Objective: To assess the potential of oral Clonidine premedication in decreasing patient discomfort during the injection of Propofol. Design: This was a comparative study of 80 ASA class 1 and II. Place and Duration of study: This study was carried out at Combined Military Hospital, Kharian. Patients and Methods: This was a study of 80 ASA class 1 and 2 patients of similar age group. Patients selected were from amongst those undergoing elective gynaecological surgery, specifically Diagnostic Dilatation and Curettage. These patients were selected by non-probability convenience sampling. The patients were randomly assigned, by means of a random table, to one of the two groups of 40 patients each. Group ‘A’ patients were given oral Clonidine, 300mg two hours before induction of anaesthesia by Propofol injection. Group B’ patients were given 0.01 to 0.02mg/kg plain Lidocaine just before Propofol induced anaesthesia. Non-invasive systolic arterial blood pressure (ni-SBP), non-invasive diastolic arterial blood pressure (ni-DBP) and heart rate were recorded in the ward about 120 min [before administration of oral Clonidine in group-A] in both groups. Measurements were repeated in the operating theatre before induction of anaesthesia. Patients in Group-Â were given one tablet Catapres [Clonidine, 300mg] with a sip of water, two hours before induction of anaesthesia and they were observed in the Post Anaesthesia Care Unit during this period, while their pulse and blood pressure were monitored. Patients in group-B were not premedicated with Clonidine. They were injected 0.01 to 0.02mg/kg injection plain lidocaine, through the injection port of an 18-gauge cannula, as premedication just before propofol monitoring was done as for group-A. Before administration of propofol, the patient was requested to rate immediately any sensation of pain during injection as none (0), mild (1), moderate (2) or severe (3), also called the Verbal Rating Scale (VRS). Results: The results showed both groups to have similar pain score, and differences were deemed statistically not significant by the analysis. Conclusion: Our results imply that Clonidine makes an excellent premedication with Propofol for short gynaecological procedures.
INTRODUCTION

Propofol a phenol derivative, was identified as a potentially useful intravenous anaesthetic agent in 1980, and became available commercially in 1986. It is more expensive than thiopental or methohexitol, but has achieved great popularity because of its favorable recovery characteristics and its antiemetic effect. Chemical structure is 2, 6-Di-isopropylphenol.

Anaesthesia is induced within 20-40 s after i.v. administration. Recovery of consciousness is rapid and there is a minimal ‘hangover’ effect even in the immediate post-anaesthetic period. Pain on injection occurs in up to 40% of patients.

Pain is an unpleasant sensory and emotional experience with actual and potential tissue damage.

Among the more common methods of measuring pain are the visual analogue scale, the verbal rating scale, and the numerical rating scale. The verbal rating scale consists of a list of adjective describing pain. This provides for fewer possible responses than does the analogue scale and, accordingly, may be less sensitive. Induction of anaesthesia with propofol involves assessment of adequate sedation by loss of verbal contact with the patient; therefore, the drug is injected slowly. Thus subjects have adequate time to rate the pain according to the simple verbal rating scale.

A lot of ways have been employed to provide relief from injection pain. These include intravenous retention of lidocaine, intravenous retention of fentanyl, and fentanyl as premedication, intravenous retention of tramadol, premedication with remifentanil, pretreatment with ketorolac and venous occlusion, and pretreatment with Nafamostat mesilate, a kallikrein inhibitor.

Of all these lidocaine premedication has been the most widely used. Clonidine, the prototype α2-agonist, was originally developed in the early 1970s for its potential use as a nasal decongestant. It rapidly found favour as a useful anti-hypertensive agent, however, with the advent of the ACE inhibitors and more selective α2-adrenergic antagonists, Clonidine has been relegated to no better than third line alternative for this purpose. It has, however, remained an intriguing compound that has been shown to be efficacious in a wide range of applications, from analgesia, sedation and reduction in post-operative shivering, to the control of symptoms during alcohol, nicotine and opioid withdrawal. Clonidine premedication reduces the intraoperative requirement for opioids and volatile anesthetics. Clonidine also reduces the induction dose of IV anesthetics. While much work has been published pertaining to the use of Clonidine as an adjunct to anaesthesia and pain management, few reports address its specific use as a sedative unrelated to anaesthesia. Its use as a sedative/anxiolytic in the intensive care setting is now relatively commonplace, particularly after long-term sedation with opiates and/or benzodiazepines, evidence exists that Clonidine is effective in the relief of withdrawal symptoms from these agents. Reliable data on i.v dosing, sedative efficacy and the effect on outcome in the intensive care setting are lacking. Presence of α2-receptors has been demonstrated in the substantia gelatinosa of the human spinal cord, often in close association with μ-opioid receptors. Again, α2-agonist-mediated analgesia can be enhanced in the presence of α2-agonists. The MAC-sparing effect of i.v and oral Clonidine has been well documented and as such again provides further evidence for their complex interactions with other CNS depressants.

