

A COMPARATIVE STUDY BETWEEN RECTAL DICLOFENAC PLUS PARACETAMOL AND INJECTABLE TRAMADOL FOR POSTOPERATIVE PAIN MANAGEMENT IN OPEN/LAPAROSCOPIC APPENDECTOMY

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ABSTRACT

Both rectal diclofenac and paracetamol are commonly used to treat acute postoperative, but combining them to improve the quality of analgesia is controversial. This study aimed to detect whether the preoperative combined administration of rectal diclofenac and paracetamol is superior to injectable tramadol alone, is effective in postoperative pain management.

METHODS

57 patients were randomly assigned to receive the suppository 1 hr. prior to surgery. In the first 24 hrs. postoperatively, pain was assessed using the visual analogue pain scale (VAS). If the patients experienced a pain score of 5 or more, tramadol 50 mg IV was given. The total dose of tramadol and number of doses required were recorded. Patients who received the rectal diclofenac-paracetamol combination experienced a lower pain scale and a decreased need for tramadol compared with those receiving tramadol alone.

RESULTS

The overall VAS score and consumption of injectable tramadol was lower in the group receiving the rectal suppository. The mean VAS score in group 1 at 4, 8 and 24 hours was lower than those in group 2, this difference was statistically significant ($p < 0.000$).

CONCLUSIONS

Patients receiving the rectal diclofenac-paracetamol combination experienced significantly a lower pain as compared with patients getting only injectable analgesics. The need for injectable analgesics was also found to be reduced in the immediate postoperative period in the patients receiving rectal suppository.

KEYWORDS

Diclofenac-paracetamol Suppository, VAS scale, Injectable Tramadol.

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INTRODUCTION: Postoperative pain is usually an acute pain, sharp in character which starts with the surgical trauma and ends with tissue healing. Unrelieved acute pain results in potentially life-threatening adverse physiological effects and may also cause psychological disturbances. In the modern day concept, postoperative care essentially includes an effective relief from pain, suffering, anxiety, and sleeplessness. Thus, the outcome of postoperative recovery is greatly influenced by effective pain management. Multidisciplinary pain trails are being developed. The concept of pre-emptive analgesia is important in combating postoperative pain. Postoperative pain is a major concern because it affects multiple systems and induces

physiological, immunological, and psychological changes.^(1,2)

Despite many advances in the provision of pain services, acute pain after surgery remains a serious cause of severe suffering that is often undermanaged despite our best efforts.⁽³⁾ Acute pain can be persisted, the tissue damage of surgery setting up pathophysiological processes in the peripheral and central nervous system that may produce chronicity.⁽⁴⁾ The association between surgery, acute pain and ongoing severe chronic pain is well defined.^(5,6) There is therefore a pressing need of advances in the agents and techniques we can use to improve analgesia efficacy, and perhaps reduce the incidence of chronic suffering after surgery.

Pain management in the perioperative period has been traditionally based on opiates. Considering their side effects (respiratory depression, nausea, vomiting and histamine release), new drugs, opiate-sparing drugs, and novel techniques were introduced for treatment. A multimodal approach has been suggested to improve postoperative analgesia and to reduce the opioid-related side-effects.⁽⁷⁾

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Non-opioids play an ever increasing role in the treatment of postoperative pain. Different classes of analgesics exert their effects through different mechanisms. A combination of analgesics from different classes may provide additive analgesic effects with fewer side effects than when a single therapeutic drug is used.⁽⁹⁾ Paracetamol is frequently used as non-opioid analgesic in postoperative pain and has a morphine-sparing effect. Its mechanism of action is not fully understood, but it is generally accepted that paracetamol is a centrally acting drug.⁽⁸⁾ Diclofenac is a commonly used analgesic, that has analgesic, anti-inflammatory properties and exerts its action via inhibition of prostaglandin synthesis by inhibiting cyclooxygenase-1 and cyclooxygenase-2 with relative equipotency.⁽⁹⁾ In clinical practice, NSAIDs and paracetamol are widely used together, but whether such a combination actually offers a significant improvement analgesia is controversial.^(10,11) Both rectal diclofenac and paracetamol are commonly used to treat acute postoperative pain but combining them to improve the quality of analgesia is controversial. This study aimed to detect whether the preoperative combined administration of rectal diclofenac and paracetamol suppository reduces the need for injectable analgesics in the postoperative period.

OBJECTIVE: To detect if the preoperative combined administration of rectal diclofenac and paracetamol suppository is superior to injectable analgesics alone for the management of postoperative pain after open/laparoscopic appendectomy.

MATERIALS AND METHODS: 50 patients, scheduled for open/laparoscopic appendectomy were recruited to this randomised trial of which 25 were to receive rectal

combination of diclofenac 100 mg and paracetamol 1.5 g, which were given as a suppository 1 hour prior to surgery and the remaining 25 didn't receive pre-emptive analgesia.

