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Combination Of Suppository Diclofenac And Intravenous Morphine Infusion In Post-Caesarean Section Pain Relief - A Step Towards Balanced Analgesia?

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ABSTRACT

Post-Caesarean section analgesia can be achieved by morphine infusion. NSAIDs are frequently administered to relieve uterine cramps. This study is aimed at assessing the efficacy of the combination of suppository diclofenac and morphine infusion in post-Caesarean section pain relief. General anaesthesia was given to 60 patients who were randomly allocated into two groups: group A received 100 mg suppository diclofenac before surgical incision and morphine infusion 1.5 mg per hour postoperatively while group B received only morphine infusion 1.5 mg/H postoperatively.

Pain assessment was done by an unbiased observer on arrival of the patients in the recovery room, then 6 hours, 12 hours and 24 hours later.

Pain relief was found to be better in group A, with group B requiring more supplemental analgesia. Apart from better analgesic effect for wound pain, group A also had more favourable scores for uterine cramping pain.

The incidence of nausea or vomiting was similar in both groups. No respiratory depression was observed in both groups. Two cases of increased bleeding (one from each group) were observed, both receiving conservative treatment. The conclusion: suppository diclofenac improved the analgesic efficacy of morphine infusion in post-Caesarean analgesia.

Keywords: balanced analgesia, suppository diclofenac, NSAIDs, Intravenous morphine, post-Caesarean analgesia

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INTRODUCTION

Patients after Caesarean section suffer from two kinds of acute pain: wound pain and spasmodic uterine contraction pain[1-3]. Analgesic efficacy of NSAIDs either on their own or in combination with opioids is well known[4,5]. NSAIDs have also been used to relieve uterine cramps[2,3]. Therefore, NSAIDs can potentially enhance the analgesic effect of opioids without accentuating the adverse effects of opioids. Here, the effect of 100 mg suppository diclofenac in addition to morphine infusion of 1.5 mg/H is evaluated to see whether this combination is superior to morphine infusion alone in the provision of post-Caesarean section analgesia.

METHOD

This is a randomised double blind study (with the approval of the Hospital Ethics Committee) comprising 60 patients of ASA physical status I and II coming in for elective lower segment Caesarean section. They were divided equally into two groups, ie, A and B. They were premedicated with ranitidine on the night before the operation as well as on the morning of operation.

General anaesthesia was instituted; induced in rapid sequence with thiopentone/suxamethonium and maintained with nitrous oxide/oxygen/isoflurane and atracurium. Intravenous morphine 10 mg and syntocinon 10 U were given after delivery. General anaesthesia was reversed with atropine/neostigmine and all patients were extubated at the end of the procedure.

Group A received suppository diclofenac 100 mg after the induction of anaesthesia but before surgical incision while group B did not.

On arrival in the recovery room, intravenous morphine 1.5 mg/H was started in both groups. The patients were asked about the intensity of wound pain and uterine pain on arrival in the recovery room and 6 hours, 12 hours and 24 hours subsequently.

Wound pain was scored by an unbiased investigator according to the following:

0 = no pain
1 = mild pain, not restricting activity
2 = moderate pain, significantly restricting activity
3 = severe pain, allowing only minimal mobility and
4 = excruciating pain, absolutely incapacitating

Uterine contraction pain was scored in accordance with the following:

0 = No contraction
1 = Mild contraction pain
2 = Severe contraction pain

Rescue medication was standardised as pethidine 20-50 mg intramuscularly every 6 hours at the patients' request.

Vital signs (blood pressure, heart rate and respiratory rate) were monitored hourly for 24 hours.

Table I - Clinical data of the two study groups

	A	B
Weight (kg)	68.3 ± 10.9	69.1 ± 11.6
Height (cm)	156.4 ± 5.5	154.7 ± 6.3

Values of weight and height mean values ± SEM

No significant differences between 2 groups (*t* tests)

Table II - Side effect

Side effect	Gp A (n=30)	Gp B (n=30)
Nausea and vomiting	10	13
Bleeding	1	1
Respiratory depression	0	0

No significant differences between the two groups in nausea and vomiting (χ^2 test) and bleeding (Fisher exact test).

Table III - Pethidine requirement in each group

	Group A	Group B
Patients requiring treatment	5 (total dose 145 mg)	16 (total dose 805 mg)

$p < 0.05$ between the 2 groups requiring treatment (χ^2 - test).

Respiratory depression was taken as the respiratory rate of less than 8/min. Bleeding was regarded as abnormal when the obstetrician decided to use oxytocics to increase uterine tone.

Importantly, patients with bronchial asthma, known drug allergy to NSAIDs, peptic ulcer disease, bleeding tendency, liver or kidney diseases were excluded from the study. Similarly patients with complicated obstetric history like pregnancy-induced hypertension and antepartum haemorrhage were excluded.

Data are expressed as mean values ± SEM for patients' weight and height with *t*-tests being used for their evaluation. The pain scores as well as the incidence of nausea or vomiting were evaluated with χ^2 tests. The significance of increased bleeding was assessed by Fisher exact test. The number of patients requiring rescue medication was evaluated with χ^2 test. A ρ value of less than 0.05 was considered significant.

