Study Of The Effect Of Paracetamol In Reducing Postoperative Morphine Consumption By Patient Controlled Analgesia After Abdomenoplasty.

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Background. Trials should not stop to found the proper pain killer that can effectively replace or reduce the use of narcotic analgesics to avoid their known side effects, most important is physical dependence. Paracetamol (perfalgan) is a promising parentral form of paracetamol. The aim of this work is to study the sparing effect of paracetamol on morphine consumed by the patients undergoing abdomenoplasty using patient controlled analgesia pump (PCA).

Methods. Eighty female patients were randomly arranged in two groups (40 each). They were scheduled for surgical abdomenoplasty. The first group received paracetamol 1 5mg/kg intravenous infusion after induction and every 6 hours in the first post operative day. The second group received placebo. Both groups received the same anesthetic management and PCA settings postoperatively. The study variables were morphine consumption, pain at rest and activity (coughing), patient satisfaction throughout the first postoperative day and reporting of any adverse effects.

Results. From this study it is found that the use of paracetamol infusion on regular bases both intraoperatively and 6 hours postoperatively reduced morphine requirements by more than 30%.

Conclusions. From this work it is concluded that the use paracetamole infusion reduces the need for morphine in postoperative analgesia.

Keywords: analgesia, paracetamole, patient controlled analgesia, morphine, abdomenoplasty, postoperative.

INTRODUCTION

Effective pain relief after surgery is an essential element of good postoperative management. The management of acute pain has improved over the last few years. The use of morphine by titration in the post-anesthesia care unit (PACU) is often the first step in postoperative pain management. This approach provides rapid analgesia but is associated with frequent adverse effects (nausea, vomiting, urine retention, pruritus and respiratory depression) also it shows a wide inter-individual variability in morphine requirements and may prolong patient stay in the PACU(1,2).

Non-opioid analgesics as paracetamol and non-steroid anti-inflammatory drugs (NSAIDs) are proposed for pain relief. Postoperative administration of paracetamol or its prodrug, propacetamol, has been used to decrease pain(3-7). Paracetamol is a peripherally acting analgesic commonly used in multimodal post-operative pain management to reduce the need for more potent analgesics with their unwanted side-effects (5). Paracetamol infusion bottles (Perfalgan) are available now for intravenous infusion as analgesic for the treatment of postoperative pain. Consequently, it has become very common to use non-opioid analgesics in association with morphine(9) to obtain a morphine sparing-effect and hopefully, a decrease in morphine-related adverse effects. This concept is supported by several studies that emphasize the role of multimodal analgesia(1,2).

The aim of this work is to calculate the sparing effect of paracetamol on the amount of morphine needed for postoperative pain relief, after abdomenoplasty.

PATIENTS AND METHODS

This study was done on 80 adult female patients presented for abdomenoplasty at the operating theatre of Zayed Military Hospital under general anesthesia, ASA class I and II. All patients of the study were
operated by the same surgical staff. Criteria for exclusion were as follows: age above 50 yr, ASA status III or IV, known allergy to paracetamol, non educated non cooperative patients, or who were having language barrier (with no Arabic or English speaking). Taking the approval of the local ethical committee, and written informed consent from the patients, patients were arranged randomly into two equal groups. The first group we called (Para group) and the second (Placebo group). All patients received anesthesia using propofol and remifentanil in a target controlled infusion way based on achieving and maintaining a pre determined plasma drug concentration. Para group received paracetamol infusion (peralgan vial) 15mg/kg body weight over 20 minutes after induction and then six hourly in the first post operative day. The other group received placebo.

Muscle relaxation was maintained guided by train of four stimulus (TOF). Before the end of surgery by about 30 minutes, 0.1mg/kg morphine was given intravenously. At end of surgery, anesthesia stopped, reversal of relaxation guided by TOF.

