ABSTRACT

Objective: In this study, we sought to assess the pattern of analgesic usage, adequacy of pain management, side effects, and analgesic drug interactions in the post-emergency cesarean surgery setting.

Methods: This was a prospective observational study of 80 patients who underwent emergency cesarean surgery at the Obstetrics and Gynecology Department of the Rumah Sakit Umum Pusat Nasional Cipto Mangunkusumo (RSUPN-CM) between July 2015 and January 2016. Adequacy of pain management during the first 3 post-operative days was assessed using Pain Management Index. Relation between pain intensity during activities and rest with patient characteristic was assessed using Chi-squared test and Fisher’s exact test.

Results: Nineteen patients (8.7%) were prescribed two types of nonsteroid anti-inflammatory drugs concomitantly, and 41.8% received inappropriate analgesics at a lower frequency. Most patients experienced pain with numerical rating scale score >3 in the first 24 h post-surgery: 59 patients (73.75%) experienced pain during activities and 7 patients (8.75%) during rest.

Conclusion: Post-emergency cesarean surgery pain management at RSUPN-CM was not optimal. Most patients did not receive adequate pain management in the first 24 h post-surgery.

Keywords: Pain management, Emergency cesarean surgery, Numerical rating scale.
RESULTS
A total of 92 patients underwent cesarean surgery at the RSUPN-CM during the study reference period. Of these, 80 patients were included in this study. One patient was discharged; therefore, the total number of subjects on day 2 was 79. Total patients analyzed on day 3 were 60. All patients in this study underwent cesarean surgery under spinal anesthesia with bupivacaine 0.5% (12.5 mg) plus fentanyl (25 mcg). A majority of patients in this study (71.25%) were unemployed, 88.75% were covered by National Health Insurance, and 82.5% of patients had not undergone prior cesarean surgery (Table 1).

Total number of analgesics and accuracy of usage based on dosage
About 87.5% of patients received one type of analgesic during the first 24 h during 3 days of treatment, 19 patients (8.7%) were administered two analgesics (nonsteroidal anti-inflammatory drug [NSAID]+NSAID) simultaneously, whereas 2 patients (0.9%) were administered NSAID+low-dose opioid (tramadol) (Table 2). During 3 days of treatment, the analgesic dosage prescribed was generally correct. Subtherapeutic dosage was prescribed in patients who received two analgesics, i.e., tramadol for 2 days of treatment.

Analgesic prescription frequency
The most frequently prescribed analgesic frequency on the 1st day of treatment was thrice a day (60%), whereas 6 patients (7.5%) were given analgesic just once a day (Table 2). In the first 24 h, 12 patients were administered more than one type of analgesic, whereas one patient was not administered any analgesic. Of 67 patients who were administered only one type of analgesic during the first 24 h, 41.8% received inappropriate analgesic and at a lower frequency than that recommended by the guidelines.

Mode of administration
The most commonly used mode of analgesic administration on day 1 and day 2 was as rectal suppository (91.25% and 32.91%, respectively). The percentage of patients who were administered oral analgesics increased from day 1 (1.25%) to day 3 (43.33%). A similar pattern was observed with respect to percentage of patients who did not receive analgesic (1.25% on day 1 and 46.67% on day 3) (Table 2).

Pain intensity
The intensity of pain experienced during activities showed a decreasing trend; 66.25% of patients felt moderate pain on day 1 as against 5% on day 3. On day 1, 7.375% of patients experienced pain with NRS score >3. The same pattern was observed with respect to pain intensity during rest; 8.75% of patients felt moderate pain on day 1 as against 0% on day 3. On day 1, 8.75% of patients experienced pain with NRS score >3 (Fig. 1). (Table 3) shows that peripertive analgesics used, paracetamol alone or in combination with tramadol, have significant influence on pain intensity during activity (p: 0.016), but not during relax.

Adequacy of pain management
The adequacy of pain management was assessed using PMI. A total of 59 (73.75%) patients were inadequately treated (PMI score was minus). NRS scores during activities on day 1 were included in the calculation of PMI.