RESULTS

There was no difference in the data between the two groups in terms of weight and height (Table I).

Significant differences between the two groups in terms of both wound pain and uterine contraction pain were noted at the sixth, twelfth and twenty-fourth hours.

Group A had lower wound pain and uterine contraction pain scores from 6 hours after the conclusion of the operation until 24 hours after surgery (Figs 1 & 2).

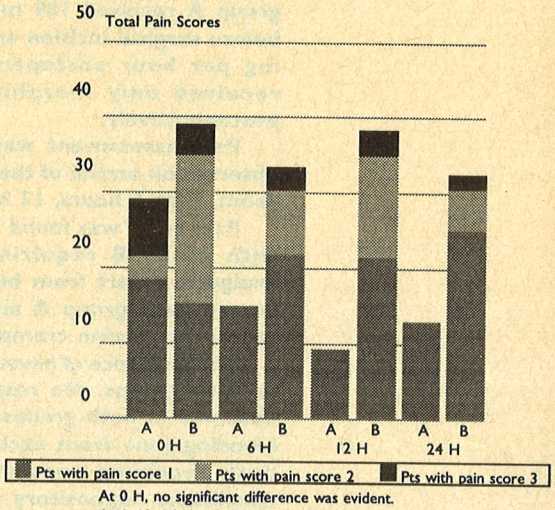
Nausea and/or vomiting occurred frequently in both groups (ie, about 1/3 of the patients) but there was no significant difference between the two groups. Respiratory depression was not observed in either group. Both groups had one patient requiring syntocinon infusion and therefore there was no significant difference in terms of increased bleeding between the two groups (Tables II & III).

DISCUSSION

The finding that the combination of diclofenac and morphine was superior to morphine alone in analgesic quality in the 6-24 hour period indicates that diclofenac contributes to additional relief of both wound pain and uterine contraction pain.

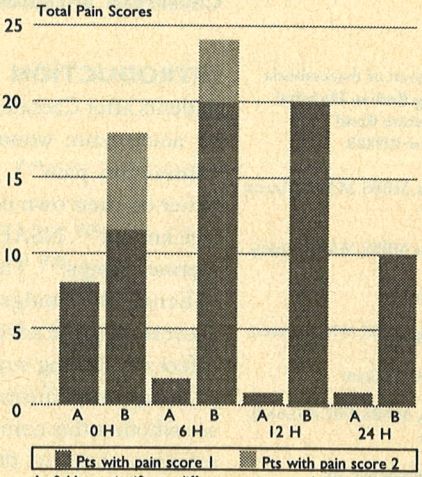
In this study, patients who had been given diclofenac required less pethidine and had lower pain scores, a finding which was consistent with other studies which showed the opioid sparing effect of NSAIDs[6-8]. Uterine contraction pain relief was also more effectively accomplished by diclofenac, indicating the contribution of NSAIDs to the relief of uterine cramps as shown in other studies[3,4,9,10].

Fig 1 - Total incisional wound pain scores in the two groups



At 0 H, no significant difference was evident.
At 6, 12, 24 H, $p < 0.05$ between the two groups (χ^2 - test).

Fig 11 - Total uterine contraction pain in the two groups



At 0 H, no significant difference was noted.
At 6, 12, 24 H, $p < 0.05$ between the two groups (χ^2 - test).

The NSAIDs were thought to exert their analgesic effect by the inhibition of prostaglandins synthesis. Apart from this "peripheral mechanism", a central anti-nociceptive effect of NSAIDs has also been postulated[11-13]. Diclofenac possesses anti-inflammatory, anti-oedema, antipyretic and analgesic properties[14,15]. Increased peripheral endorphin levels was also found after diclofenac treatment although this contribution to the overall analgesic effect should be further investigated[16]. Moreover, NSAIDs have been found to neither cause respiratory depression nor psychomimetic effect[11,17]. Addiction liability is also low[18].

The risk of postpartum haemorrhage in relation to NSAIDs is a theoretical one, considering the possibility of diclofenac increasing bleeding time and reducing platelet aggregation[19,20]. However, diclofenac-induced post- operative bleeding is rare in clinical practice[1,19,20].

NSAIDs have been used to relieve postpartum uterine cramps and post-episiotomy pain without significant side-effects. NSAIDs are not readily distributed to breast milk because being weak acids they are readily ionised in the range of pH of breast milk (pH 6.9 to 7.6).

CONCLUSION

In conclusion, the combination of morphine infusion and suppository diclofenac enhances the analgesic quality after Caesarean section. While opioid analgesia is the cornerstone, the foundation of pharmacological postoperative pain management, it should not be viewed in isolation. The question should not be NSAIDs or opioids but rather NSAIDs and opioids[5]. The concept of balanced, multi-modal analgesia is one which the anaesthetist must be very familiar. The guidelines to minimise the incidence and severity of acute pain (developed under the sponsorship of the Agency for Health Care Policy and Research, Public Health Service, US Department of Health and Human Services) recommend that in few cases should we be providing analgesia using a single agent[21]. Balanced analgesia is polypharmacy, but the combination of pharmacological agents may produce better analgesia with fewer side effects[7,17,22-24].

