Comparison of diclofenac sodium with indomethacin suppositories for mediolateral episiotomies

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Summary

Objective: The study was carried out to compare the analgesic effect of diclofenac sodium and indomethacin suppositories for management of right mediolateral episiotomy repair. *Method:* A total of 70 patients who gave birth vaginally with right mediolateral episitomy were randomly assigned to receive 100 mg diclofenac sodium suppositories/day (G1, n = 35) or 100 mg indomethacin supposotories/day (G2, n = 35) after episiotomy repair and postpartum for three days. Pain ratings were recorded before, the first hour and 24 hours after medication. The verbal rating scale (VRS) and visual analog scale (VAS) were used for pain recording. The independent T test, Mann-Whitney U and Wilcoxon rank test were used for statistical analysis and Spearman correlation analysis was used for comparison between VRS and VAS. *Results:* Diclofenac sodium was a more effective analgesic than indomethacin suppositories for right mediolateral episiotomy pain. For G1 the first hour VRS was 2.6 ± 0.5 points and VAS 4.9 ± 0.8 points; for G2 the first hour VRS was 3.4 ± 0.6 points VAS 6.6 ± 1.2 points; this difference was statistically significant ($p < 0.05$, Mann-Whitney U test). For G1 at the 24th hour VRS was 1.2 ± 0.4 points and VAS 2.4 ± 0.9 points; for G2 at the 24th hour VRS was 2 ± 0.7 points and VAS was 3.4 ± 1.3 points; the difference was statistically significant ($p < 0.05$, Mann-Whitney U test). The first and 24th hour pain scores (VAS1-VAS24, VRS1-VRS24) were decreased dramatically for both groups ($p < 0.05$, Wilcoxon rank test). A positive correlation was obtained between the first and 24th hour VRS and VAS by Spearman correlation analysis ($r_s = 0.9$, n = 70, $p = 0.000$). *Conclusion:* The two analgesics were effective after episiotomy repair, however diclofenac sodium suppositories may be the preferred choice because they were more effective.

Key words: Diclofenac sodium; Indomethacin; Mediolateral episiotomy; Pain.

Introduction

Severe perineal pain during vaginal delivery is associated with lacerations or episiotomy. Treatment is usually by local anesthesia and oral or rectal analgesics [1-5]. Perineal pain, especially three days after vaginal delivery, can poorly effect the daily (movement, micturation, defecation, lactation) activities of women [6].

Both diclofenac sodium and indomethacin are nonselective nonsteroidal anti-inflammatory drugs (NSAID) that inhibit prostaglandine synthase via cyclooxygenase 1 (COX-1) and 2 (COX-2) [7, 8]. Inhibition of prostaglandin synthase leads to anti-inflammatory and antinociceptive effects [9, 10]. Odigie [4] *et al*. used 2 x 100 mg of indomethacin suppositories for post episiotomy pain and found them effective in their study. Searles and Pring [5] reported effective usage of 100 mg diclofenac suppositories for second degree perineal tears or episiotomy.

Our purpose in designing the study was to compare the analgesic effect of diclofenac sodium and indomethacin suppositories for right mediolateral episiotomy (MLE) that are often used for analgesia however have different action mechanisms.

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Material and Methods

Seventy patients with spontaneous vaginal deliveries and MLE were randomly (randomized number table used), one-side blinded, and prospectively divided into two groups. Group 1: (n = 35) was composed of patients medicated by diclofenac sodium suppositories (Voltaren, 100 mg diclofenac sodium, Novartis, Istanbul, Turkey), Group 2: (n = 35) was composed of patients medicated by indomethacin suppositories (Endol, 100 mg indomethacin, Deva, Istanbul, Turkey). Permission was given by the Firat University Medicine Faculty Ethical Commitee (ethical standards declared in Helsinky in 1983 were followed) for the study. All patients were informed about the study and gave written permission.

Exclusion criteria of the study were chronic renal failure, coagulopathy, non steroidal anti-inflammatory intolerance or allergy, episiotomies longer than 5 cm, forceps delivery and perineal tears. Age, length, gravida, abortus, length of the episiotomy, reoperation duration and presence of hematoma in the MLE region were recorded. Right after MLE reoperation 100 mg rectal suppositories were administered. The verbal rating scale (VRS) and visual analog scale (VAS) were used for pain score at rest, the first and 24th hour after medication. VRS scoring: No pain = 0 point, mild = 1 point, medium = 2 points, severe = 3 points, very severe = 4, intolerable = 5 points. A 100 mm ruler was used for VAS: 0 mm = no pain and 100 mm = very severe pain [11]. Control pelvic examinations were performed on postpartum day 1 and patients were released and prescribed 100 mg suppositories daily for two more days.

For statistical analysis the SPSS 9.0 computer programme (Microsoftware, Chicago, IL USA) was used. Continuous and ordinal data were established as mean ± standard deviation (SD). For comparison of independent groups, the Mann-

Whitney U test was used for ordinal data and continuous data were determined by the independent T-test. The chi-square test was used for nominal data, and repeated measurements in the groups were analyzed by the Wilcoxon-rank test; $p < 0.05$ was considered as statistically significant. Spearman corelation analysis was used for analysis between VRS and VAS (r_s, n, p).

