

Original article:

Effect of Combined Paracetamol and Dexamethasone on Pain and Postoperative Nausea Vomiting

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Abstract:

Background : Pain and Postoperative Nausea and Vomiting (PONV) are surgical side effects. Pain management can use opioids and non-opioids. Opioids have side effects such as nausea, vomiting, pruritus, somnolence, and respiratory depression, so other alternatives are needed to reduce pain. Paracetamol is an analgesic while dexamethasone is anti-inflammatory and anti-emetic. This study was to determine whether the combination of paracetamol and dexamethasone was more effective in dealing with pain and PONV after cesarean section than paracetamol. **Materials and Methods :** This was an experimental study employing post-test only control group design, using two study groups. Group PD (combined paracetamol and dexamethasone) was treated using dexamethasone 8 mg and paracetamol 1 gram intravenously, while the group P (paracetamol) was treated using paracetamol 1 gram intravenously. Data of Pain and PONV were collected using the Wong Baker Faces Scale, Numeric Rating Scale, and a frequency table for PONV at the 4th, 6th, 12th, and 24th hours of postoperative administration. The data were analyzed using Mann Whitney test. **Results :** The results of this study found that the multimodal administration of combined paracetamol and dexamethasone was better in reducing the pain compared to administration of a paracetamol at 4th, 6th, 12th, and 24th hours of post cesarean section (p <0.05). Multimodal administration of combined paracetamol and dexamethasone was better reduced the incidence of PONV compared to that of paracetamol at the 4th hour of post cesarean section (p <0.05). The multimodal use of combined paracetamol and dexamethasone had resulted fewer use of opioid and anti-emetic frequencies compared to that of paracetamol. **Conclusion :** The combined paracetamol and dexamethasone was more effective to reduce pain and PONV in samples with post cesarean section.

Keywords: pain, PONV, paracetamol, dexamethasone

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Background

Cesarean section is the removal of a baby with an incision in the abdominal wall¹. The postoperative effects include pain caused by tissue or organ lesions, stretching, and nerve compression that can cause neuropathic pain². Acute inflammation due to tissue damage has an important role in the development of postoperative pain, nausea, and vomiting³. Pain management after surgery has its own difficulties despite the acute pain that can be predicted to occur after surgery⁴. Opioids and non-opioids can be used for pain management. The use of opioids has side effects such as nausea, vomiting,

pruritus, somnolence, and respiratory depression⁵. The American Society of Anesthesiologists (ASA) combines non-opioids in the form of paracetamol, with or without adjuvant analgesics in the form of dexamethasone as first-line pain management⁶. Moderate to severe acute pain can occur after surgery with an incidence of 30-80%⁴. The percentage of acute pain after cesarean section is around 85%, whereas in vaginal delivery only 57%⁷. Acute pain, if not treated properly, can increase catabolism, heart rate, and blood pressure, thus causing immunosuppression. Inadequate treatment of acute pain can also prolong healing

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time which has an impact on the increase in the cost of hospital care⁸. The breastfeeding and interaction processes between the mother and her baby can be disrupted if acute pain after cesarean section is not handled properly². Poor management of acute pain can cause nerve damage, which is a risk factor for chronic pain. Postoperative nausea and vomiting can occur in 30% of patients with the highest incidence of the first 6 hours⁹. If postoperative nausea and vomiting still continue to occur, they can lead to dehydration, electrolyte imbalance, tension in the sutures, and aspiration pneumonia¹⁰. Prevention of postoperative pain needs to be done well, so that acute pain does not change into chronic pain. The provision of multimodal analgesics before the surgical procedure is necessary to deal with the pain and reduce the use of opioids¹¹.

The administration of multimodal analgesics can be a combination of paracetamol and dexamethasone. Paracetamol is an analgesic or anti-pyretic which can inhibit the activity of the cyclooxygenase enzyme, which leads to inhibition of the prostaglandin production, equivalent to the NSAID (Non-Steroid Anti-Inflammatory Drug). The study conducted by Kartapraja (2016)¹² reported that paracetamol is less effective at reducing pain and requires the initiation of analgesics more quickly than parecoxib. Another trial shows that multimodal analgesic administration between dexamethasone in combination with morphine and paracetamol can reduce pain and opioid use significantly compared to the combination of morphine and paracetamol, but it does not eliminate the inflammatory process¹³. Another analgesic commonly administered is dexamethasone, which is a glucocorticoid class of drugs that has anti-inflammatory and anti-emetic effects that can be used as a prevention of postoperative nausea and vomiting. Glucocorticoids can reduce edema and postoperative pain⁸. The study of Mohtadiet al. (2014)³ suggested that the use of single-dose dexamethasone can significantly reduce post-laparoscopic cholecystectomy pain significantly compared to placebo. The study of Cardoso (2013)¹⁴ proved that dexamethasone is also useful to prevent PONV after cesarean surgery.