The primary outcomes were visual analogue pain scores measured at 0, 2, 4, 6 and 24 hours after surgery and the time of first administration and also total amount of injectable analgesics used in the first 24 hours after surgery. A 10 cm visual analogue scale (VAS) was used to assess pain intensity at rest and compared between the two groups and analysed statistically.

Inclusion Criteria:

- Age above 18 years.
- Patients posted for laparoscopic/open appendectomy.
- Written informed consent.

Exclusion Criteria:

- Patient refusing.
- Asthma.
- Known allergy or contraindication to the study drugs.
- Kidney or hepatic dysfunction or haemorrhagic diathesis.

METHOD: Suppositories contained of 50 mg diclofenac plus 325 mg paracetamol, which were then inserted per rectally one hour prior to the surgery and before the induction of anaesthesia. The operation was performed by the same surgeon.

After the surgery, patients were transferred to the post-anaesthetic care unit, and their pain scores and opioid usage were measured and recorded on arrival and at 4, 6, 8, 24 hours after surgery. The results from both the groups were tabulated and analysed.

STATISTICAL ANALYSIS:

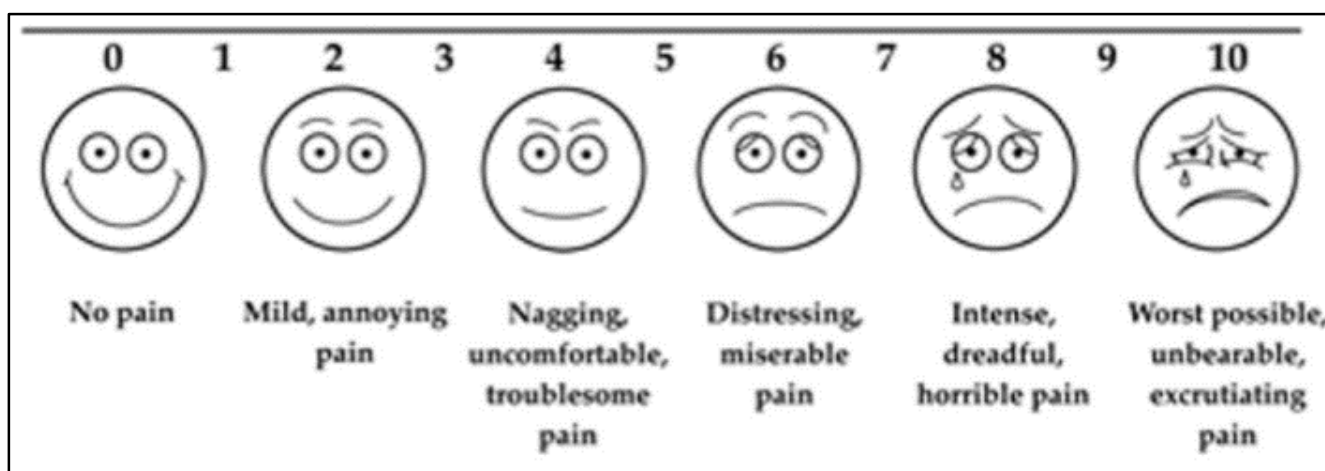
Independent T-Test

	Group	N	Mean	Std. Deviation	t	p
2 hrs.	1	26	5.73	.874	2.571	0.013
	2	31	5.19	.703		
4 hrs.	1	26	4.00	.632	-8.302	0.000
	2	31	5.61	.803		
8 hrs.	1	26	4.31	.679	-4.033	0.000
	2	31	5.42	1.259		
12 hrs.	1	26	4.62	.983	-1.238	0.221
	2	31	4.94	.964		
24 hrs.	1	26	4.15	.464	-8.265	0.000
	2	31	5.52	.724		

Table 1

Independent Samples Test										
		Levene's Test for Equality of Variances		t-test for Equality of Means					95% Confidence Interval of the Difference	
		F	Sig.	T	Df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
2 hrs.	Equal variances assumed	1.631	.207	2.571	55	.013	.537	.209	.118	.956
	Equal variances not assumed			2.522	47.769	.015	.537	.213	.109	.966
4 hrs.	Equal variances assumed	4.582	.037	-8.302	55	.000	-1.613	.194	-2.002	-1.224
	Equal variances not assumed			-8.478	54.807	.000	-1.613	.190	-1.994	-1.232
8 hrs.	Equal variances assumed	16.204	.000	-4.033	55	.000	-1.112	.276	-1.664	-.559
	Equal variances not assumed			-4.236	47.568	.000	-1.112	.262	-1.639	-.584
12 hrs.	Equal variances assumed	.094	.761	-1.238	55	.221	-.320	.259	-.838	.198
	Equal variances not assumed			-1.235	52.908	.222	-.320	.259	-.840	.200
24 hrs.	Equal variances assumed	11.659	.001	-8.265	55	.000	-1.362	.165	-1.693	-1.032
	Equal variances not assumed			-8.580	51.692	.000	-1.362	.159	-1.681	-1.044