Results

Sociodemographic characteristics of the patients were similiar (Mann-Whitney U test) in both groups. MLE length and MLE reoperation duration of the patients were also similiar (independent T test) in both groups (non significant).

Primigravidas were 60% in Group 1 (G1) and 74% in Group 2 (G2) and no statistically significant differences were obtained (X^2 test) (Table 1).

No hematoma or complications were seen in MLEs.

For G1 one-hour VRS was 2.6 ± 0.5 points and VAS was 4.9 ± 0.8 points; for G2 one-hour VRS was 3.4 ± 0.6 points and VAS was 6.6 ± 1.2 points and this difference was statistically significant ($p < 0.05$, Mann-Whitney U test).

For G1 the 24th hour VRS was 1.2 ± 0.4 points and VAS was 2.4 ± 0.9 points; for G2 VRS was 2 ± 0.7 points and VAS was 4 ± 1.3 points ($p < 0.05$, Mann-Whitney U test). The first and 24th hour pain scores (VAS1-VAS24, VRS1-VRS24) were decreased dramatically for both groups ($p < 0.05$, Wilcoxon rank test).

A positive correlation was obtained between the first and 24th hour for VRS and VAS scores by Spearman's correlation analysis ($r_s = 0.9$, n = 70, p = 0.001).

Table 1. — *Data on sociodemographic characteristics, episiotomy length and reoperation duration. Values are shown as mean ± SD, and n, % ( ).*

Parameter	G1	G2	*p*
Age (years)	25 ± 6	24 ± 4	ns
Length (cm)	158 ± 4	159 ± 3.6	ns
Gravida	1.9 ± 1.2	1.7 ± 1.3	ns
Parity	0.9 ± 1.2	0.6 ± 1.1	ns
Live birth	0.9 ± 1.1	0.5 ± 0.9	ns
Primigravida	21 (60)	26 (74)	ns
Multigravida	14 (40)	9 (26)	ns
MLE length (cm)	3.6 ± 0.6	3.7 ± 0.5	ns
MLE reoperation duration (min)	20 ± 3	19.8 ± 3.2	Ns

ns = not significant, Independent T test, Mann-Whitney U test or X^2 test.

Discussion

Diclofenac sodium suppositories had more effective analgesia than indomethacin suppositories for early- and late-term perineal pain occurring after MLE. Consequently diclofenac sodium suppositories may be proposed for post MLE pain.

We quantified our study by using both VRS and VAS scales that are generally used in analgesia studies. A positive correlation was obtained between VRS and VAS by Spearman's correlation analysis.

Odigea *et al*. [4] administered 2 x 100 mg indomethacin suppositories to 30 patients and placebo to another 30 patients and evaluated the pain at 15, 30, 60 and 90 minutes. No patients complained about pain after MLE reoperation in the study group, however in the placebo group patients felt variable pain. Our first hour findings correlated with this study. We thought that pain after MLE would poorly effect the quality of life so we did not design any placebo group.

Seckin *et al*. [12] administered 100 mg indomethacin suppositories vaginally and could not establish any analgesia pain at 15, 30, 60, and 90 minutes when compared with placebo. The administration way of drugs and maximum pain point on VRS (3 points) differed from our study and that may have altered the results. In our study the administration route was rectal and maximum points on VRS were 5. Searles and Pring [5] administered 100 mg diclofenac suppositories to 100 cases and found that average pain score markedly decreased on the first, second and third days when compared with a control group, which is compatible with our findings. Both diclofenac sodium and indomethacin are non selective non steroidal anti-inflammatory drugs. They inhibit prostaglandin synthesis and thus act as anti-inflammatory analgesics [7, 8].

Diclofenac and other nonsteroidal anti-inflammatory drugs (ketorolac, metamizole, nimesulide and meloxicam) have analgesic effects independent from prostaglandin, which is why these analgesics have different analgesic properties.

Diclofenac activates the L-arginine-NO-cGMP-potassium channel and inhibits the hydrogen channel [13-16]. Potassium channel opening leads to hyperpolarization and increased intracellular cGMP. Hyperpolarization causes desensitation and cGMP has an analgesic effect. Indomethacin does not act in this way, which may be the explanation as to why diclofenac sodium suppositories were more effective analgesics in our study.

Inhibition of hydrogen ion channels show an analgesic effect especially when topical medications (suppositories) were applied [13]. However, indomethacin does not have any effect on these channels.

These two medications have been compared especially in rheumatoid arthritis cases. Wafin *et al*. [17] reported similiar analgesic effects of 100 mg diclofenac and 100 mg indomethacin suppositories. However these were for joint pain (hand, elbow, finger and knee), not perineal. Topical diclofenac sodium has an analgesic effect on the perineum. Diclofenac sodium increases both plasma and brain β-endorphin levels [18, 19]. Increased β-endorphin decreases pain [20]. Thus analgesia effects of diclofenac sodium were marked in our cases.