A comparison between dexamethasone and paracetamol has not been done. This study aims to prove whether the combination of paracetamol and dexamethasone is better than a single dose of paracetamol in reducing pain and PONV (Post-Operative Nausea and Vomiting) after cesarean section.

Material and Method

The study belongs to the experimental research with the post-test only control group design. The population in this study included patients who were going to deliver a baby by cesarean section in 2019 at Sultan Agung Islamic Hospital Semarang. The patients who underwent cesarean section were given an explanation of the study to be conducted before being given the informed consents. The patients who agreed with the informed consents were then identified for the inclusion and exclusion criteria.

The sample size in this study was 20 people. There were two groups in this study, namely the paracetamol-dexamethasone combination group (PD) given 8-mg intravenous dexamethasone 30 minutes before induction and 1-gram intravenous paracetamol immediately after induction, and the single paracetamol group (P) given paracetamol 1 gram immediately after induction. Measurements of pain and PONV were performed at the 4th, 6th, 12th, and 24th hours using the Wong Baker Faces Scale, Numeric Rating Scale, and a frequency table for nausea and vomiting.

The data obtained were processed using the SPSS for Windows program. Shapiro Wilk's and Levene's tests were used for the normality and homogeneity tests. The data were not normally distributed and not homogeneous. Then, the Mann Whitney test was performed with the result of $p < 0.05$, implying that there were significant differences between the two treatment groups.

Results

The comparative test of pain and PONV scores between the two treatment groups was carried out with the Mann Whitney test.

Table 1. Mann Whitney Test Result of Pain Data

		Mean	Std. Deviation	P
PAIN 4	P	6.40	0.51	0,014*
	PD	5.60	0.69	
PAIN 6	P	5.50	0.52	0,042*
	PD	4.80	0.78	
PAIN 12	P	4.10	0.99	0,038*
	PD	3.10	0.99	
PAIN 24	P	3.10	0.56	0,014*
	PD	2.40	0.51	

*significantly different based on Mann Whitney test

Table 1 depicts the results of the Mann Whitney test of pain scores between the single paracetamol group and the paracetamol-dexamethasone combination group at the 4th, 6th, 12th, and 24th hours of postoperative cesarean section which show significantly different results ($p < 0.05$).

Table 2. Mann Whitney Test Result of PONV Data

		Mean	Std. Deviation	p.
PONV 4	P	0.90	0.31	0,008*
	PD	0.30	0.48	
PONV 16	P	0.00	0.00	1,000
	PD	0.00	0.00	
PONV 12	P	0.00	0.00	1,000
	PD	0.00	0.00	
PONV 24	P	0.00	0.00	1,000
	PD	0.00	0.00	

*significantly different based on Mann Whitney Test

Table 2 depicts the results of the Mann Whitney test of PONV scores between the single paracetamol group and the paracetamol-dexamethasone combination group at the 4th hour of postoperative cesarean section which show significantly different results ($p < 0.05$).

Table 3. Frequency of Opioid Administration for the Single Paracetamol Group and the Paracetamol-Dexamethasone Combination Group

		GROUP		Total
		P	PD	
Administration of Opioid 4	Yes	10 (66.7%)	5 (33.3%)	15 (100.0%)
	No	0 (0.0%)	5 (100.0%)	5 (100.0%)
Administration of Opioid 6	Yes	5 (71.4%)	2 (28.6%)	7 (100.0%)
	No	5 (38.5%)	8 (61.5%)	13 (100.0%)
Administration of Opioid 12	Yes	0 (0%)	0 (0%)	0 (0%)
	No	10 (50.0%)	10 (50.0%)	20 (100%)
Administration of Opioid 24	Yes	0 (0%)	0 (0%)	0 (0%)
	No	10 (50.0%)	10 (50.0%)	20 (100%)

Table 3 describes the frequency of administration of opioids at the 4th hour of postoperative cesarean section to 15 patients, consisting of 10 patients in the single paracetamol group (66.7%) and 5 patients in the paracetamol-dexamethasone combination group (33.3%). The administration of opioids at the 6th hour of postoperative cesarean section was performed on 7 patients, consisting of 5 patients in the single paracetamol group (71.4%) and 2 patients in the paracetamol-dexamethasone combination group (28.6%). Opioids were not administered at the 12th and 24th hours of postoperative cesarean section.

