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INTERNATIONAL ARCHIVES OF MEDICINE
SECTION: GYNECOLOGY AND OBSTETRICS
ISSN: 1755-7682

2015
Vol. 8 No. 133
doi: 10.3823/1732

Acetaminophen and the Pain Management in Cesarean Post-Operatory

REVIEW

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Abstract

Effective post-caesarean pain relief is important, once this promotes a better and faster recovery and can diminish the hospital expenses. Paracetamol *(acetaminophen)* is the most commonly used drug to treat fever or pain, both as an over the counter drug as well as in the hospital setting. Many works demonstrated the efficacy of Paracetamol as analgesic in pregnancy: Paracetamol infusion and the diclofenac intramuscular injection have analgesic efficacy similar to the intravenous pethidine. In a pregnant, 34 years, history of Non-Hodgkin Lymphoma in 5 years remission and with Tail Syndrome Equine manifestations the analgesia was maintained with Paracetamol, magnesium Dipyrone and, intercalary with Paracetamol, tramadol; a case of a nulliparous, 39 weeks, with arteriovenous malformations and whose postoperative analgesia was assured with Paracetamol by intravenous three peridural bolus of ropivacaine and morphine.However, acetaminophen is associated with risks for women and her baby: neurodevelopmental and behavioral disorders; reduced gross motor skills, delay in walking, increased activity, reduced communication skills, and attention-seeking or aggressive behavior; Recent studies also suggest that acetaminophen is a hormone disrupter. Future studies comparing the usage of Paracetamol and other possible combinations are necessary, provided that they have significant statistical samples and standard tools accepted internationally to measure pain levels.

Keywords
Acetaminophen, Cesarean, Management, Pain, Post-Operatory.

Caesarean delivery is one of the most commonly performed surgical procedures and postoperative pain is a great concern for women [1]. Effective post-caesarean pain relief is important, once this promotes

a better and faster recovery and can diminish the hospital expenses [2].

It causes significant discomfort to women, which can lead to difficulties in mobility and subsequent problems, such as, an increased risk of venous thrombosis, and by interfering with optimal interaction with the newborn in the immediate postpartum period; shallow breathing and splinting may result in atelectasis and predispose to pneumonia; pain has psychological sequel [3, 4], and, also, promotes delay in feeding outset [2] **(Figure 1)**.