Table 2



57 patients with Acute Appendicitis were admitted and were scheduled to undergo emergency laparoscopic or open appendectomy, they were assigned to either groups randomly. Group 1 consisted of the patients who received rectal diclofenac and paracetamol suppository 1 hour before the surgery began, and the group 2 belonged to them who didn't get the suppository, instead had only injectable analgesics (tramadol 50 mg IV) for postoperative

management. The postoperative pain was analysed using the visual analogue scale (VAS) at 2, 4, 8, 12 and 24 hours, compared using independent and standard t test. It was noted that the mean VAS scores at the end of 4, 8, 12 and 24 hours were lower in the group 1, with it being significant at the end of 4, 8 and 24 hours postoperatively ($p < 0.000$).

The overall tramadol consumption between the groups was compared, and it was found that the suppository group was given 550 mg and the other consumed 2700 mg.

DISCUSSION: Millions of patients undergo surgery each year and benefit from the knowledge, skills, and sophisticated technology that characterise most aspects of modern surgical treatment. Though essential, effective pain control is sadly suffering a lacuna despite advances in pathophysiology, pharmacology, and development of newer modalities of pain management. Postoperative pain is undertreated for varied reasons viz., lack of knowledge regarding effective dose ranges, duration of action of opioids and unfounded fear of respiratory depression and addiction. Nonsteroidal anti-inflammatory drugs (NSAIDs) occupy a pivotal role in the arena of postoperative pain management because of their opioid sparing property. Paracetamol is the most widely used centrally acting NSAID in paediatric age group because of its wide margin of safety. The combination of diclofenac and paracetamol has been shown to decrease narcotic consumption after operation in adults.^[12,13]

Montgomery and colleagues reported that the use of this combination has been shown to reduce the amount of morphine required for adequate analgesia postoperatively by about one-third compared with paracetamol alone in patients undergoing elective abdominal procedures.^[12] The dose of paracetamol used was higher than the usual adult oral dose (1.5g) as the bioavailability was lower in suppositories and only a single preoperative dose was administered and plasma concentrations known to reduce fever did not produce better pain relief and were only achieved after twice the conventional dose was administered. Analgesic plasma concentrations have yet to be determined but may be higher than those associated with antipyresis.

It has been reported that because of the mode of action of NSAIDs, it is preferable that they are given prophylactically before the synthesis of prostaglandin is initiated by tissue trauma.^[13] Morton and O'Brien demonstrated that concurrent administration of diclofenac in patients receiving patient-controlled analgesia (PCA) morphine has a highly significant morphine sparing effect, although they failed to demonstrate any extra additive effect of paracetamol.^[14] Our finding is similar to those of other investigators who demonstrated a reduction of opioid consumption after diclofenac and paracetamol.^[13,14,15]

In our study, the drugs were given 1 hr. prior to surgery and needed amount of morphine was significantly reduced in combination therapy group. In our study, the most significant pain reduction occurred at early hours after surgery, when the pain is at its peak. This can be attributed to peak plasma concentration of administered drugs (diclofenac and paracetamol), that after rectal administration (prior to surgery), reach their peak plasma concentration after 2-3 hrs., therefore explaining their peak clinical effect in 4 hours after administration.

In Moussa and Riad study, the effect of diclofenac alone or diclofenac-paracetamol was compared.^[16] Paracetamol is the most widely used centrally acting NSAID because of its wide margin of safety. There is evidence in the literature that paracetamol^[17] was safely used up to a dose of 90 mg/kg/day. Diclofenac is a potent NSAID, which marks the

first line of defence in combating acute pain even today. Diclofenac inhibits the release of prostaglandins which sensitise the nociceptors to other inflammatory mediators.

There is abundant evidence in the literature proving the effectiveness of diclofenac in postoperative pain management.^(18,19,20) When two different agents targeted at a single pharmacological effect are used in synergism, the said combination allows the reduction in the dose of individual drugs without compromising on the quality of the effect, rendering a wider margin of safety. Thus in our study, we sought to compare the effectiveness of the combination of paracetamol and diclofenac with that of paracetamol alone in combating postoperative pain. We opted for the rectal route of administration as it is painless and well tolerated. In our study, the most significant pain reduction occurred at early hours after surgery, when the pain is at its peak.

This can be attributed to peak plasma concentration of administered drugs (diclofenac and paracetamol), that after rectal administration (prior to surgery), reach their peak plasma concentration after 2-3 hrs., therefore explaining their peak clinical effect in 4 hours after administration. In the study, the drugs were administered before operation, and it showed effective reduction of pain with combination therapy.

CONCLUSION:

1. According to our study, patients receiving the rectal diclofenac-paracetamol combination experienced significantly lower pain in first 24 hours after surgery as compared with patients getting only injectable analgesics.
2. The need for injectable analgesics was also found to be reduced in the immediate postoperative period in the patients receiving rectal suppository.

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