Side effects of analgesics and their interactions
Ten of the 80 patients experienced side effects such as nausea and dizziness. On the basis of the Naranjo Adverse Drug Reaction Probability Scale, these symptoms were likely caused by NSAIDs. Only one patient experienced nausea, which was likely attributable to ketoprofen.

Potential analgesic interactions were observed on day 3. Of the 32 analgesics used on day 3, potential drug interactions of two drugs (ketoprofen and sodium diclofenac) with bisoprolol were observed.

Relation between pain intensity control and patient characteristics
There was no significant association of pain intensity control during activities or rest in the first 24 h treatment with a history of the previous cesarean surgery, duration of surgery, age of patients, educational level, or ethnicity (Table 1).

Table 1: Characteristics of the study population

| Characteristic | Total | % |
|----------------|-------|---|
| Occupation     |       |   |
| Unemployed     | 57    | 71.25 |
| Employed       | 23    | 28.75 |
| Fee system     |       |   |
| National health insurance | 71 | 88.75 |
| Private        | 9     | 11.25 |
| Pregnancy status|   | |
| Primigravida   | 27    | 33.75 |
| Multigravida   | 53    | 66.25 |
| Age (years)    |       |   |
| <30            | 41    | 51.25 |
| ≥30            | 39    | 48.75 |
| Educational level|   | |
| ≤Middle school | 25    | 31.25 |
| ≥High school   | 55    | 68.75 |
| History of previous surgery | | |
| Yes            | 14    | 17.5 |
| No             | 66    | 82.5 |
| Duration of surgery | | |
| ≤60 min        | 54    | 67.5 |
| >60 min        | 26    | 32.5 |
| Ethnicity      |       |   |
| Javanese       | 38    | 47.5 |
| Batavinese     | 29    | 36.25 |
| Others*        | 13    | 16.25 |
| Indication for emergency cesarean surgery | |
| Premature rupture of membranes | 36 | 45 |
| Severe preeclampsia-eclampsia | 17 | 21.25 |
| Others*        | 27    | 33.75 |
| Perioperative analgesics | | |
| Paracetamol 1 g IV | 35 | 43.75 |
| Paracetamol 1 g IV+Tramadol 100 mg IV | 35 | 43.75 |
| Paracetamol 1 g IV+Tramadol 50 mg IV | 1 | 1.25 |
| Paracetamol 1 g IV+Dextrometorfan 50 mg IV | 4 | 1.25 |
| Paracetamol 1 g IV+Ketorolac 30 mg IV | 4 | 5 |
| Ketorolac 30 mg IV | 1 | 1.25 |
| Tramadol 100 mg IV | 3 | 3.75 |
| Total          | 80    | 100 |

*Sumateranese, Ambonnese, and Kupangnese, *Antepartum bleeding, fetal distress, intrauterine growth restriction, Kala I opening, atonia uteri, intrauterine infection, cephalopelvic disproportion, HIV, transverse lie fetus

Table 2: Characteristics of analgesic prescription

| Parameters | Day-1 | Day-2 | Day-3 |
|------------|-------|-------|-------|
| Type of analgesics | | | |
| One type of analgesic | 70 (87.5) | 51 (64.56) | 30 (50) |
| Combination of analgesics | | | |
| NSAID+NSAID | 9 (11.25) | 8 (10.13) | 2 (3.33) |
| NSAID+low-dose opioid | - | 2 (2.53) | - |
| No use of analgesic | 1 (1.25) | 18 (22.78) | 28 (46.67) |
| Frequency | | | |
| Once a day | 6 (7.5) | 30 (37.98) | 17 (28.33) |
| Twice a day | 24 (30) | 16 (20.25) | 9 (15) |
| Three a day | 48 (60) | 14 (17.72) | 5 (8.33) |
| Four times a day | 1 (1.25) | 1 (1.27) | 1 (1.67) |
| No use of analgesic | 1 (1.25) | 19 (22.78) | 26 (46.67) |
| Mode of administration | | | |
| Rectal suppository | 65 (81.25) | 26 (32.91) | 3 (5) |
| Rectal suppository+oral | 11 (13.75) | 15 (18.99) | 3 (5) |
| Suppository+IV | 2 (2.5) | 0 (0) | 0 (0) |
| Oral | 1 (1.25) | 20 (25.32) | 26 (43.33) |
| No use of analgesic | 1 (1.25) | 18 (22.78) | 28 (46.67) |
| Total | 80 (100) | 79 (100) | 60 (100) |