Chemical structure is C9H9Cl2N3 · HCl, with a molecular weight of 266.56. Since its analgesic effect significantly reduces the injection pain it would make a worthy premedication for propofol based anaesthesia.
OBJECTIVES
To study the effectiveness of oral Clonidine premedication in decreasing patient discomfort during the injection of Propofol and to compare its efficacy with Lidocaine in terms of pain relief on Propofol injection.

STUDY DESIGN
Comparative.

MATERIALS AND METHODS
This Comparative study was conducted at Combined Military Hospital, Kharian from 1st February 2002 to 30th May 2002. Approval was taken from hospital ethics committee. This was a comparative study of 80 ASA class 1 and 2 patients of similar age group.

Patients were selected during preanaesthesia assessment. Patients undergoing dilatation and curettage under General Anaesthesia, of 25-40 years of age, weighing 60 to 70 kgs were selected. Patients requiring any other premedication, patients taking sedative or analgesic drugs, sympatholytic medication, having neurological or cardiovascular disease, known to be sensitive to propofol and, overly apprehensive or unwilling patients were excluded from the study.

These patients were selected by non-probability convenience sampling. Informed consent was obtained on a consent form. These patients were randomly assigned, by means of a random table, to one of the two groups of 40 patients each.

During the pre-anaesthetic visit, patients were thoroughly examined and only ASA 1 patients were selected. The patients were briefed about the study. Written consent was obtained from each patient. The method of assessing pain was explained to each patient and how they are going to grade their pain, if felt, in that scale.

Two hours before induction of anaesthesia in both the groups the rating of pain, if felt, was again carefully explained to the patients. An 18-gauge Teflon cannula was inserted into the cephalic vein of the non-dominant hand, without infiltration of local anaesthetic, about 180 min before the induction of anaesthesia. The cannula was used for i.v. infusion of Ringer’s lactate solution. Non-invasive systolic arterial blood pressure (ni-SBP), non-invasive diastolic arterial blood pressure (ni-DBP) and heart rate were recorded in the ward about 120 min before the time for administration of oral Clonidine. Measurements were repeated before induction of anaesthesia.

Patients in Group-A were given Clonidine 300mg [one tablet Catapres] with a sip of water, two hours before induction of anaesthesia and they were observed in the Post Anaesthesia Care Unit during this period, while their pulse and blood pressure were monitored.

Patients in group-B were not premedicated with Clonidine. They were injected 0.01 to 0.02mgkg-1 injection plain lidocaine, through the injection port of an 18-gauge cannula, as premedication just before induction with propofol. Before administration of propofol, the patient was requested to rate immediately any sensation of pain during injection as none (0), mild (1), moderate (2) or severe (3), according to the Verbal Rating Scale (VRS).

As induction of anaesthesia with propofol involves assessment of adequate sedation by loss of verbal contact with the patient and the drug is injected slowly. Therefore our subjects had adequate time to rate the pain according to the simple scale being used. Their observations were duly recorded.
Table-II. Performance for data recording (Performa B)

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<td>Pain Score</td>
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**RESULTS**

The variable, pain score, was noted at time of injecting propofol in both groups using the Verbal Rating Scale (VRS).

The other three variables recorded were Non-invasive systolic arterial blood pressure (ni-SBP), non-invasive diastolic arterial blood pressure (ni-DBP) and heart rate. Statistical analysis was performed using the unpaired student’s t-test and the chi-square test. SPSS package was used for this purpose. A P value <0.05 was considered statistically significant.