Management in post anesthesia care unit (PA CU):
All nurses in the postanaesthesia care unit (PACU) and in the wards had been trained to assess pain using the VAS (0-10 Cm, hand-held slide-rule type)(8) When patients had difficulty in manipulating the VAS, nurses were allowed to use a numerical rating scale (0-10 Cm)(9). The nurses that administered the drug were different from those who assessed the pain so that the later were unaware whether the patient received paracetamol or placebo. A strict protocol of i.v. morphine titration had been implemented in the PACU as a nurse controlled analgesia (NCA) to keep pain score below 3 according to visual analogue pain scale (VAS) (10,11) As soon as the patients were awake, they were questioned about the presence of pain (at least every 15 mm) and asked to rate pain intensity. When the pain score increased to more than 3, intravenous morphine was given every 5 mm in 2 mg increments. Pain relief was defined as VAS less than 3. Clinical monitoring included arterial blood pressure, heart rate, pulse oximetry (SpO₂), respiratory rate (RR) measurements, and sedation according to the Ramsay score(10) When the patient was asleep (Ramsay score >2) no attempt was made at arousal, and the patient was considered as having adequate pain relief. Morphine titration was stopped if the patient had a RR lower than 10 breaths per minute (bpm) and/or a SpO₂ lower than 95%, and/or experienced a serious adverse event related to morphine administration (allergy, vomiting, severe pruritus)(11,2). If there was ventilatory depression (RR less than 10 bpm), naloxone (intravenous boluses of 0.04 mg) was administered until RR was greater than 12 bpm. The decision for the patient to leave the PACU was taken by the anesthetist after

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the nurse had checked that the patient fulfilled the Aldrete criteria\textsuperscript{(11)} and was not suffering from emesis, severe pain or major postoperative bleeding. Before discharge from PACU the patient reminded to use patient controlled analgesia pump, (Lfe Care, PCA infuser, Abbott laboratories USA) by pressing the button each time she needs pain relief, (they first learned to do so in the preoperative visit). PCA pump adjusted to deliver 2mg boluses, with 7 minutes lock out interval. After 24 hours of discharge, the amount of morphine used by the patient was calculated and also the amount of morphine required by the patients in the PACU to keep their pain score below 3 on VAS. Pain score by VAS was measured each hour in the first post operative day.

Statistical analysis was done after data collection. Data are expressed as mean (± standard deviation) for quantitative variables normally distributed, categorical variables were compared using the chi-squared test and continuous variables were compared using the Student t test.

**RESULTS**

There were no differences between the two groups as regard the distribution of the patient’s physical characteristics including sex, age, weight and height (Table I). As regards the type of surgery, abdominoplasty was the procedure for all patients done by the same surgical team. There was no significant difference of the mean anesthesia time in both groups (Table I).

There were insignificant differences in mean blood pressure and heart rate values during the whole period of the study in both groups.

Pain scores showed insignificant difference between both groups during the first post operative day. Pain was estimated by VAS every hour, all the time it was below three. VAS assessment was cancelled during periods of calm sleep of the patients and VAS considered <3.

The amount of morphine required by placebo group was significantly higher than Para group both in PACU and in the ward, (Table II). Placebo group required 14.55 (3.25) mg of morphine while Para group required 9.36 (2.45) mg of morphine (34.5% lower, \( P < 0.05 \)), during their stay in the PACU. In the first post operative day, Placebo group consumed 25.36 (5.21) mg of morphine which is significantly higher than Para group who consumed (32.4 % lower) of morphine 15.7 (4.1) mg (\( P < 0.05 \)).

None of the patients showed morphine adverse effects.

**Table I: Physical characteristics of the patients studied**

<table>
<thead>
<tr>
<th></th>
<th>Paracetamol group mean ±(SD)</th>
<th>Placebo group mean ±(SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>34.6 (6.5)</td>
<td>35.9 (4.7)</td>
</tr>
<tr>
<td>Weight(Kg)</td>
<td>95.6 (5.47)</td>
<td>94.3 (6.33)</td>
</tr>
<tr>
<td>Height (Cm)</td>
<td>155.3 (4.9)</td>
<td>156.2 (4.4)</td>
</tr>
<tr>
<td>BMI</td>
<td>38.51 (2.3)</td>
<td>39.17 (2.2)</td>
</tr>
<tr>
<td>Duration of anesthesia (mm)</td>
<td>185.7 (25.2)</td>
<td>190.5 (30.11)</td>
</tr>
</tbody>
</table>

