informed consent obtained from all patients. Prospective double-blind study was performed on 120 patients. Pre-anaesthetic evaluation was carried out in detail which included general examination, systemic examination, airway examination, spine examination. All baseline investigations were done including hemoglobin, complete blood count, blood sugar, serum urea, creatinine and urine routine. The patients were divided randomly by computer generated numbers in three groups as mentioned above.

Exclusion Criteria: patients with history of allergy to propofol, neurological disorders or altered sensorium or those on anti-psychotropic medication and patient with cardiac conduction abnormalities.

A good intravenous line with 20 gauge intracath was established and started with ringer lactate solution at the rate of 200ml/hr and premeditated with inj. Atropine 0.01mg/kg. Monitors like, pulse oxymeter and sphygmomanometer were attached and basal readings were noted.

The venous drainage was occluded manually at arm, the test drug (either normal saline or lignocaine or ondansetron) was administered over 5sec. The arm compression was released after exactly 1 min. Pulse, blood pressure and O₂ saturation were noted and 1/4 of calculated induction dose of propofol (2mg/kg) was administered slowly over 5sec. Independent anesthesiologist who was unaware of pretreatment drug administered noted the following observation:

1. SEDATION SCORE:

Awake	=1
Awakening in response to vocal commands	=2
Awakening in response to touch	=3
Awakening in response to painful stimulus	=4
No response to painful stimulus	=5
Severe respiratory depression	=6

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It was pre decided that patients with sedation score of >3 would be excluded from study, however none of the patients in our study had sedation of >2 with 1/4th calculated dose of propofol.

2. Assessment of pain Using:

I. Verbal pain score:

No pain experienced	=0
Mild pain or soreness	=1
Moderate pain with grimacing	=2
Severe pain associate with withdrawal of limbs	=3

II. Face pain score:

3. Haemodynamic parameters were noted including- pulse, blood pressure, o2 saturation and other adverse reaction.

This one time observation made at 30 sec. after injecting 1/4 dose of propofol following this remaining dose of propofol was administered.

OBSERVATION: The mean age, weight, height and duration of surgery in all groups were comparable and statistically not significant.

After pretreatment with designed drug, all patients were given test dose (1/4) dose of propofol followed by full dose of propofol. During this procedure pulse rate and systolic blood pressure were monitored.

The mean change in pulse rate and systolic blood pressure during the procedure were comparable and was statistically not significant.

All patients were enquired about occurrence and severity of pain after test dose (1/4th) of Propofol intravenously. The group wise incidence and severity of pain as per Verbal Pain Score was shown in Table:

Verbal Pain Score	Group I	Group II	Group III
No pain	0(0.00%)	27(67.50%)	24(60.00%)
Mild pain	02(5.00%)	10(25.00%)	12(30.00%)
Moderate pain	16(40.00%)	03(7.50%)	04(10.00%)
Severe pain	22(55.00%)	0(0.00%)	0(0.00%)

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The incidence of pain was also evaluated according to statistical analysis and the values are shown in Table:

Score			Group				F value	P value
	I		II		III			
	Mean	S.D.	Mean	S.D.	Mean	S.D.		
Verbal pain score	2.3	0.68	0.35	0.52	0.5	0.68	96.125	P<0.05 significant

The incidence of pain was also evaluated with Face pain score (Wong-Baker) shown in Table:

Face pain score	Group I	Group II	Group III
No pain	00(0.00%)	27(67.50%)	29(72.50%)
Mild pain	05(12.50%)	13(32.50%)	10(25.00%)
Moderate pain	19(47.50%)	00(0.00%)	01(02.50%)
Severe pain	11(27.50%)	00(0.00%)	00(0.00%)
Very severe pain	05(12.50%)	00(0.00%)	00(0.00%)
Worst possible pain	00(0.00%)	00(0.00%)	00(0.00%)

Face pain score was also evaluated statistically as shown in Table:

Score	Group						F value	P value
	I		II		III			
	Mean	S.D.	Mean	S.D.	Mean	S.D.		
Face pain score	4.8	1.74	0.65	0.94	0.55	1.01	99.83	P<0.05 Significant

During intravenous administration of Propofol all patients were observed for incidence of adverse effects related to drugs as shown in Table:

Adverse effects	Group I	Group II	Group III
Hypersensitivity or rash	01	01	01
Hypotension	00	00	00
Bradycardia	00	00	00
Cardiovascular collapse	00	00	00
Myoclonus	01	00	00

DISCUSSION: Nowadays anaesthesiologists are expected to provide their services with safe, uncomplicated accepted technique of anaesthesia to patient.

Here the patient expects painless, uncomplicated technique of anaesthesia for their operative procedures.

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The incidence and severity of pain on injection may be more when intravenous cannulation is performed in small veins. Hypertonic drugs, size of needle, site of injection, speed of injection and many other factors are important to produce pain on injection.

Again pain on injection is considerably more at extremes of age. In paediatric patients many times uncooperation may result in multiple pricks and more incidence of pain. In geriatric patients overall pain threshold is decreased giving rise to more incidence of pain.

Propofol (2, 6, di isopropyl phenol) was introduced in practice of anaesthesia as an induction agent in early 1970's. It gains popularity due to its rapid induction, complete anaesthesia and rapid recovery. The merits of Propofol on one side were stigmatized due to its demerits as pain on injection, hypersensitivity reaction and cardiovascular collapse. Many authors have noted pain on injection of Propofol and claimed it due to its physical properties and chemical constituents.

