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PRE-EMPTIVE PAIN CONTROL; COMPARISON OF KETOROLAC AND DICLOFENAC SODIUM



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ABSTRACT... Introduction: Opioid related side effects have encouraged the use of analgesic drugs that are devoid of these problems. **Objective:-** This study was done to compare the analgesic efficacy of Ketorolac and diclofenac in 60 adult patients of age group ranging between 30 to 45 years of age body wt 50-60kg belonging to ASA I and II grade. **Material and Methods:** Patients were scheduled for elective gynecological procedure (laparoscopic tubal ligation) under general anaesthesia. They were divided into two equal groups using non-probability convenience sampling technique. Each group comprised of 30 patients. Group A received Ketorolac 10 mg I/V with local infiltration of 0.5% Bupivacaine and group B received IM Diclofenac sodium 75 mg after local infiltration 0.5% bupivacaine as in Group A ½ hourly before surgery. Post operatively patients were observed after 30 minutes in the recovery room for pain relief for two hours. Mean pain scores were noted in the recovery area using visual analog scale with need for supplementary analgesic after awakening from general anaesthesia. Vital signs were monitored. **Result:** Results were analyzed by using SPSS-8 package by applying Student Test and chi Square Test. There was statistically significant difference between two groups regarding their mean pain score. **Conclusion:** The patients who received Ketorolac I/V (Group A) had longer pain free time interval and request for first analgesic supplement was made after 90 minutes compared to a shorter interval of 60 minutes in Group-B, who received intramuscular diclofenac sodium.

Key words: Opioid, Laparoscopic, Ketorolac.

INTRODUCTION

The word analgesia meaning insensibility to pain comes from Greek word 'a va no'. Through the ages herbs and plants have been used as analgesics by most cultures¹. Pain is a combination of severe discomfort, fear,

autonomic changes, reflex activity and suffering. Postoperative pain differs from other types of pain in that it is usually transitory with progressive improvement over relatively short time course. This renders the condition more easily amenable to therapy than is the case for

chronic types of pain. The relief of pain during surgery is the aim of anaesthesia. Any expertise required in this field should be extended into the postoperative period.

Anaesthesiologist is in unique position to treat acute postoperative pain. Training and knowledge of opioid, non-opioid and local anaesthetic pharmacology, as well as the understanding of pain pathways and mechanism and the experience with the regional anaesthesia is necessary to optimize the management of acute pain. The opioid analgesics are particularly effective in conditions where the effective component of pain i.e. pain suffering is prominent. In contrast NSAID interact with the reaction leading to the production of pain producing inflammatory responses in the region of peripheral nociceptors although their central action is increasingly recognized². The mechanism of actions of various NSAID is inhibition of this prostaglandins mediated amplification of chemical and mechanical irritants on the sensory pathway. NSAID interfere with prostaglandins biosynthesis by inhibition of enzyme cyclo-oxygenase. By doing this cyclo-oxygenase inhibitors block the nociceptive response to endogenous mediator of inflammation³.

After being neglected for a long time, post-operative analgesia is developing considerably at present. A wide range of resources including antipyretics, NSAID, morphine agent and opioid agonists, antagonist allow to great variation of sensitivity between individuals. New technique such as PCA's and spinal morphine therapy are becoming essentials for intense pain. New concepts have appeared such as treatment units for acute pain while others are gaining new momentum like prophylaxis of postoperative pain. Relief of surgical pain with nominal side effects is primary goal. The various drugs and techniques of their administration have varying degree of success.

The conventional use of intermittent intramuscular injection of opioids is known to be less than ideal in most circumstances. Intravenous injection of opioids provides fewer fluctuations in the quality of analgesia but they require the use of more sophisticated infusion devices

and experienced personals for optimal use. Extra dural analgesia using local anaesthetics or opioids may be used but may be associated with hypotension and delayed respiratory depression.

Several studies have reported the successful use of non-steroidal anti-inflammatory agent in the treatment of postoperative pain and in the reduction of opioid requirement when these used in combination with these drugs^{4,5}. They produce few side effects especially absence of sedative or respiratory depression, and lower incidence of nausea and vomiting dizziness etc.