Table 4. Frequency of Anti-Emetic Administration for the Single Paracetamol Group and the Paracetamol-Dexamethasone Combination Group

		GROUP		Total
		P	PD	
Administration of Anti-Emetic 4	Yes	9 (75.0%)	3 (25.0%)	12 (100.0%)
	No	1 (12.5%)	7 (87.5%)	8 (100.0%)
Administration of Anti-Emetic 6	Yes	0 (0%)	0 (0%)	0 (0%)
	No	10 (50.0%)	10 (50.0%)	20 (100%)
Administration of Anti-Emetic 12	Yes	0 (0%)	0 (0%)	0 (0%)
	No	10 (50.0%)	10 (50.0%)	20 (100%)
Administration of Anti-Emetic 24	Yes	0 (0%)	0 (0%)	0 (0%)
	No	10 (50.0%)	10 (50.0%)	20 (100%)

Table 4 describes the frequency of administration of anti-emetics at the 4th hour to 12 patients, consisting of 9 patients in the single paracetamol group (75.0%) and 3 patients in the paracetamol-dexamethasone combination group (25.0%). Anti-emetics were not administered at the 12th and 24th hours.

Discussion

This result is relevant to that of Kamath and Lasrado's study in India in 2014, which shows that the use of intravenous paracetamol is more effective than intravenous butorphanol in managing pain in obstetric and gynecological operations¹⁵. The study conducted by Choy and Isquandar (2014) shows that giving multimodal analgesic paracetamol can reduce pain significantly compared to placebo¹⁶. Paracetamol is a p-aminophenol derivative, which has an analgesic effect by inhibiting the cyclooxygenase enzyme (COX) weakly in the peripheral, and therefore inhibits prostaglandin synthesis that can reduce pain¹².

This result is also relevant to the study conducted by Mohtadiet *al.* (2014) about the use of a single dexamethasone that can reduce pain significantly after laparoscopic cholecystectomy than the use of placebo³. The study of Badawy and Sakka in 2015 suggests that dexamethasone given as multimodal can reduce pain and PONV after abdominal hysterectomy significantly compared to placebo⁸. The study of Cardoso *et al.* (2013) shows that the use of dexamethasone is also useful for preventing PONV after cesarean section¹⁴. Dexamethasone is a glucocorticoid class of drugs, which inhibits the enzyme phospholipase A2 so that it inhibits the release of arachidonic acid to produce the cyclooxygenase enzyme (COX), which results in the formation of prostaglandins as a mediator of pain not occurring. Dexamethasone is also an anti-inflammatory that reduces inflammation due to afferent nerve stimuli to the vomiting center¹⁷. Multimodal analgesics are a combination of several drugs given before the surgical procedure that are needed to deal with the pain and reduce the use of opioids¹¹. Badawy and Sakka (2015) state that acute pain must be treated adequately so as not to prolong healing time that will not lead to the increase in the hospital-treatment cost⁸. Postoperative pain is an effect caused by tissue or organ lesions, stretching, and nerve compression². Acute inflammation due to tissue damage has an important role in the development of postoperative pain, nausea, and vomiting³.

The limitations in this study include differences

in pain and PONV thresholds in each individual because it is subjective, the analysis of side effects after the drug administration that has not done yet, and additional analgesics and anti-emetic that cannot be controlled.

Conclusion

The administration of combined paracetamol and dexamethasone could manage pain and PONV after cesarean section better than that of a single paracetamol. The frequency of opioid use after cesarean section is higher in the single paracetamol than in the paracetamol-dexamethasone combination. The frequency of anti-emetic use after a cesarean section is higher in the single paracetamol than in the paracetamol-dexamethasone combination.

Conflict of Interest:

The authors declare that they have no competing interests. The authors alone are responsible for the writing and content of this paper.

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Author Contribution:

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Ethical clearance

The ethical clearance of this study was issued by Bioethical Commission of Medical and Health Allied Research, Faculty of Medicine Universitas Islam Sultan Agung Semarang

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Reference:

