Article (Original Investigation)

Effectiveness of A Single Dose of Epidural Morphine for Postpartum Perineal Pain

A Randomized Controlled Trial

Mao Mao, MD, MSc; Zhaohui Wang, MD, MSc; Caijuan Li, MD, MSc; Nan Wang, MD, MSc; Shanwu Feng, MD, MPH; Shiqin Xu, MD, MPH; Xiaofeng Shen, MD, MPH; Xian Wang, MD, MSc

OBJECTIVE

The purpose of this study was to identify the effectiveness of a single dose of epidural morphine for postpartum perineal pain, and the incidence of side effects.

MATERIALS AND METHODS

After institutional review board approval and patient consent, a total of 200 parturients with perineal trauma undergoing epidural analgesia were randomized into three groups: C, M1, and M2, wherein sole saline 10ml, morphine 1mg dissolved in saline 10ml, or morphine 2mg dissolved in saline 10ml was epidurally given immediately after umbilical cord clamp, respectively. Within 24 hours after vaginal delivery, perineal pain at rest and movement evaluated with present pain intensity (PPI) as well as the time to the first request for additional analgesia were recorded. Besides, epidural morphine related side effects including nausea, vomiting, pruritus, and urinary retention were observed as well.

RESULTS

The proportion of women with moderate and severe pain at rest was significantly lower in groups M1 and M2 compared to group C (4.5 & 0% vs. 20.6%, respectively). Meanwhile, the proportion of women with moderate and severe pain at movement was also significantly lower in groups M1 and M2 compared to group C (10.4 & 12.3% vs. 55.9%, respectively). Further, the proportion of women who require for additional analgesics in the first 24 hours after vaginal delivery in groups M1 and M2 was lower compared with group C (9.0 & 7.7% vs. 52.9%, respectively). The average time to first request for additional analgesia after delivery was prominently longer in groups M1 and M2 compared to group C (12.79±5.49 & 15.61±4.90 h vs. 7.17±3.84 h, respectively). No significant difference was found between groups M1 and M2 with regard to morphine efficacy. However, epidural morphine 2mg remarkably increased the incidence of nausea, vomiting, and pruritus compared to sole saline ($P<0.05$), and the incidence of nausea and pruritus compared to morphine 1mg ($P<0.05$).

CONCLUSIONS

Epidural morphine 1mg could decrease the proportion of moderate-severe PPI pain, prolong the time to first request for additional analgesia, and have fewer side effects.■

KEYWORDS Perineal trauma; Perineal pain, Epidural morphine

Sci Insigt. 2017; 2017:e00067. doi:10.15354/si.17.ar062

Author Affiliations: Author affiliations are listed at the end of this article.

Correspondence to: Dr. Xian Wang, Department of Anesthesiology, Obstetrics and Gynecology Hospital Affiliated to Nanjing Medical University, Nanjing 210004, China
Email: wangxian2002@126.com

Postpartum perineal pain is highly correlated with perineal trauma, which is associated with various risk factors, such as episiotomy, perineal laceration, macrosomia, instrumental delivery, or uterine involution (1). The incidences of perineal pain in parturients after delivery were 88.2% and 24.9% in postpartum day 1 and 7, respectively (2), and postpartum perineal pain significantly interfered women's daily activities, even sitting and urinating. However, perineal pain has not been relieved effectively. The typical treatment is oral analgesics, but a multimodal analgesic regimen could decrease the need for systemic analgesics after postpartum perineal pain (3).

Morphine is a traditional opioid drug, which characteristically slow diffusion and long duration in epidural analgesia makes it widely used in postoperative pain management. A single dose of epidural morphine could continuously relieve severe pain for the first 24 hours, and thus considered to be an improvement for postpartum analgesia (4).

Nowadays, more than 90% parturients would like to choose epidural labor analgesia in our hospital. We designed this randomized, double-blinded, placebo-controlled study to evaluate the efficacy of low dose of epidural morphine on postpartum pain management and its adverse reactions after vaginal delivery.