Administration before surgery may cover some protectable action against prostaglandins synthesis resulting from surgical insult⁶. Residual analgesia in the recovery period may also reduce opioid requirements. Recent evidence suggests that surgical incision and other various peri-operative events may induce prolonged changes in central neural function that later contribute to postoperative pain. Noxious stimulus induced neuroplasticity can be prevented or pre-empted by the administration of analgesic (Diclofenac sodium, Ketorolac) prior to injury.

These drugs are used to evaluate their analgesic effects in the immediate postoperative period. Aspirin was introduced as an analgesic in 1899. Recently DR John Bonka an anaesthesiologist established the first pain clinic in 1950. In Pakistan acupuncture was introduced by Brigadier S M Saleem 1972 and first pain clinic was opened in 1979 in Rawalpindi⁵.

PURPOSE OF STUDY

- * Evaluate the analgesic effect of single bolus dose of diclofenac and ketorolac in immediate post anaesthesia period in the patients undergoing gynaecology operation.
- * Find whatever these non-narcotic have opioid sparing effect.

PATIENTS AND METHOD

STUDY DESIGN

This Experimental comparative study with no randomization was conducted in Gynaecology Operation Theatre, Nishtar Hospital, Multan during period from January 2002 to December 2002. Sixty patients were included in the study. All patients belonged to ASA-I or II, age range between 30 and 40 years & body weight 50-60 kg. Patients with significant concomitant disease who were ASA-III and IV, with severe pain before surgery were already taking strong or weak analgesic, medication, obese, with history of allergy to NSAID or with biochemical evidence of hepatic disease were not included in the study.

Duration of anaesthesia noted. All patients received standard general anaesthesia. They received oral diazepam 5-10 mg on the morning of surgery. Anaesthesia was induced with thiopentone 4-5 mg/kg and suxamithonium 1 mg/kg to facilitate tracheal intubation. Anaesthesia was maintained on IPPV with 0.5-1% halothane and 60% N₂O in O₂ after 0.5 mg/kg tracrrium or vecuronium .15 mg/kg. After producedure neuromuscular block was antagonised with neostigmine and atropine. Monitoring done during general anaesthesia was e.g. automatic blood pressure, pulse rate, pulse oxymetry and ECG.

RESULTS

There were 30 patients in each group. Mean pain score was noted 30 min after completion of operation using VAS and McGill questionnaire. Lower pain score was noted in recovery room after I/V ketorolac (in group A) than after I/M Dicloran (group B). Majority of the patients experienced no pain, some had mild pain and none had severe pain after I/V ketorolac, whereas after I/M dicloran, proportionately greater number had mild to severe pain and fewer had no pain. Difference between the mean pain scores was statistically significant.

The time interval for first request for analgesia postoperatively after awakening from anaesthesia, was greater after I/V Ketorolac (Group A) than after I/M

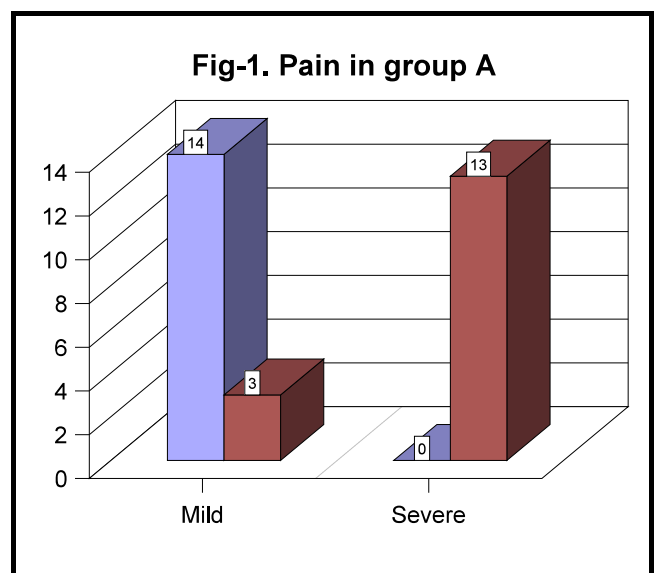
dicloran (Group-B). The number of doses required was also less in this group than in those who recieved dicloran.