In conclusion, after vaginal deliveries with right mediolateral episiotomies diclofenac sodium suppositories may be the first choice as a more effective analgesic than indomethacin suppositories.

References

[1] Hedayati H., Parsons J., Crowther C.A.: "Rectal analgesia for pain from perineal trauma following childbirth". Cochrane Database Syst. Rev., 2003, (3), CD003931.

[2] Harrison R.F., Brennan M.: "Evaluation of two local anaesthetic sprays for the relief of post-episiotomy pain". *Curr. Med. Res. Opin*., 1987, *10,* 364.

[3] Daftary S.N., Mehta A.C., Nanavati M.: "A controlled comparison of dipyrone and paracetamol in post-episiotomy pain". *Curr. Med. Res. Opin*., 1980, *6*, 614.

[4] Odigie E.A.: "Effectiveness of indomethacin (indocid) suppositories as post-episiotomy analgesia". *Int. J. Gynaecol. Obstet*., 1988, *26*, 57.

[5] Searles J.A., Pring D.W.: "Effective analgesia following perineal injury during childbirth: a placebo controlled trial of prophylactic rectal diclofenac". *Br. J. Obstet. Gynaecol*., 1998, *105,* 627.

[6] Ghosh C., Mercier F., Couaillet M., Benhamou D.: "Quality-assurance program for the improvement of morbidity during the first three postpartum days following episiotomy and perineal trauma". *Acute pain*., 2004, *6,* 1.

[7] Vane J.R., Botting R.M.: "Mechanism of action of anti-inflammatory drugs". *Scand. J. Rheumatol*., Suppl. 1996, *102,* 9.

[8] Warner T.D., Giuliano F., Vojnovic I., Bukasa A., Mitchell J.A., Vane J.R: "Nonsteroid drug selectivities for cyclo-oxygenase-1 rather than cyclo-oxygenase-2 are associated with human gastrointestinal toxicity: a full in vitro analysis". *Proc. Natl. Acad. Sci USA,* 1999, *96,* 7563. Erratum in: *Proc. Natl. Acad. Sci USA*, 1999, *96,* 9666.

[9] Tonussi C.R., Ferreira S.H.: "Mechanism of diclofenac analgesia: direct blockade of inflammatory sensitization". *Eur. J. Pharmacol*., 1994, *251*, 173.

[10] Bjorkman R.: "Central antinociceptive effects of non-steroidal anti-inflammatory drugs and paracetamol. Experimental studies in the rat". *Acta Anaesthesiol. Scand*. Suppl., 1995, *103*, 1.

[11] Aguilar J.L., Rincon R., Domingo V., Espachs P., Preciado M.J., Vidal F.: "Absence of an early pre-emptive effect after thoracic extradural bupivacaine in thoracic surgery". *Br. J. Anaesth*., 1996, *76,* 72.

[12] Seckin B., Avsar F., Parlakyigit E., Aksakal O.: "Effects of indomethacin suppository and lidocaine pomade for the relief of post-episiotomy pain". *Int. J. Gynaecol. Obstet*., 2002, *78*, 159.

[13] Voilley N., de Weille J., Mamet J., Lazdunski M.: "Nonsteroid anti-inflammatory drugs inhibit both the activity and the inflammation-induced expression of acid-sensing ion channels in nociceptors". *J. Neurosci*., 2001, *21*, 8026.

[14] Lazaro-Ibanez G.G., Torres-Lopez J.E., Granados-Soto V.: "Participation of the nitric oxide-cyclic GMP-ATP-sensitive K(+) channel pathway in the antinociceptive action of ketorolac". *Eur. J. Pharmacol*., 2001, *426*, 39.

[15] Ortiz M.I., Torres-Lopez J.E., Castaneda-Hernandez G., Rosas R., Vidal-Cantu G.C., Granados-Soto V.: "Pharmacological evidence for the activation of K(+) channels by diclofenac". *Eur. J. Pharmacol*., 2002, *438*, 85.

[16] Rodrigues A.R., Duarte I.D.: "The peripheral antinociceptive effect induced by morphine is associated with ATP-sensitive K(+) channels". *Br. J. Pharmacol*., 2000, *129*, 110.

[17] Wafin F., Valindas E., Wuolijoki E.: "Comparison of diclofenac and indomethacin suppositories in rheumatoid arthritis". *Clin. Rheumatol*., 1984, *3*, 67.

[18] Martini A., Bondiolotti G.P., Sacerdote P., Pierro L., Picotti G.B., Panerai A.E. *et al*.: "Diclofenac increases beta-endorphin plasma concentrations". *J. Int. Med. Res*., 1984, *12*, 92.

[19] Sacerdote P., Monza G., Mantegazza P., Panerai A.E.: "Diclofenac and pirprofen modify pituitary and hypothalamic beta-endorphin concentrations". *Pharmacol. Res. Commun*., 1985, *17,* 679.

[20] Stein C., Hassan A.H., Lehrberger K., Giefing J., Yassouridis A.: "Local analgesic effect of endogenous opioid peptides". *Lancet,* 1993, *342*, 321.

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