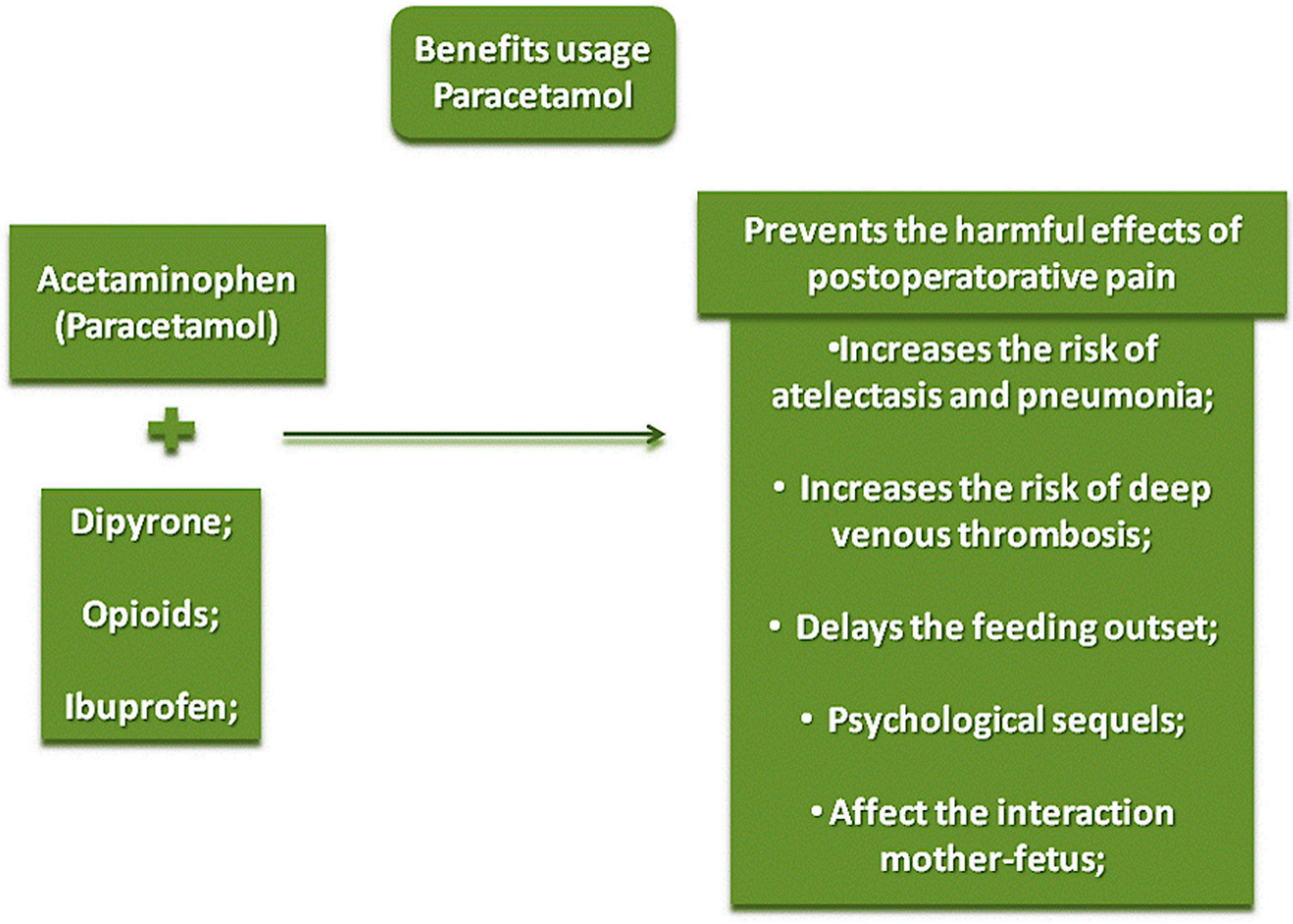
Furthermore, the chemicals used to treat or to prevent the postoperative pain can lead to outcomes to the newborn through the breast-feeding [5].

Due to the relevance of this clinical symptom, the Agency for Healthcare Research and Quality's (AHRQ), the American Pain Society and the Joint Comission on Accreditation on Healthcare Organizations (JCAHO) advocates that, to control the pain in an ideal manner, it is necessary to regularly and adequately measure it, in the same clinical ambience in which the vital signals are measured, being defined as "the fifth vital signal" [7].

There are diverse analgesic schemes to the treatment of the postoperative pain in cesarean. The biggest part of the schemes described is based on the usage of the combination of two or more drugs, which usually can be associated to an important augment on the global cost of the surgery [8]. Generally, the used drugs are: anti-inflammatory as Paracetamol and Dipyrone, opioids, anticonvulsants, antidepressants, neuromuscular blockers, clonidine, ketamine and lidocaine [9].

Paracetamol *(acetaminophen)* is the most commonly used drug to treat fever or pain, both as

Figure 1: Benefits of the usage of Acetaminophen (Paracetamol) in postoperative cesarean pain.



an over the counter drug as well as in the hospital setting [10]. This drug is a p-aminophenol derived, being the metabolic product of fenacetina and acetanilide [11], whose action mechanism is based in the indirect activation of the receptors CB1 of cannabinoid system, a complex system of neurotransmitters related to energetic balance, emotional alterations, pain, hyperthermia and hyperphagia [12]. Paracetamol can be administered either in monotherapy or as part of a multimodal approach, resulting in more effective temperature control when combined with non-steroidal anti-inflammatory drugs (NSAIDS) or equivalent analgesia with lower opioid exposure [13, 14].

Idehen et al., [15] relate that the Paracetamol infusion and the diclofenac intramuscular injection have analgesic efficacy similar to the intravenous pethidine, wherein this combination can be a good substitute for pethidine in the management of post caesarean pain. Buhagiar et al., [16] utilized the Paracetamol as chosen drug to control the pain in their study, which investigated predictors of post-caesarean section pain and analgesic consumption in 65 pregnant women over 36 weeks in Malta

Study [17] demonstrated that pain relief was maintained with repeated boluses of local anesthetic combined with oral paracetamol *(acetaminophen)* and ibuprofen unless contraindicated in received ultrasound-guided transversus abdominis plane catheters for post-cesarean delivery analgesia. Study performed by Derry, Derry e Moore [18] concluded that the usage of ibuprofen plus Paracetamol combinations provided better analgesia than either drug alone (at the same dose), with a smaller chance of needing additional analgesia over about eight hours, and with a smaller chance of experiencing an adverse event.