NSAID: Nonsteroidal anti-inflammatory drug, IV: Intravenous
Table 3: Relationship between pain intensity control and patient characteristics

| Parameters                      | Pain intensity during activities | p-value | Pain intensity during relax | p-value |
|---------------------------------|----------------------------------|---------|-----------------------------|---------|
|                                 | Uncontrolled (NRS >3)            |         | Controlled (NRS ≤3)         |         |
| History of cesarean surgery     | 50                               | 0.504*  | 6                           | 1.000*  |
| Yes                             | 9                                |         | 1                           |         |
| No                              | 16                               |         | 6                           |         |
| Duration of surgery             | 20                               | 0.654*  | 3                           | 0.676*  |
| >60 min                         | 20                               |         | 4                           |         |
| ≤60 min                         | 39                               |         | 5                           |         |
| Age                             | 29                               | 0.904*  | 3                           | 1.000*  |
| ≥30 years                       | 29                               |         | 4                           |         |
| <30 years                       | 30                               |         | 11                          |         |
| Educational level               | 16                               | 0.181*  | 0                           | 0.092*  |
| ≤ SLTP                          | 16                               |         | 7                           |         |
| ≥ SLTA                          | 43                               |         | 48                          |         |
| Perioperative analgesics         | 21                               | 0.016*  | 2                           | 0.673*  |
| PCT 1 gr IV                     | 21                               |         | 4                           |         |
| PCT 1 gr+Tramadol 100 mg IV     | 30                               |         | 3                           |         |
| Frequency of analgesics prescription | 19                         | 0.560*  | 3                           |         |
| Inappropriate                   | 19                               |         | 7                           |         |
| Appropriate                     | 29                               |         | 10                          |         |

*Chi-squared, #Fisher’s exact test; p<0.05; PCT: Paracetamol

Fig. 1: Pain intensity during activities and relaxation

and adequacy of analgesic prescription frequency. The proportion of patients with controlled pain among those who received perioperative paracetamol 1 g IV was higher than that among patients who received perioperative paracetamol 1 g+tramadol 100 mg IV (p=0.016).

DISCUSSION

In this study, most patients were prescribed NSAIDs (99.01%), whereas two patients received tramadol as the second analgesic. Similar results were reported from an online survey by Tagaloa et al. conducted through the members of Society of Obstetric Anesthesia and Perinatology; the results showed that 81% of patients were administered NSAIDs for pain management post-cesarean surgery [3]. Similarly, in a descriptive study by Tennant et al. in Jamaica, 80.3% of patients were administered NSAIDs after surgery [4].

In this study, 19 patients (8.7%) were prescribed two types of NSAIDs simultaneously with a similar frequency of administration. This result is lower than that reported from a prescription pattern survey in Pakistan (2014) in which 60% of patients were prescribed a combination of two types of NSAIDs [5]. Due to similar mechanism of action and other pharmacodynamic considerations, the NSAID+NSAID combination is not recommended according to the WHO conceptual framework of analgesic ladder for post-operative pain management [6]. Besides, concomitant use of more than one type of NSAIDs increases the risk of toxicity and peptic ulcer [7]. A pharmacovigilance study in France (2004) showed that the use of two types of NSAIDs increases the risk of gastrointestinal bleeding, disorder of liver function, and acute kidney disease [8].

In this study, 28 (41.8%) patients received less than the recommended frequency of analgesics on day 1. Guidelines from the American Pain Society recommend analgesic prescription based on schedule in the early period after surgery, especially during the first 24 h, to prevent and control pain [9]. In addition, guidelines from the American Society of Anesthesiologists (2004) also recommend the use of NSAIDs, COX-2 inhibitors, or acetaminophen based on schedule in all patients in the absence of any contraindications [10]. On the basis of these guidelines, the prescription frequency was inadequate in 41.8% of patients and 73.75% of patients felt severe pain during the 24 h after surgery; therefore, the pain management was not optimal.