**Table II: Morphine consumption in the two groups in PACU and the first postoperative day, presented as Mean ± ( SD).**

<table>
<thead>
<tr>
<th></th>
<th>Paracetamol group mean (SD)</th>
<th>Placebo group mean (SD)</th>
<th>%difference between the two groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine consumption in PACU (mg)</td>
<td>9.36 (2.45)</td>
<td>14.55 (3.25*)</td>
<td>34.5%</td>
</tr>
<tr>
<td>Morphine consumption in the ward in first post operative day (mg)</td>
<td>15.7 (4.1)</td>
<td>25.36 (5.21)*</td>
<td>32.4%</td>
</tr>
</tbody>
</table>

* means that there is statistical significant difference and \( p <0.05 \).
DISCUSSION

In this study we demonstrated a sparing effect of paracetamol of more than 32% on morphine needed to relieve postoperative pain in the first postoperative day. During this study we relied on the use of patient controlled analgesia which is a proven safe and reliable method to relieve postoperative pains. We fixed all variables in both groups regarding the range of BMJ, sex, surgical procedure, surgical team, and a tight range of time of surgery and anesthesia, to better clarify the effect of the only variable left which is the use of paracetamol. Also the rate of paracetamol infusion was fixed to 15 minutes duration to have the best effect as proved by Moller et al (13) who concluded from their study that paracetamol, administered as a 1 5-mm infusion, is a fast-acting analgesic agent. It is more effective in terms of onset of analgesia than a faster rate of infusion or a similar dose of oral acetaminophen.

Aubrun et al(4), confirmed that propacetamol (which is a prodrug of paracetamol) induces a morphine sparing-effect ranging from 18% up to 46%. They also observed that the degree of this effect depends on the intensity of postoperative pain: the value was 37% in patients with moderate postoperative pain vs 18% in patients with severe postoperative pain. The morphine-sparing effect of propacetamol has been reported as 46% after total hip replacement, 37% after knee ligamentoplasty and 26% after vertebral disc surgery.

On the other hand, In a recent study, Verchère and colleagues(14) failed to demonstrate a postoperative analgesic effect of intraoperative propacetamol administration, after remifentanil anesthesia for supratentorial craniotomy. Pain after supratentorial neurosurgery was too severe and paracetamol was insufficient to relieve it.

Affected by the relation between the severity of postoperative pain expected and the success of paracetamol in saving some of morphine needed by the patients, Michèle Binhasl et al(15) studied mammoplasty which was chosen because postoperative pain is moderate. They proved that intraoperative propacetamol administration with remifentanil based anesthesia improved significantly early postoperative pain by sparing morphine and shortening the delay to achieve pain relief.

Many studies failed to prove that paracetamol given rectally immediately after induction of anesthesia(17) or at the end of gynecological surgery(18) or orally before surgery(19,22) improved early postoperative analgesia. The negative results of these studies may be explained by many factors such as the low initial pain score in the control group(17,18,21,23) and the difference in the route used for paracetamol administration(17,22). An other hypothesis to consider is the use of long-acting opioid such as fentanyl that might have contributed to the early post-operative analgesia(20,24). In our study, remifentanil was used intraoperatively because of its very short half life so no postoperative overlap of analgesic effect.

In other studies propacetamol was administered at the beginning of skin closure, which corresponds to one hour before the end of surgery. This delay may be insufficient to achieve pain control immediately after tracheal extubation, as the peak effect of intravenous propacetamol was shown to occur only two hours after its administration(25).

In conclusion, intraoperative paracetamol administration in women undergoing abdominoplasty significantly reduced (by about 32%) early postoperative morphine consumption, used for pain control in recovery room, and in first postoperative day. It is recommended to be used intraoperatively and postoperatively for pain management.

REFERENCES

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