MATERIALS AND METHODS

After approval by the Ethics Committee of Nanjing Medical University and signed in-formed consent, parturients with episiotomy or 2-degree laceration, at least 18 years old receiving epidural labor analgesia, ASA I, with a single gestation in vertex presentation at term were eligible for enrollment. Patients were excluded if they met one of the following criteria: a history of gestational diabetes mellitus, gestational hypertension, asthma, opioid allergy, or any reasons of epidural puncture tube failure. And the following data were recorded in postpartum 24 hours: maternal age, height and weight, gestational age, neonatal weight, use of dolatin at the time of labor analgesia, duration of total labor, episiotomy or 2-degree laceration, breast feeding, use of instrumental delivery, the proportion of women with moderate to severe PPI pain intensity at rest or at movement, and time to first request for additional analgesic; and the adverse outcomes.

Patients were randomized into 3 groups by a random number table in a double-blinded manner. After umbilical cord clamping and visual analogue scale (VAS) pain score assessment of labor analgesia, patients received a 10 mL volume of epidural solution consisting of saline (group C), 1mg morphine (group M1), or 2mg morphine (group M2). The epidural catheter was removed after drug administration. Respiratory rate was monitored every hour for the first 12 hours and then every 4 hours for 12 hours. Treatments, such as waking up or oxygen uptake, will be taken if respiratory rate<10 times per minute. In addition, women could request additional analgesics for breakthrough perineal pain. Ondansetron 8mg was given intravenously to treatment serious vomiting or pruritus. Urinary retention was defined by the need for catheterization, but parturient with indwelling catheters placed immediately after delivery was excluded from this analysis.