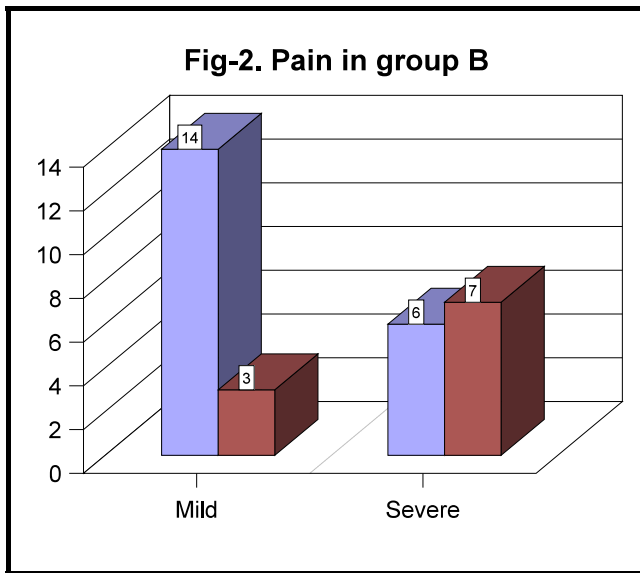
Mean arterial pressure, heart rate and respiratory rate were also noted at the time of assessment of mean pain scores and higher values were revealed after I/M dicloran than after I/V Ketorolac.

The incidence of side effects also differed in two groups and it was higher in patients receiving I/M dicloran. The side effects mainly comprised of nausea, vomiting and sweating.

Group	Group A	Group B
Age in years	37.8±9	39.1±7
Weight in Kg	53.7±3	51.9±2
Height	57"±6	55"±2

	Pain Group A	Pain Group B
N Valid	30	30
Missing	0	0





DISCUSSION

The use of NSAID in the pre operative period is increasing. This may obviate the need of opioids along with their unwanted side effects. As studies indicate injectable agents like Ketorolac, diclofenac and indomethacin, all have clinically useful analgesic efficacy especially for mild to moderate pain⁷. Many of these drugs have well known side effects such as gastric ulceration, impaired coagulation and alteration of renal function.

For this study we used a type of surgery such as tubal ligation because we thought that major surgery would complicate our study model. Infact Laparoscopic surgery is a highly non-invasive operation and tissue damage, performance time and technique do not vary significantly in patients. The postoperative pain induced by this type of surgery has a major visceral component, owing to surgical handling and diaphragmatic. Irritation by dissolved CO₂ and a minor component, that is somatic in origin owing to the hole made with trocar in the abdominal wall⁸.

Postoperative pain of lesser intensity occurred with preoperative piroxicam in a study⁹. He used piroxicam in patients coming for gynecological surgery before induction of anaesthesia. He showed that postoperative visual analog pain scores were lower on admission to the

recovery ward in patients given piroxicam preoperatively. Postoperative analgesia requirements were also reduced therefore, in these patients. This type of surgery provoked pain that is less intense and shorter in duration and this had led to use of pain scale visual analogue scale (VAS).

This study was designed to assess and compare the pre-emptive analgesic efficacy of Ketorolac and Diclofenac sodium. Pre-emptive analgesia is given in an attempt to reduce excitability of the peripheral and central nervous system during nociceptive input, thereby reducing central and peripheral sensitization.

In a study it has showed that early block of the nociceptive input with local anaesthetics is more effective if local anaesthetics were given before surgery than after surgery¹⁰. In another it was compared the analgesic and Opioid sparing effects of three intervenous non-steroidal anti-inflammatory drugs. He showed that Opioid analgesic request was 42% less with Ketorolac and Diclofenac sodium, than with other NSAID as Ketoprofen¹¹.

The central sensitization prolongs and increases sensitivity to noxious stimuli over an expanded receptive field. Repetitive noxious stimuli provoke a progressively escalating response in the cord and further magnify the pain. Hyperalgesia and reflex hyper excitability caused by sensitization of the nervous system also occur in surgical patient suggesting a potential for pre-emptive analgesia in human beings. The hyperalgesic effect of various protanoids varies considerably. After a rapid onset the effects of prostacyclins (PGI₂) only last for approximately 30 min, where as PGE₁, and PGE₂ cause hyperalgesia for upto 3 hours after a slow onset. This effect may pass before the maximum effect on pain threshold has reached when using inhibitors of prostaglandin synthesis.

The mean pain score was noted in this study in the immediate postoperative period (30 minutes after anaesthesia). It is possible that benefits of pre-emptive treatment are evident considerable time after conclusion

of surgery.