Many works demonstrated the efficacy of Paracetamol as analgesic in pregnancy. Duarte et al., [19] related a case of a pregnant, 31 weeks, Gest IV, Para IV, epileptic, hypertensive and chronic alcoholic, that suffered acute infarct of myocardium and whose postoperative cesarean analgesia was assured through the operative wound infiltration with 10mL of ropivacaine in 10 $mg.mL^{-1}$, 1 g of Paracetamol by venous way in 8/8h and peridural infusion of morphine-1 0.12 $mg.h^{1}$ through an elastomeric infuser for 48 hours. Carvalho et al., [20] approached a case of a nulliparous, 39 weeks, with arteriovenous malformations and whose postoperative analgesia was assured with 1 g Paracetamol by intravenous way in 6/6h and three peridural bolus of 10 mL ropivacaine 1.2 $mg.mL^{-1}$ and morphine 0.2 $mg.mL^{-1}$ in 12 in 12 hours (until 36 hours post-cesarean), getting a satisfactory pain control. Duarte et al., [21] described a case of a pregnant, 34 years, history of Non-Hodgkin Lymphoma in 5 years remission and with Tail Syndrome Equine manifestations after the application of morphine and methylprednisolone in epidural space, the analgesia was maintained with Paracetamol 1g IV in 6/6h, magnesium Dipyrone 2g in 100 mL of NaCl 0,9% IV in 6/6h and, intercalary with Paracetamol, tramadol 50 mg IV in 8/8h.

Pharmacokinetics of intravenous Paracetamol has been estimated following caesarean delivery. Although limited to a loading dose shortly after surgery, the results are clinically relevant [22]. Other pharmacokinetic aspect of Paracetamol is that its passage to breast milk is very low. Despite the mother take the maximum recommended diary dose (4g), only 5% of the therapeutic dosage (60mg/kg/day) remain in the milk. The nursling has active enzymes to the Paracetamol metabolization [23].