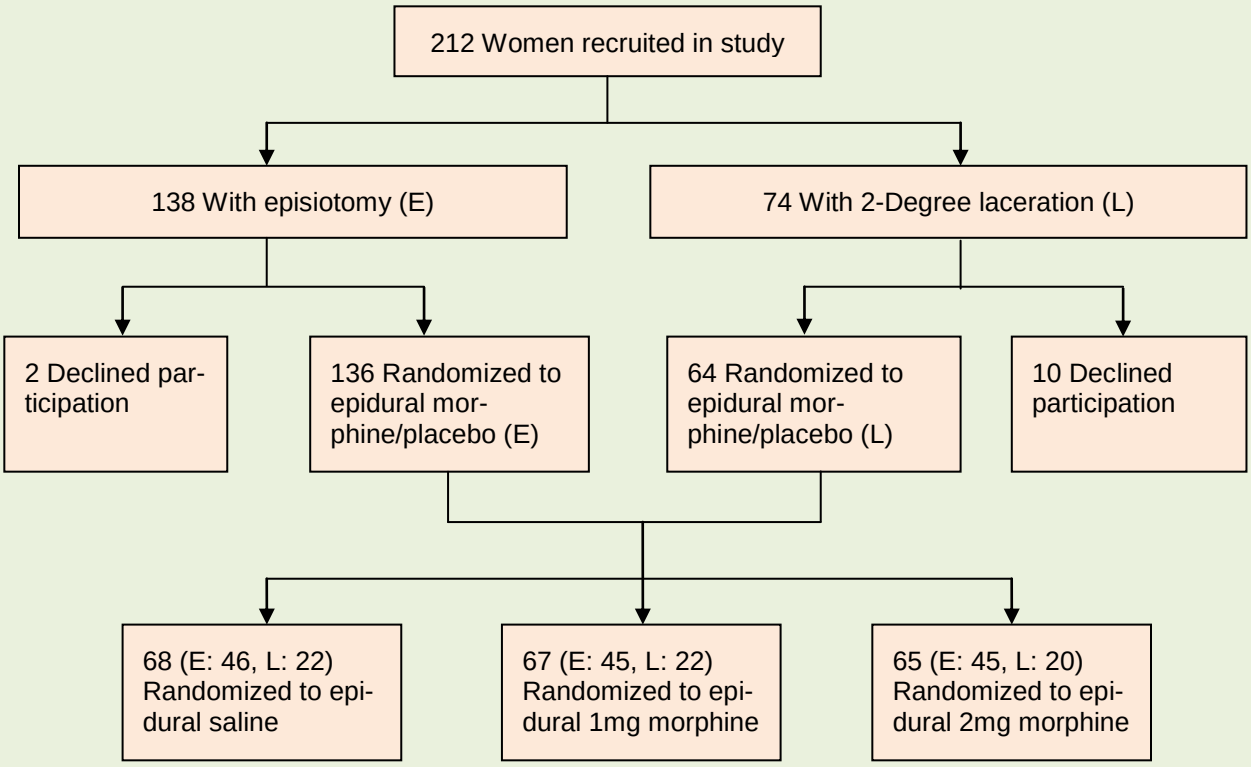
STATISTICAL ANALYSIS

Data are expressed as mean ± standard deviation or n (%). All continuous variables such as maternal age, height and weight, and time to first request for additional analgesic were evaluated using analysis of one-factor analysis of variance (ANOVA), with Bonferroni or Dunnett's T3 post hoc test for correcting multiple comparisons according to the variance homogeneity. Chi-square or Fisher's exact test for difference in proportions was used to compare the incidence of the primary and secondary outcomes, if appropriate. Significance level for the primary outcome was defined as $P<0.05$, whereas secondary outcome P values were adjusted using Bonferroni corrections for multiple testing. All analyses were done using the SPSS 18.0.

RESULTS

Two hundred and twelve women were included and data were collected between December 2015 and January 2017. Figure 1 provides the CONSORT flow diagram of this study and reasons for exclusion. About 136 women with episiotomy and 64 women with 2-degree laceration agreed to participate in the study. Some participants were excluded due to a long-term use of analgesic for dysmenorrhea. Two hundred women who delivered vaginally were randomized to

Figure 1. Consort Flow Diagram



receive epidural saline (46 with episiotomy, 22 with 2-degree laceration), 1mg morphine (45 with episiotomy, 22 with 2-degree laceration) and 2mg morphine (45 with episiotomy, 20 with 2-degree laceration). There was no difference in demographic variables among the three groups (Table 1). Women participated in the study were all Asia primiparous patients, with an average maternal age of 28 year, and body mass index (BMI) of 25-26 kg/m^2. The mean maternal VAS pain score during labor analgesia was <3, and no difference in three group (P>0.05, data not shown in details).

Table 2 has shown the analgesic efficacy and side effects. The proportion of women with moderate and severe pain at rest was significantly lower in groups M1 and M2 com-pared to group C (P<0.05). Meanwhile, the proportion of women with moderate and severe pain at movement was also significantly lower in groups M1 and M2 compared to group C (P<0.05). Besides, the proportion of women who require for additional analgesics in the first 24 hours after vaginal delivery in groups M1 and M2 was lower compared with group C (P<0.05). Compared with group C, the aver age time to first request for additional analgesics after delivery was longer in groups M1 and M2 (P<0.05). No significant difference was found between groups M1 and M2 with regard to morphine efficacy.

The incidence of side effects related to epidural morphine, except urinary retention, differed among three groups (Table 2). Epidural morphine 2mg remarkably increased the incidence of nausea, vomiting, and pruritus compared to sole saline (P<0.05), and the incidence of nausea and pruritus compared to morphine 1mg (P<0.05).

DISCUSSION

Giving epidural morphine 1 or 2 mg in women with perineal trauma can significantly decrease the proportion of women with moderate to severe PPI pain score compared with that of group C in the first 24 hours. Moreover, epidural morphine can also decrease the proportion of women requesting for additional analgesia, and prolong the time interval to first request for additional analgesia. However, 2mg morphine can increase the incidence of adverse effects, especially nausea and pruritus at the same time.

Our earlier study demonstrated that perineal pain occurred more commonly in women with primiparous, high BMI, epidural analgesia and episiotomy

Table1. Demographic Variables

Variable	Group C (N=68)	Group M1 (N=67)	Group M2 (N=65)	P Value
Perineal trauma				
Episiotomy	46 (67.6%)	45 (67.2%)	45 (69.2%)	0.97
2-Degree laceration	22 (32.4%)	22 (32.8%)	20 (30.8%)	
Maternal characteristics				
Age (year)	28.19±3.18	28.73±3.59	28.72±3.22	0.56
BMI (kg/m^2)	25.75±2.73	25.42±2.99	26.23±2.42	0.23
Labor and birth variables				
Gestational age (day)	277.62±7.06	276.60±7.96	275.14±13.94	0.37
Neonatal weight (g)	3316.76±303.79	3328.66±366.89	3378.00±349.59	0.55
Length of labor (min)	568.37±196.79	561.91±195.20	538.82±175.04	0.64
Dolatin	2 (2.9%)	3 (4.5%)	4 (6.2%)	0.67
Operative delivery	0 (0%)	2 (3.0%)	3 (4.6%)	0.17
Breast feeding	59 (86.8%)	62 (92.5%)	62 (95.4%)	0.19

Values are reported as n (%) or mean ± SD.