On day 1 and day 2, most patients (81.25% and 32.91%, respectively) were administered analgesic through rectal suppository, and on day 3, 3 patients (5%) were administered analgesic through suppository. Oral route was shown to be better than the parenteral route for administration of NSAIDs for post-operative pain management [11]. Oral prescription is easier to administer, safe, and cheap [12]. Intramuscular and rectal administration is associated with local side effects, and parenteral administration is associated with a high risk of bleeding. Most doctors still prescribe NSAIDs through parenteral route even if the patients can consume through oral route; this is largely attributable to pharmacokinetic considerations because parenteral administration is associated with faster onset of action [13]. If paracetamol with or without NSAID, is not adequate in relieving pain, administration of short-term tramadol could be considered. However, this drug should be avoided in patient with high risk of convolution, such as severe pre eclampsia, since tramadol decreases convulsion threshold and might elicte seizure [14].

This study showed that most patients during treatment experienced pain during activities (NRS score >3). On day 1, 59 patients (73.75%) still experienced pain with NRS score >3, which decreased to 17 (21.52%) patients and 3 (5%) patients on day 2 and day 3. These findings differ from those reported by Ismail et al.; in their study, 39.9% of patients experienced moderate-severe pain during activities. This difference may be attributable to the fact that in their study, 94% of patients were prescribed opioids through parenteral infusion (pethidine/tramadol/morphone) and 74.8% of patients received additional sodium diclofenac rectal suppository (100 mg) twice a day [15].

On the basis of pain targets of the Joint Commission on Accreditation, pain score should not be >3 during rest or activities. The Royal College...
of Anaesthetists recommends that >90% of females should have post-operative visual analog scale score of 0–3 [16]. Therefore, the management of pain after emergency cesarean surgery in our study population was not optimal as 73.75% of patients still felt pain during activities (NRS score >3) and 7 patients (8.75%) still felt pain during rest (NRS score >3).

On the basis of the PMI method, 59 (73.75%) patients did not receive adequate pain management. Similar results were reported by Shen et al. from China; in their study, 60.2% of post-surgery patients were treated inadequately, as assessed by PMI [17]. In a survey conducted in a hospital in Ethiopia, 80.1% of post-surgery patients received inadequate treatment to manage post-surgery pain [2]. Inadequacy of pain management based on PMI depends on prescription or the use of opioids because it could lead to negative PMI scores.

The number of patients with controlled pain intensity among those who received perioperative paracetamol 1 g IV was higher than that among those who received paracetamol 1 g+tramadol 100 mg IV (14 vs. 5); Fischer's exact test showed a significant difference (p=0.016). This result is surprising because the latter regimen should be more effective in pain control. The discrepancy may be attributable to the variability in the use of analgesics in the operating room and the relative small sample size (70 patients). Further studies are required to compare the pain intensity control post-surgery with paracetamol 1 g IV and paracetamol 1 g+tramadol 100 mg IV.

Two potential drug interactions (ketoprofen and sodium diclofenac with bisoprolol [beta-blocker]) were observed in this study. Concomitant use of NSAIDs and bisoprolol may decrease the antihypertensive efficacy of bisoprolol. The use of NSAIDs may lead to increase in blood pressure and lower the antihypertensive efficacy of drugs such as diuretics, ACE inhibitors, ARB, and beta-blocker by 50% [18,19]. NSAIDs inhibit prostaglandin synthesis, which act as vasodilators, both in systemic circulation and in kidneys; therefore, NSAIDs may lead to water and sodium retention and decrease the activity of renin. All these factors play a role in increasing blood pressure [20].

This study had several limitations such as variation in the use of analgesics, assessment of pain intensity 24 h after surgery, and the small sample size (70 patients). All these factors may have introduced an element of bias. Furthermore, the relation between pain intensity management with paracetamol 1 g IV prescription compared with paracetamol 1 g+tramadol 100 mg IV should be assessed in a future study.

CONCLUSION

Post-emergency cesarean surgery pain management was not optimal. Most patients (73.75%) did not receive adequate pain management at 24 h after surgery.

CONFLICTS OF INTEREST

All authors declare that they have no conflicts of interest.

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