The success rate in maintaining analgesia in the Clonidine group was 72% as compared to only 7.5% incidence of moderate pain and 20% of slight pain. While the success rate in maintaining analgesia in the Lidocaine group was 90% as compared to only 2.5% incidence of moderate pain and 7.5% of slight pain. As evident the results showed no statistically significant difference in the pain scores of the two groups. A chi-square test was applied on both groups for pain score. The 20% incidence of slight pain in the Clonidine group, rather than moderate or severe pain, puts the two groups in balance. While the incidence of moderate pain was, 7.5% and 2.5% in the Clonidine and lidocaine groups respectively. There was no significant relationship between the pain score and time to onset of pain. It was also observed that the patients administered Clonidine had a comparatively more stable haemodynamic profile.
**DISCUSSION**

The study was aimed at ascertaining the efficacy of oral Clonidine premedication in decreasing the pain of Propofol injection.

Propofol is an induction agent with a profile significantly better than the older drugs. Its onset of action is gauged by the loss of verbal contact with the patient. Recovery of consciousness is rapid and there is minimal hangover. It has anti-emetic properties and there is no problem of postoperative nausea and vomiting.

Propofol is distributed rapidly, and blood concentrations decline exponentially. Clearance of the drug from plasma is greater than would be expected if the drug was metabolized only in the liver, and it is believed that extra-hepatic sites of metabolism exist, and its effective half-life is short 30-60 min. Propofol has been used successfully for sedation during regional analgesic techniques and during endoscopy.

Propofol is the most suitable agent for total I/v anaesthesia. Propofol has been used successfully by infusion to sedate adult patients for several days in ICU. The level of sedation is controlled easily, and recovery is rapid {usually < 30min} Airway obstruction and known hypersensitivity to the drug are probably the only absolute contraindications.

But there is the problem of Pain on injection which occurs in up to 40% of patients. A lot of work has gone into the ways to solve this problem but till now the only method being used is the injection of local anaesthetic [lidocaine] before propofol. At times no pain relief is used. Clonidine an α2-agonist is known to decrease induction doses of i.v. anaesthetics and to decrease intraoperative opioid and volatile anaesthetic requirements for maintenance of anaesthesia and decreases peri-operative catecholamine concentrations and promotes peri-operative haemodynamic and adrenergic stability.

Due to these facts it is gaining popularity as a premedication, therefore its analgesic effects on propofol injection have been investigated. For our study we chose patients under going diagnostic Dilatation and Curettage in addition to being in ASA grade-1. Due to an ethical objection raised to our original plan of having a control group with no premedication, the controls were given lidocaine, and the study became comparative. The Verbal Rating Scale was utilized to assess pain, before the patient fell asleep.

It was observed that the patients in both groups were largely comfortable and few complained of pain. Among those experiencing discomfort only a few felt ‘moderate pain’, while the rest were in the ‘some pain’ category. It can be assumed that Clonidine premedication decreases the pain of Propofol injection. It was also seen that the Clonidine group had on an average lower heart rate and blood pressure at the time of induction, which is a stressful time for most patients.

Previous studies have demonstrated that oral Clonidine administered before anaesthesia increases the analgesic
effects of opioids after operation\textsuperscript{10} and reduces anaesthetic\textsuperscript{20} and/or opioid requirement\textsuperscript{10} during the perioperative period, Clonidine at induction reduces shivering after general anaesthesia\textsuperscript{11} and that Clonidine attenuates the haemodynamic responses to noxious stimuli such as tracheal intubation\textsuperscript{22}. Because of these beneficial properties, Clonidine is a useful premedication. Our results demonstrate the efficacy of oral Clonidine for pain on injection of propofol.

With our study a newer more logical and wholesome approach is identified that provides for the above as well as giving all the benefits of Clonidine as premedication.

**CONCLUSION**

As apparent from the results there was no significant difference between the two groups thereby supporting our hypothesis that of oral Clonidine premedication decreases patient discomfort during the injection of Propofol. Thus our results imply that Clonidine makes an excellent premedication with Propofol for short gynaecological procedures.

Our study was limited to a particular class of patients and a certain kind of surgical procedure . It needs to be duplicated in diverse condition to fully bring out the implications of the technique.

Furthermore we stuck to oral Clonidine as it was the form used in previous studies and it was the only form available to us. The results should also be sought with injectable and transdermal Clonidine.

**REFERENCES**


ORAL CLONIDINE


Only the person who has faith in himself is able to be faithful to others

Erich Fromm