Table 2. Analgesic Efficacy and Side Effects

Outcome	Group C (N=68)	Group M1 (N=67)	Group M2 (N=65)
Moderate to severe PPI pain, n (%)			
At rest	14 (20.6%)	3 (4.5%)*	0 (0%)*
At movement	38 (55.9%)	7 (10.4%)*	8 (12.3%)*
Request for additional analgesia			
The proportion for additional analgesia, n (%)	36 (52.9%)	6 (9.0%)*	5 (7.7%)*
Time to first request for additional analgesia (hr)	7.17±3.84	12.79±5.49*	15.61±4.90*
Side effects, n (%)			
Nausea	1 (1.5%)	3 (4.5%)	11 (16.9%)*$^{\#}$
Vomiting	0 (0%)	8 (11.9%)*	11 (16.9%)*
Pruritus	2 (2.9%)	10 (14.9%)*	26 (40%)*$^{\#}$
Urinary retention	8 (11.8%)	16 (23.9%)	10 (15.4%)

Data presented as n (%) or mean ± SD. *P<0.05，compared with group C. $^{\#}$P<0.05, compared with group M1.

And episiotomy was proved to be an independent predictor associated with perineal pain postpartum 1 day according to the logistic regression (RR=2.05, 95%CI 0.95-4.42) (2). It had demonstrated that between postpartum day 1 and 7, multiparous women experienced 10%–30% less perineal discomfort than that of primiparous women (5-6). So, we choose the primiparous women as our objects in the study, avoiding a potentially unequal distribution of primiparous patients in each group.

The number of women undergoing vaginal delivery in our hospital is 15,000 in 2016, and the incidence of lateral episiotomy is high for 40%. About 6,000 women underwent perineal pain, and somnipathy, daily activity limitation, postpartum depression and sexual dysfunction related complication. The most effective treatment improved perineal pain is drug analgesia, especially opioid. Compared with oral or i.v. administration, the incidence of adverse effects in neuraxial administration were obviously decreased (7). Morphine has been considered as the 'gold standard' single dose neuraxial opioid owing to its postoperative analgesic efficacy and prolonged duration of action. The optimal 'single shot' in trathecal dose appears to be 0.075-0.15mg and the ideal 'single shot' epidural morphine dose is 2.5-3.75mg in USA (8-9). But the ideal dose is not a 'Chinese optimal dose', the ethnic differences in the mu-opioid receptor gene (OPRM1) break the balance between the conflicting demands of providing optimal analgesia while minimizing dose-related adverse effects (10). Asians are sensitive to opioids. Therefore, the epidural analgesia dose of morphine should be decrease and better to begin with 1-2mg for Chinese women.

The new practice guidelines for respiratory depression associated with neuraxial opioid administration reminds the dangerous behind neuraxial morphine (11). While no one occurred respiratory depression for first 24 h in all 200 women in this study, the incidence of respiratory depression with the use of epidural morphine is lower compared with those patients in post cesarean delivery analgesia in Crowgey's study (1 event per 1429 cases) and has been estimated 0% and 0.07%(12), respectively. For the above differences, the main reason maybe the sample size is small. We have detected a difference in the incidence of nausea, vomiting and pruritus, but not urinary retention. Administration of epidural morphine began with doses between 1-2mg, and the incidence of pruritus was between 14.9% and 40% and nausea/vomiting between 16.4% and 33.8%. Obviously, the proportion of moderate-severe PPI pain in 2mg morphine is similar to 1mg, but the incidence of side effects is higher. So, 'the Chinese optimal dose' is tending to 1mg morphine.

In conclusion, epidural morphine is an effective method for perineal pain management in women with perineal trauma (included episiotomy and 2-degree laceration). A single dose of epidural morphine 1mg could decrease the proportion of moderate-severe PPI pain, prolonged the time to first request for additional analgesia, and with fewer side effects.

