A Comparative Study of Intravenous Diclofenac and Combination of Intravenous Paracetamol with Intravenous Diclofenac for the Postoperative Pain Management

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Abstract

Context: The search for an ideal drug for post operative analgesia is ongoing. Paracetamol is commonly used drug for this purpose in different routes.

Aims: To assess and compare the quality and duration of postoperative pain relief with intravenous Diclofenac and combination of intravenous Diclofenac and Paracetamol.

Settings and Design: This prospective randomized comparative study was conducted in the department of anaesthesiology in a medical college & hospital.

Methods and Material: The study subjects were 60 male patients, aged between 20 and 40 years, of American Society of Anesthesiology (ASA) grade I scheduled for inguinal hernia repair, under spinal subarachnoid block anaesthesia. They were randomly allocated to receive either 75mg of Diclofenac in 100ml of normal saline as intravenous infusion (Group D) or 75mg of Diclofenac in 100ml of normal saline followed by 1000mg of Paracetamol as intravenous infusion (Group DP). The cases were observed for pain intensity, time of first rescue anlgesia requirment & total doses of rescue analgesia requirement. The study subjects were also observed for any change in haemodynamic and respiratory parameters & adverse effects.

Statistical analysis used: The data using SPSS 17 version. Data were expressed as Mean and Standard Deviation and data were also analysed by using Test of Association (chi-square test). 'P' value less than 0.005 & 0.0001 was considered as significant & highly significant respectivelly.

Results: The pain score and number of doses of rescue analgesia requirement were significantly less in the DP group ($p<0.001$). The time of first rescue analgesia requirement was significantly shorter in the D Group. There were no differences in vital parameters & adverse reactions in between two groups.

Conclusions: A combination of Diclofenac 75mg along with 1000mg of Paracetamol given as a slow intravenous infusion, for post operative pain relief, gives a better quality, longer duration of analgesia, with lesser number of rescue analgesia, compared to infusion of 75mg of Diclofenac alone.

INTRODUCTION

Postoperative pain is considered as a form of acute pain owing to surgical trauma with an inflammatory reaction, initiation of an afferent neuronal barrage. Post operative pain is an unpleasant sensory, emotional and mental experience which is precipitated as a result of surgery and isoften associated with autonomic, endocrine-metabolic, physiological and behavioral response. [(1)]

Pain if inadequately relieved can result in various complications like atelectasis / pneumonitis/hypoxaemia, deep vein thrombosis, delayed recovery of bowel function, myocardial ischemia and infarction, urinary retention and residual psychological trauma. [(2)] Therefore it is important to totally relieve the patient from the pain sensation after surgery. [(3)]

Various treatment modalities are now available for controlling postoperative pain which include intravenous opioids, patient –controlled analgesia, regional catheters and

adjuvant therapies (cryotherapy, minor analgesics, and NSAIDs). Conversely, these approaches have lots of limitations and technical use which could limit its use. [4]

Nonsteroidal anti-inflammatory drugs (NSAIDs) are one of the widely used drug class for the relief of pain and inflammation. They act by inhibition of prostaglandin synthesis. However, the uses of NSAIDs group of drugs have increased risk of gastrointestinal and cardiovascular complication as compared with non- NSAIDs use. Paracetamol is an opioid sparing, short acting analgesic, used orally, rectally and intramuscularly. The mechanism of action of paracetamol was unknown till recently, when two important researchers unequivocally demonstrated that the analgesic effect of paracetamol is due to indirect activation of cannabinoid receptors. [5, 6] Diclofenac is an NSAID used orally, rectally, and as deep intramuscular injection. A combination is available commercially in the oral form but not intravenously. Each of these analgesic drugs is available as separate intravenous preparation.

There are limited numbers of studies in literature with combination of diclofenac and paracetamol for postoperative anlgesia. Therefore we planned for the present study.Our aim was two fold: (1) To assess and compare the quality and duration of postoperative pain relief with intravenous Diclofenac and combination of intravenous Diclofenac and Paracetamol. (2) To assess whether addition of Paracetamol to Diclofenac improve the quality and duration of postoperative analgesia.