Overall pain on injection of Propofol ranges from 25 to 100% at vein on dorsum of hand (Stark R.D. et al 1986, Scott R.P.F. et al 1988, Johnson R.A. et al 1999 [7,8,9]) and 3 to 26% only when injected into proximal veins.

G. Gehan et al 1991^[10] quoted that pain on injection of Propofol was attributed to the stabilizing agent Cremophor EL but persisted even though replaced by soyabean oil (Brooker J et al 1985 and McCulloch M.J. et al 1985).^[11,12]

To overcome this pain on injection, McCulloch M.J. et al 1985^[12] suggested injection in large veins. Hiller S.C. et al 1996^[13] suggested decreasing speed of injection, dilution in 5% dextrose or 10% intralipid or pretreatment with narcotics or thiopentone before Propofol administration. All those workers have carried out their studies on various methods but no one has pointed out a single method applicable in all patients with success.

Pretreatment with Lignocaine with venous conclusion was found to decrease the incidence and severity of pain on injection of Propofol. (S.N. Hansen et al 1988^[1], Yew W.S. et al 2005, Nyman Y et al 2005, Kam E et al 2004^[2,3,5]). Lignocaine hydrochloride due to its membrane stabilizing action along with blocking of sodium channels was well accepted and routinely administered drug to alleviate pain on Propofol injection (Yew W.S. et al 2005, Kunt Z.O. et al 2004.^[2,14]

S.P. Ambesh et al 1999^[15] and Reddy M.S. et al 2001^[16] have tried pretreatment with Ondansetron to alleviate pain on Propofol. They claimed that Ondansetron acts as 5HT₃ antagonist and blocks sodium channels to brain neurons.

In present study number of patients was in age range of 16 to 45 years. Paediatric and geriatric patients were not included due to their anticipated uncooperation and difficulties encountered during choice of vein.

The patient's selection for operative procedures requiring general anaesthesia were of ASA grade I and II as the incidence of pain may not be tolerated to associated medical disorders.

All patients were pre-medicated with only Inj. Atropine 0.01mg/kg of body weight. No other premedication in form of sedatives or narcotic analgesic were administered because they may interfere with evaluation of pain on Propofol injection, as accordance to above authors.

In all patients intravenous line was established with 20 G angiocath on dorsum of hand with adequate size of vein.

Because small size vein may contribute for resistance during administration of Propofol as it is in form of emulsion resulting in intimal damage and more pain. In contrast large vein may alleviate pain due to dilution effect.

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According to groups the test drug were given as pretreatment in 2ml solution over 5 seconds followed by venous occlusion at arm for 1 minute according to R.A. Johnson et al 1990 [9] and S.P. Ambesh et al 1999 [15]. After pretreatment test dose of Propofol (1/4th of calculated induction dose) was injected over 5 seconds.

According to Hiller S.C. et al 1996 [13] speed of injection directly correlates with pain on injection that's why speed of test drug and Propofol were kept constant as 5 seconds. Initial test dose of Propofol given was only 1/4th dose to exclude those patients having sedation score more than 3, to evaluate verbal pain score and face pain score up to its optimization.

Verbal pain score applicable to assess pain perceived by the patient and self-reporting of pain severity scoring system when used in adults correlates well and are more reliable.

In present study group II (Lignocaine group) no pain was noted in 67.50% and in group III (Ondansetron group) was 60% by verbal pain score when group II and III were compared for quality of pain alleviation there was no difference and was statistically not significant. These observations are similar to S.P. Ambesh et al 1999 and Reddy M. S. et al 2001. [15,16]

Objective analysis of pain on injection following Propofol was also evaluated with Face pain score. Face pain score assessment is mainly applicable to paediatric patients but Craig and Patric reported the facial reaction for the first time in adults in 1995 [17]. According to Face pain score group II (Lignocaine group) no pain was noted in 67.50% of patients and in group III (Ondansetron group) 72.50%, the difference between two groups was statistically not significant. Our observations were in accordance with W. Klement et al 1991 and S.P. Ambesh et al 1999. [18,15]

The mean change in pulse rate and systolic blood pressure were significant in lignocaine and Ondansetron group when compared to normal saline group. This cardiovascular stability may be secondary to membrane stabilizing action which blocks the sensitivity of myocardium to further stimulation mediated by sympathetic stimulation due to any cause such as pain. Similar observations were made by S.P. Ambesh et al 1999 and Reddy M. S. et al 2001. [15,16]

The incidence of adverse reaction were negligible in our study may be attributed to selection of patients of ASA grade I and II only.

CONCLUSION: To conclude it is mandatory to decrease the incidence of pain following Propofol injection which is said to be unavoidable with its use. Pretreatment with either Lignocaine or Ondansetron can be used to alleviate incidence of pain on Propofol injection with cardiovascular stability and minimal side effects.

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AUTHORS:

1. Prashant J. Pachore
2. Sonal A. Chaudhari
3. Abhimanyu S. Tarkase
4. Ganesh K. Nikam

PARTICULARS OF CONTRIBUTORS:

1. Assistant Professor, Department of Anaesthesia, SRTR Government Medical College, Ambajogai.
2. Assistant Professor, Department of Anaesthesia, SRTR Government Medical College, Ambajogai.
3. Associate Professor, Department of Anaesthesia, SRTR Government Medical College, Ambajogai.

4. Assistant Professor, Department of Anaesthesia, SRTR Government Medical College, Ambajogai.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Prashant J. Pachore,
8 Panhalgad, SRTR,
Government Medical College Campus,
Ambajogai-431517, District Deed.
Maharashtra.
Email: pachorepj@rediffmail.com

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