ACKNOWLEDGEMENTS

We thank doctors Zhaohui Wang and Caijuan Li for their patient work in data collection and language correction.■

ARTICLE INFORMATION

Author Affiliations: Department of Anesthesiology, Obstetrics and Gynecology Hospital Affiliated to Nanjing Medical University, Nanjing, 210004, China.

Author Contributions: All authors have full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: All authors.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: All authors.
Critical revision of the manuscript for important intellectual content: All authors.
Statistical analysis: N/A.
Obtained funding: N/A.
Administrative, technical, or material support: All authors.
Study supervision: Wang X.

Conflict of Interest Disclosures: All authors declared no competing interests of this manuscript submitted for publication.

Role of the Funder/Sponsor: Nanjing medical university of science and technology development fund projects, No.2014NJMU091.

Jiangsu provincial science and technology department of clinical medicine fund projects, No. BL2014016

How to Cite This Paper: Mao M, Wang Z, Li C, Wang N, Feng S, Xu, S, Shen X, Wang X. Effectiveness of a single dose of epidural morphine for postpartum perineal pain: A randomized controlled trial. Sci Insigt 2017; 2017:e00067.

Digital Object Identifier (DOI):
http://dx.doi.org/10.15354/si.17.ar062.

Article Submission Information: Received, April 17, 2017; Revised: May 13, 2017; Accepted: May 16, 2017.

REFERENCES

1. Temtanakitpaisan T, Bunyacejchevin S, Koyama M. Obstetrics anal sphincter injury and repair technique: a review. J Obstet Gynaecol Res 2015; 41:329-333.
2. Wang X, Shen J, Feng SW. Xue X, Xu SQ. A prospective study of perineal pain after vaginal delivery. Chin J Pain Med 2014; 20: 490-493.
3. Wong CA. Advances in labor analgesia. Int J Women Health 2009; 1:139-154.
4. Wang X, Xu S, Feng S. Postpartum perineal pain in the absence of obstetric anal sphincter injuries: A prospective observational study. Sci Insigt 2013; 4:69-74.
5. Macarthur A, Macarthur C. Incidence, severity and determinants of postpartum perineal pain: a prospective cohort study. Am J Obstet Gynecol 2004; 191:1199-1204.
6. Leeman L, Rogers R, Borders N, Teaf D, Qualls C. The Effect of Perineal Lacerations on Pelvic Floor Function and Anatomy at 6 Months Postpartum in a Prospective Cohort of Nulliparous Women. Birth 2016; 43:293-302.
7. Dichtwald S, Ben HM, Papismedov L, Hazan S, Cattan A, Matot L. Intrathecal morphine versus intravenous opioid administration to impact postoperative analgesia in hepato-pancreatic surgery: a randomized controlled trial. J Anesth 2017; 31:237-245.
8. Sultan P, Gutierrez MC, Carvalho B. Neuraxial morphine and respiratory depression: finding the right balance. Drugs 2011; 71:1807-1819.
9. Capdevila X, Moulard S, Plasse C, Peshaud JL, Molinari N, Dadure C, Bringuier S. Effectiveness of Epidural Analgesia, Continuous Surgical Site Analgesia, and Patient-Controlled Analgesic Morphine for Postoperative Pain Management and Hyperalgesia, Rehabilitation, and Health-Related Quality of Life After Open Nephrectomy: A Prospective, Randomized, Controlled Study. Anesth Analg 2017; 124: 336-345.
10. Tan EC, Lim Y, Teo YY, Goh R, Law HY, Sia AT. Ethnic differences in pain perception and patient-controlled analgesia usage for postoperative pain. J Pain 2008; 9:849-855.
11. Apfelbaum JL, Horlocker TT, Agarkar M, Connis RT, Hebl JR, Nickinovich DG, Palmer CM, Rathmell JP, Rosenquist RW, Wu CL. Practice Guidelines for the Prevention, Detection, and Management of Respiratory Depression Associated with Neuraxial Opioid Administration: An Updated Report by the American Society of Anesthesiologists Task Force on Neuraxial Opioids and the American Society of Regional Anesthesia and Pain Medicine. Anesthesiology 2016; 124:535-552.
12. Crowgey TR, Dominguez JE, Peterson LC, Allen TK, Muir HA, Habib AS. A retrospective assessment of the incidence of respiratory depression after neuraxial morphine admin-istration for postcesarean delivery analgesia. Anesth Analg 2013; 117:1368-1370.