1. Sumelung, V., Kundre, R. & Karundeng, M. *Faktor-Faktor yang Berperan Meningkatkan Angka Kejadian Sectio Caesarea di Rumah Sakit Umum Daerah Liun Kendage Tahuna*. Factors Contributing to the Increased Incidence of Caesarean Sectio in the General Hospital of Kendun Tahuna Regional Hospital *Ejournal keperawatan* **2**, 1-7 (2014).
2. Borges, N.D.C., Pereira, L.V., Moura, L.A., De Silva, T.C. & Pedroso, C.F. Predictors for Moderate to Severe Acute Postoperative Pain after Cesarean Section. *Pain Research and Management*, 1-6 (2016).
3. Mohtadi, A., *et al.* The Effect of Single-Dose Administration of Dexamethasone on Postoperative Pain in Patients Undergoing Laparoscopic Cholecystectomy. *Anesthesiol. Pain Med.* **4**, 1-4 (2014).
4. Pöpping, D., *et al.* Effectiveness and safety of postoperative pain management: a survey of 18 925 consecutive patients between 1998 and 2006 (2nd revision): a database analysis of prospectively raised data †. *British Journal of Anaesthesia* **101**, 832–840 (2008).
5. Grimsby, G., *et al.* A Double-Blind Randomized Controlled Trial of Continuous Intravenous Ketorolac vs Placebo for Adjuvant Pain Control After Renal Surgery. *Mayo Clin. Proc* **87**, 1089–1097 (2012).
6. Boesoirie, M.A., Oktaliansah, E. & Bisri, T. *Perbandingan Parasetamol dengan Ketorolak Intravena Sebagai Analgesia Pre-emptif terhadap Skala Nyeri Pascabedah Labioplasti pada Pasien Pediatrik*. Comparing of Paracetamol and Intravenous Ketorolac as a Pre-addictive Analgesia on the Scale for Labioplasty Postoperative Pain in Pediatric Patients. *Jurnal Anestesi Perioper* **3**, 81–86 (2015).
7. Eisenach, J.C., *et al.* Severity of Acute Pain After Childbirth, but Not Type of Delivery, Predicts Persistent Pain and Postpartum Depression. *Pain* **140**, 87-94 (2009).
8. Badawy, A. & Sakka, A. Preoperative Gabapentin Alone or in Combination with Dexamethasone on Postoperative Pain Relief After Abdominal Hysterectomies. A Randomized Controlled Trial. *Egypt. J. Anaesth* **31**, 107-113 (2015).
9. Jelting, Y., *et al.* Preventing Nausea and Vomiting in Women Undergoing Regional Anesthesia for Cesarean Section : Challenges and Solutions. *Local Reg Anesth* **Aug 9**, 83-90 (2017).
10. Jadon, A., Sinha, N., Agrawal, A. & Jain, P. Effect of Intravenous Dexamethasone on Postoperative Nausea-Vomiting (PONV) after Intrathecal Morphine during Caesarean Section. *SOJ Anesthesiol Pain Management* **3**, 1-5 (2016).
11. De Oliveira, G.J., Almeida, M., Benzon, H. & McCarthy, R. Perioperative Single Dose Systemic Dexamethasone for Postoperative Pain. *Anesthesiology*. 2011 Sep; **115**(3):575-88 **Sep 115**, 575-588 (2011).
12. Kartapraja, R.D., Fuadi, I. & Redjeki, I. *Perbandingan Efek Pemberian Analgesia Pre-emptif Parecoxib dengan Parasetamol terhadap Nyeri Pascaoperasi Radikal Mastektomi Menggunakan Numeric Rating Scale*. Comparison of the Effect of Parecoxib Pre-addictive Analgesia and Paracetamol on Radical Mastectomy Postoperative Pain Using Numeric Rating Scale. *Jurnal Anestesi Perioper* **4**, 111-116 (2016).
13. Musba, A., Tanra, H., Yusuf, I. & Ahmad, R., (2015). The Effect of Dexamethasone on the Dynamics of Inflammation, Cortisol and analgesia in Lower Limb Surgery. *Journal of Pain and Relief* **4**, 1-6 (2015).
14. Cardoso, M.M.S., Leite, A.O., Santos, E.A. & Gozzani, J.L. Effect of Dexamethasone on Prevention of Postoperative Nausea, Vomiting and Pain After Caesarean Section: A Randomised, Placebo-Controlled , Double-Blind Trial. *European Journal of Anesthesiology* **30**, 102-105 (2013).
15. Kamath, V. & Lasrado, A. Efficacy and safety of intravenous acetaminophen versus intravenous butorphanol as post-operative analgesic in obstetrics and gynecology: a comparative study. *International Journal of Advances in Medicine* **1**, 222-229 (2014).
16. Choy, Y. & Isquandar, A. Effectiveness of tramadol/ paracetamol compared with etoricoxib as postoperative analgesia in day care surgery. *Southern African Journal of Anaesthesia and Analgesia* **20**, 155-159 (2014).
17. Erlangga, M.E., Sitanggang, R.H. & Bisri, T. *Perbandingan Pemberian Deksametason 10 mg dengan 15 mg Intravena sebagai Adjuvan Analgetik terhadap Skala Nyeri Pascabedah pada Pasien yang Dilakukan Radikal Mastektomi Termodifikasi*. Comparison of Administration of Intravenous Dexamethasone 10 mg and 15 mg as Analgesic Adjuvant to Post-Surgical Pain Scale in Patients Performing Modified Radical Mastectomy. *Jurnal Anestesi Perioperatif* **3**, 146-154 (2015).