In a study it was observed that the postoperative analgesic effects of diclofenac given as premedication with bupivacain in day case athroscopy. There was decrease in VAS pain score of knee pain after diclofenac sodium even after 2 hours post operatively¹².

Comparison of the efficacy of a multimodal analgesic regimen and single drug therapy with I/V PCA morphine after Cesarean delivery with spinal anesthesia was done. Pain score were lower in the group who received multimodel pain treatment incisional infiltration with bupicaine and ibuprofen + acetaminophen¹³.

In study of I/V diclofenac Vs ketorolac for a pain relief after thoracoscopic surgery showed that diclofenac and ketorolac were equally effective in reducing total morphine consumption (61% and 52%) respectively. Adverse effects were similar and minor variability in plasma concentration of ketorolac was detected compared with diclofenac¹⁴.

In present study the time interval for first analgesic request was longer in group A (I/V ketorolac 90 minutes) than group B (I/M diclofenac sodium) 60 minutes. The statistical difference between pain scores of these groups was significant (mean score group A 1.5 VS group B 2.6).

In a study of pre-emptive analgesia with NSAID it was found that timing of analgesia made no difference to pain score or post operative analgesia requirements and that there was no preemptive effect of diclofenac and extradural local anaesthesia given before surgery¹⁵.

Present study show that both ketorolac and diclofenac are adequate for mild to moderate pain relief but ketorolac is slightly more effective in group A receiving Ketorolac (VAS1.5) compared to group B receiving I/M diclofenac(VAS 2.6) The effects of residual concentration of drugs used during operation were expected to be present during study period.

In review article of pain after laparoscopic surgery concluded that due to preemptive effects of NSAID, there was reduction in both severity of pain and loss of function which has made possible earlier discharge from hospital¹⁶.

Other parameters such as heart rate, blood pressure and respiratory rate being important indicators of haemodynamics were continuously monitored. They were slightly lower in group A (Patient receiving I/V Ketorolac) than in group B (patient receiving I/M diclofenac sodium).

Few important side effects were also noted in this study. Six patients in group A and three patients in group B suffered from Nausea and all required metoclopramide. Sweating was observed in three patients in group B. These values also correlated with lower mean pain score in group A than group B.

In a study in which the author evaluated the effects of ketorolac versus Bupivacaine co-administered during patient controlled hydromorphone epidural analgesia after thorocotomy procedures. The study revealed that Ketorolac supplementation significantly reduced the incidence of pain and narcotic requirements was also decreased along with the incidence of respiratory depression. The incidence other opioid side effects as drowsiness and nausea and vomiting was very low in patients receiving NSAID¹⁷.

Single dose ketorolac and pethidine for post-operative pain relief. It was concluded that pethidine produced significantly more drowsiness and dizziness than NSAID¹⁸.

There was another significant benefit received due to use of NSAID in our study. There was negligible incidence of hypoxaemia, which is primarily due to avoidance of respiratory depressant effect of opioid used for pain relief post operatively.

In another study of pre-emptive effect of multimodal analgesia in thoracic surgery were studied. The effects

of preemptive analgesia given before surgery (with I/V morphine, I/M diclofenac, and intercostal nerve block), appeared to be relatively modest in terms of analgesia, analgesic consumption and long-term outcome. In our study Ketorolac I/V given along with local infiltration of 0.5% bupivacaine revealed lower mean pain score post operatively. Other parameters as pulse rate blood pressure and respiratory rate were also less than in group B.

Dionne R studied intravenous ketorolac and its effects on platelet function during knee arthroscopy. His study revealed that Ketorolac affects the function of platelets¹⁸.

Our study did not reveal any effect on platelet function as revealed by normal bleeding time. Nausea and sweating showed slight but significant decrease in group A than group B and analgesic requirements are also decreased in group A than in group B. However a relatively effective analgesic regimen is equally effective whether initiated before or after surgery.

CONCLUSION

Inj. Ketorolac given I/V in bolus dose with 0.5% infiltration of bupivacaine before induction of anaesthesia had some advantage over diclofenac Na given I/M +0.5% bupivacaine, infiltration given before induction of anaesthesia for post operative delay in the 1st demand of supplementary analgesics in patients under going gynaecological surgery. This study however does not allow any significant conclusion to be drawn regarding its pre-emptive opioid sparing effect in the immediate postoperative period.

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