REFERENCES

1. Nir D, Rudick V, Chayen MS, David MP. Variations in the effect of epidural morphine in gynaecological and obstetric patients. Acta Obstet Gynecol Scand 1983; 62: 455-9.
2. Bloomfield SS, Cissel GB, Mitchell J, Barden TP. Analgesic sensitivity of two postpartum pain models. Pain 1986; 27: 171-9.
3. Bloomfield SS, Barden TP, Mitchell J. Naproxin, aspirin and codeine in postpartum uterine pain. Clin Pharmacol Ther 1977; 21: 414-21.
4. Hodsman NBA, Burns J, Blyth A, Kenny GNC. The morphine sparing effects of diclofenac sodium following abdominal surgery. Anaesthesia 1987; 42: 727-31.
5. Kantor TG. Use of diclofenac in analgesia. Am J Med 1986; 80 (suppl 4b): 64-9.
6. Lantinen J, Nuutinen L. Intravenous diclofenac coupled with PCA fentanyl for pain relief after total hip replacement. Anesthesiology 1992; 76: 194-8.
7. Gillies GWA, Kenny GNC, Bullingham RES, McAidle GS. The morphine sparing effect of ketorolac Tromethamine. Anaesthesia 1987; 42: 727-31.
8. Tigerstedt I, Tammisto T, Neuvonen PJ. The efficacy of intravenous indomethacin in prevention of postoperative pain. Acta Anaesthesiol Scand 1991; 35: 535-40.
9. Bloomfield SS, Cissel GB, Mitchell J, Barden TP. Codeine and aspirin analgesia in postpartum uterine cramps: qualitative aspects of quantitative assessments. Clin Pharmacol Ther 1983; 34: 488-95.
10. Sunshine A, Zighelboim I, Olson NZ, Sarrazin OD. A comparative oral analgesic study of indoprofen, aspirin and placebo in postpartum pain. J Clin Pharmacol 1985; 25: 374-80.
11. Willer JC, Broucker TD, Bussel B, Agnes RB. Central analgesic effect of ketoprofen in humans: Electrophysiological evidence for a supraspinal mechanism in a double-blind and cross over study. Pain 1989; 38: 1-7.
12. Ferreina SH, Lorezetti BB, Correa FMS. Central and peripheral analgesic action of aspirin-like drugs. Eur J Pharmacol 1978; 53: 39-48.
13. Jurna I, Brunek J. Central effect of non-steroidal anti-inflammatory agents, indomethacin, ibuprofen and diclofenac, determined in a fiber evoked activity in single neurons of the rat thalamus. Pain 1990; 41: 71-80.
14. Maier R, Manasse R, Rusterer L, Pirocin C, Ruegg M. The pharmacology of diclofenac sodium. Rheumatol Rehab 1979; 17 (Supp 2): 11-21.
15. Todd RA, Sorkin EM. Diclofenac sodium. A reappraisal of its pharmacodynamic and pharmacokinetic properties, and therapeutic efficacy. Drugs 1988; 35: 244-85.
16. Martini A, Bondiolotti GP, Brol D, Sacerdote P, Pierro L, Picotti GB et al. Delofenac increases beta-endorphin plasma concentrations. J Int Med Res 1984; 12: 92-5.
17. MacDonald FC, Gough KJ, Nicoll RAG, Dow RJ. Psychomotor effect of ketorolac in comparison with buprenorphine and didofenac. Br J Clin Pharmacol 1989; 27: 453-9.
18. Buckley MMT, Brogden RN. Ketorolac: Review of its pharmacodynamic and pharmacokinetic properties, and therapeutic potential. Drugs 1990; 39: 86-109.
19. Rorarius M, Miralleo J, Bare GA, Palomki E. Diclofenac versus indomethacin given as intravenous infusions; their effect on haemodynamics and bleeding time and side-effects in healthy subjects. Ann Clin Res 1985; 17: 306-9.
20. Power I, Chambers WA, Green IA, Ramage D. Platelet function after intramuscular diclofenac. Anaesthesia 1990; 45: 916-9.
21. Moote C. Techniques for post-operative management in the adult. Can J Anaesth 1993; 40: 5/RI9-R24.
22. Gwittz K, Helvie J, Young J, Rouff G. Ketorolac enhances intrathecal analgesia after major abdominal and orthopaedic surgery. Reg Anesth 1992; 17:161.
23. McQuay H, Carroll D, Watts P, Juniper RP, Moore RA. Codeine 20 mg increases pain relief from ibuprofen 400 mg after third molar surgery. A repeat dosing comparison of ibuprofen and an ibuprofen codeine combination. Pain 1989; 37:7-13.
24. Rubin P, Yee J, Murthy V, Hansen R, Pietrontak C. Ketorolac tromethamine (KT) analgesia: No postoperative respiratory depression and less constipation. Clin Pharmacol Ther 1987; 41: 182.