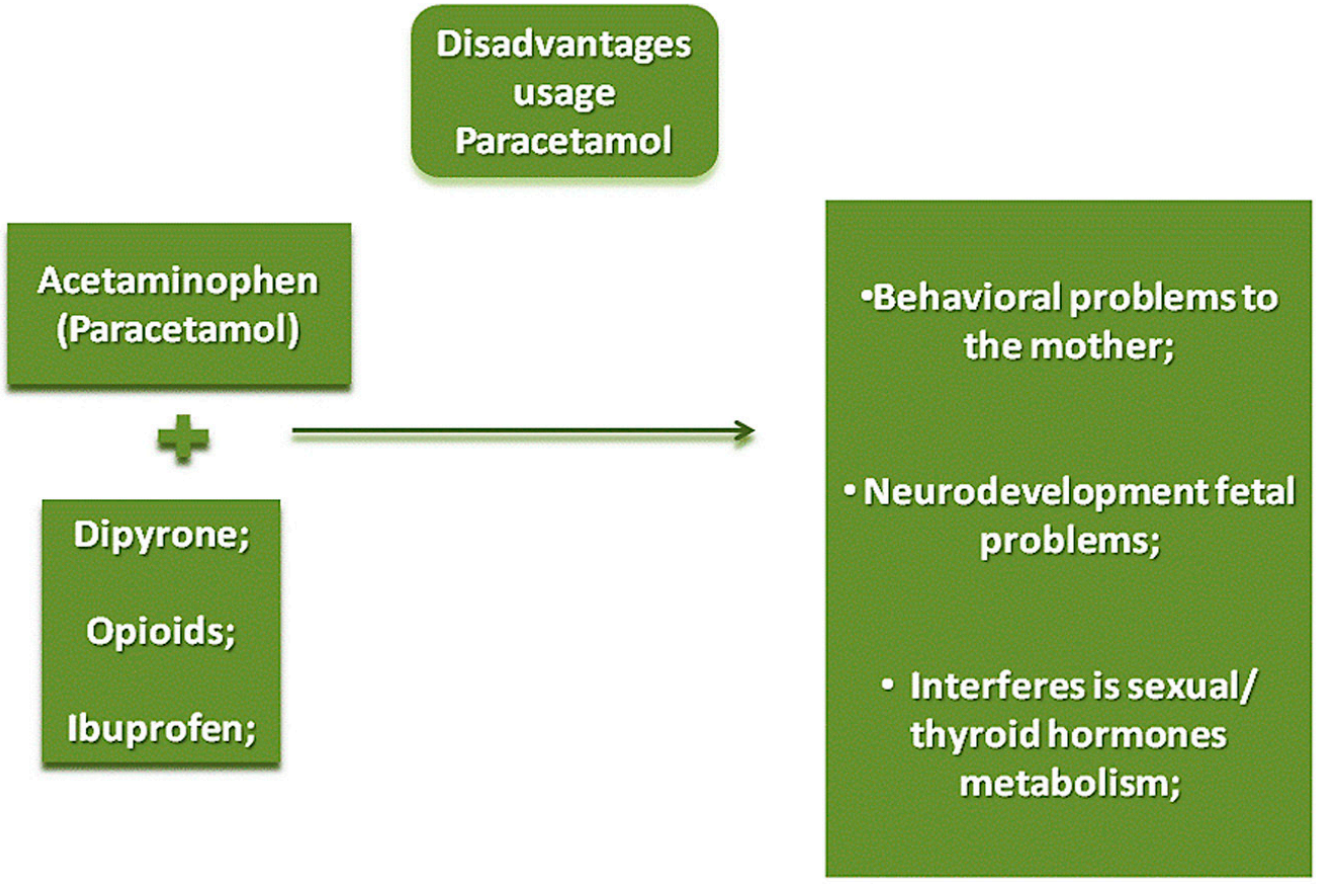
However, acetaminophen is associated with risks for women and her baby. Prospective cohort of 64.322 pregnancies show that acetaminophen use in pregnancy was associated with significantly higher scores for behavioral problems at 7 years (risk ratio 1.13, 95% CI 1.01 to 1.27) [24]. Aminoshariae e Khan [25] related prenatal exposure to acetaminophen is associated with neurodevelopmental

and behavioral disorders. Recent studies also suggest that acetaminophen is a hormone disrupter (ie, it interferes with sex and thyroid hormone function essential for normal brain development) and thus may not be considered a safe drug during pregnancy. In Brandlistuen et al., [26] that evaluated 48.631 pregnancies with a focus on 2.919 same-sex sibling pairs, acetaminophen use for 28 or more days in pregnancy correlated significantly with maternally assessed (at 3 years) reduced gross motor skills, delay in walking, increased activity, reduced communication skills, and attention-seeking or aggressive behavior **(Figure 2)**.

Mort et al., [27] warn that a large proportion (8.1%) of the 5.3 million prescriptions for opioid-Paracetamol exceeded the recommended maximum daily dose of Paracetamol (4 g/day), putting over one-quarter of a million (255 123 [18.9%]) of the 1.35 million beneficiaries receiving an opioid-Paracetamol prescription at risk of toxicity. The most frequently prescribed products that exceeded Paracetamol dosage guidelines contained dextropropoxyphene and hydrocodone. Multiple factors, including type of product (i.e. dextropropoxyphene or oxycodone-containing), geographical location (Midwest), strength of the Paracetamol in the opioid-Paracetamol product (>325 mg) and prescriber specialty (dentist, physician assistant), were associated with high-dose Paracetamol prescriptions.

As the number of women giving birth by caesarean increases throughout most of the developed world, so too is research into postoperative pain relief for these women. Like most other post-surgical populations, the new mothers need effective pain relief so they can locomote earlier, once now they have to take care of their newborn – a great responsibility. Acetaminophen provides an effecti-

Figure 2: Disadvantages of the usage of Acetaminophen (Paracetamol) in postoperative cesarean pain.



ve treatment for post-caesarean pain relief in the majority of pregnancy when associated with other medications like Ibuprofen, Opioids, Dipyrone [18-21], provided that there is no exceeding of the maximum dosage of 4g/d, being necessary to pay extreme attention in prescriptions in this crucial moment – the puerperium. Future studies comparing the usage of Paracetamol and other possible combinations are necessary, provided that they have significant statistical samples and standard tools accepted internationally to measure pain levels.

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