MATERIALS & METHODS

The Ethical Committee of the Institute permitted us to carry out the project after the approval of our methodology. Sixty male patients, aged between 20 and 40 years, of American Society of Anesthesiology(ASA) grade 1, weighing between 50-70kgs, scheduled for inguinal hernia repair, under spinal subarachnoid block anaesthesia were enrolled, in this prospective randomized study. A thorough pre-anaesthetic evaluation was done and patients with history of gastro espphageal reflu disease (GERD), liver diseases, respiratory and cardiac problems were excluded, along with patients who refused spinal anesthesia or with anticipated difficulty in spinal anaesthasia.

A written informed consent was obtained from the patients after explaining to them about the nature of the study. They were also explained about the use of the Visual Analog Scale (VAS), a 10cm scale for assessing their subjective response to pain. For no pain the score is 0 and 10 for severe pain. All were premedicated with tablet Alprazolam 0.25mg with a sip of water on the morning of surgery.

The patients were randomly allocated to 2 groups, Diclofenac Group (Group D) and Diclofenac Paracetamol Group (Group DP).

An experienced Anaesthesiologist performed the spinal block in all the patients with 3ml of 0.5% heavy Bupivacaine at L_3-L_4 interspace and the surgery was allowed to proceed. At the end of surgery, the patients were shifted to Post Anaesthesia Care Unit (PACU).

As the spinal block receded and the patients first complaint of pain, Group D received 75mg of Diclofenac in 100ml of normal saline as intravenous infusion, at the rate of 5ml/minute over 20 minutes. Group DP received 75mg of Diclofenac in 100ml of normal saline at the rate of 5ml/minute over 20minutes followed by 1000mg of Paracetamol over 20 minutes, at the rate of 5ml/minute as intravenous infusion.

From the start of the infusion, at interval of 2, 4, 6, 8hours, the patients in both groups were asked to indicate the intensity of pain in VAS. The scores were noted. When the VAS score was 5 or more, the patients were given'rescue analgesia', usually as injection Tramadol 50 mg intramusular, and the time of rescue analgesia us was noted. Any adverse effects like nausea and vomiting were watched for and recorded. A proper record was maintained regarding demographic profile, the hemodynamic and respiratory parameters and the intensity of the pain by using the VAS score. At the end of the study the data were compiled systematically and was subjected to statistical analysis. The data was analysed by a qualified statistics using SPSS 17 version. Data were expressed as Mean and Standard Deviation and data were also analysed by using Test of Association (chi-square test). 'P' value less than 0.005 & 0.0001 was considered as significant & highly significant respectivelly.

RESULTS

The mean age and mean weight in was very much comparable in between two groups (P>0.05) (Table I). Likewise, the respiratory and haemodynamic parameter remained stable throughout the period of study without any marked variation in both the groups, and statistically not significant (Table 2). Comparing the pain scores between the

two groups, Group D had a statistically very significant a VAS score as compared to Group DP (Table 3). It shows that DP Group fared better than the D group, as far as pair was concerned. Similarly the time interval between the start of drug infusion and rescue analgesia was significantly more in DP Group (Table 3). Again the number of rescue analgesia requirement in Group D was significantly more as compared to Group DP (Table 3). In Group D 21 out of a total of 30 needed rescue analgesia, out of which 3 patients at the end of the 4th hour (with an average pain score of 7.33), 12 patients at the end of the 6th hour (with an average pain score of 6.8) and 6 patients at the end of the 8th hour (with an average pain score of 6.66). In Group DP, during the eight hour period, only 5 patients out of 30 needed rescue analgesia when the pain score went above 5, and that too towards the end of the 8th hour.This too was statistically significant. There were no adverse effects like nausea and vomiting. Only one patient complained of headache in the DP Group.

Table 1

Demographic Profile of the Patients

Demographic characteristics	Group D (n=30)	Group DP (n=30)
Age in years (Mean ± SD)	33.87 ± 5.00	33.2 ± 5.15
Weight in Kgs (Mean ± SD)	60.57 ± 4.76	60.40 ± 4.99

Table 2

Haemodynamic and Respiratory parameters

Parameters	Group D (n=30)	Group DP (n=30)	'P' value
Pulse rate/minute (Mean ± SD)	79.49 ± 7.63	79.09 ± 7.55	>0.05
Mean Arterial Pressure in mm of Hg (Mean ± SD)	85.97 ± 9.91	85.63 ± 9.75	>0.05
Oxygen Saturation in Percentage (Mean ± SD)	99.40 ± 0.56	99.44 ± 0.56	>0.05

Table 3

The Quality and Duration of analgesia

Description	Group D (n=30)	Group DP (n=30)	'P' value
Pain score(VAS) (Mean ± SD)	10.34 ± 2.82	2.5 ± 2.75	<0.001
Time interval between drug infusion and rescue analgesia (in hrs) (Mean ± SD)	5.8 ± 2.94	7.6 ± 1.22	<0.05
Number of rescue analgesia used (Mean ± SD)	0.7 ± 0.47	0.1 ± 0	<0.001

DISCUSSION

Post operative pain is very acute and is an unpleasant sensory and emotional experience. Even though there are some methods of quantifying pain, there is no one single fool proof method. Pain continues to be a non quantifiable, but highly subjective and personal experience. Attempts are being made constantly to fully control post operative pain, but without compromising safety. [7]

Diclofenac is a widely used post operative analgesic, given as a 75mg deep intramuscular injection or as a slow intravenous infusion, with the limitation of not exceeding 150mg/day. [8]

Paracetamol (known as Acetaminophen in USA) is very popular in Europe as post operative intravenous infusion for pain relief, in a dose of 1000 mg, which can be repeated 6th hourly, the total dose not exceeding 4gm/day. [9, 10] In the past studies had shown that Paracetamol is a viable alternative to the NSAIDs, especially because of the low incidence of adverse effects, and should be the preferred choice in high risk patients. It may be appropriate to combine paracetamol with NSAIDs as there is decrease in dose & side effects. [11, 12]

In our study, the demographic parameters like age and weight, the physiological parameters like Heart rate, Mean Arterial Pressure and Oxygen Saturation were comparable in both Groups D and DP.

Comparing the pain scores in each group, the DP group had a far less VAS score than the D group with a statistically significant P value of < 0.001, showing that the patients who received the Diclofenac Paracetamol combination had a much better pain relief than the patients who received Diclofenac alone. Other studies in this aspect had similar findings. Kimberly A and colleages found that the scheduled

dosing of acetaminophen and hydrocodone is more effective than PRN dosing in reducing pain intensity in children following tonsillectomy.[13]Narinder Rawa & colleagues found that Tramadol/paracetamol combination tablets provided comparable analgesic efficacy with a better safety profile to tramadol capsules in patients experiencing postoperative pain following ambulatory hand surgery.[14]Ogn Ck et al in a systematic review suggested that a combination of paracetamol and NSAID may offer superior analgesia compared with either drug alone.[15]

From the time the analgesic infusion was started, till the time it took for recsue analgesia was far longer in the DP Group, again confirming the fact that the duration of pain relief was far longer in the DP Group as compare to the D Group. This finding is similar to the findings observed by other researchers. [13-15]

In the D group the requirment for rescue analgesia was early as compared to the DP group. Again the number of rescue analgesia used in both the groups seems statistically significant. The implication is that both the quality and duration of analgesia with a combination of Diclofenac and Paracetamol is better and prolonged when compared with Diclofenac alone. Other researchers had also observed similar findings. [13-16]

There were no side effects in either group, except one patient with headache in Group DP. This indicates that the safty of combine drugs is similar to diclofenac alone, a finding observed by other researchers. [16 & 17] Both Diclofenac and Paracetamol spare the side effects of opioids like respiratory depression, constipation and urinary retention.[18]Intravenous route provides quick onset of action and effective pain relief than oral or rectal route. [19]

CONCLUSION

A combination of Diclofenac 75mg along with 1000mg of Paracetamol given as a slow IV infusion, for post operative pain relief, gives a better quality, longer duration of analgesia, with lesser number of rescue analgesia, compared to infusion of 75mg of Diclofenac alone. However further studies with more number of patients and other type of surgeries is required to corelate the findings.

References

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