Analgesic efficiency of propacetamol hydrochlorid after lumbar disc surgery

P. HANS (*), J. F. BRICHANT (*), V. BONHOMME (*) and M. TRIFFAUX (**)

Summary: The influence of intravenous propacetamol hydrochlorid administration on postoperative analgesia and intramuscular opioid consumption was assessed in a randomized placebo-controlled study. Forty patients scheduled for lumbar disc surgery were randomly allocated to two groups. They were given either propacetamol 2 g or saline every 6 hours, starting at the end of procedure for a 24 hours period. The pain intensity (VAS) was not significantly different between the two groups except 3 and 4 hours after surgery, where it was higher in the paracetamol group. The cumulative narcotic consumption (pimtramide on request) was higher in the placebo group from 6 hours till 9 hours after surgery but not significantly different after 24 hours. Pimtramide administration decreased VAS score significantly in both groups while propacetamol reduced it in a significant way only when given from 12 hours after surgery.

Key words: Lumbar disc surgery; Postoperative pain; Propacetamol.


INTRODUCTION

Postoperative pain relief is a major concern for anesthesiologists (6). In practice, routine management of pain after minor or intermediate surgery involves usually repeated parenteral administration of opioid or non opioid analgesics. Among non-opioid analgesics, propacetamol hydrochlorid, a precursor of paracetamol, is a peripherally acting analgesic drug devoid of anti-inflammatory property. It can be easily solubilized and may be given intravenously. It improves analgesia after orthopedic, gynecologic or abdominal surgery (1, 4).

The present study was designed to assess the effect of systematic intravenous propacetamol administration on analgesia and intramuscular opiate consumption after lumbar disc surgery.

METHODS

After approval of the protocol by the Ethics Committee, 40 ASA I or II consenting

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patients scheduled to undergo elective lumbar disc surgery were enrolled in the study. None of these patients had known sensitivity to paracetamol, used analgesic or non-steroidal anti-inflammatory drug for 48 hours before surgery, nor suffered from gastric, renal, hepatic and hematological disorders.

Premedication consisted of hydroxyzine (1 mg.kg\(^{-1}\)), alprazolam (0.5 mg) and atropine (0.5 mg) administered orally 1 hour before surgery. All patients were anesthetized according to the same protocol. A bolus dose of sufentanil 0.2 \(\mu\)g.kg\(^{-1}\) was given i.v. 5 min. prior to induction of anesthesia. Anesthesia was induced with propofol (2 mg.kg\(^{-1}\)) and atracurium (0.5 mg.kg\(^{-1}\)). After tracheal intubation, patients were ventilated with nitrous oxide (\(N_2O\)) and oxygen (\(O_2\)) in a 60 : 40 ratio and anesthesia was maintained with enflurane 0.5% to 1%. No narcotic agent was given during the surgical procedure.

With regard to postoperative analgesia, patients were randomly allocated to 2 groups. In the first group (P; n = 20) patients received propacetamol (P) 2 g i.v. over 20 minutes every 6 h, starting at the end of surgery. In the second group (S; n = 20) patients were given saline (S). The pain intensity was assessed hourly for 14 hours by means of a Visual Analog Scale (VAS graded from 0 to 10; 0 = non pain, ... 10 = worst pain imaginable). Piritramide 15 or 20 mg according to body weight was injected intramuscularly at the patients' request in both groups.

Statistical evaluation included a two-tailed unpaired Students' t test for comparison of demographic data and duration of surgery in both groups. Differences between groups with respect to VAS scores and piritramide consumption at a given time were analysed using the Mann-Whitney rank sum test. Differences in the number of patients who required piritramide in both groups were compared using a Chi Square test. Efficiency assessment of piritramide and paracetamol were evaluated using the Wilcoxon signed-rank test. Statistical significance was assumed at the conventional 5% level.

**Results**

Demographic data and duration of surgery are listed in Table I. The two groups were similar in age, weight, height, sex ratio and duration of surgery.

**Table I**

Demographic data and operative details (*)

<table>
<thead>
<tr>
<th>Demographic data and durations of surgery</th>
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<tr>
<td>Age (year)</td>
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<tr>
<td>38.3 ± 9.4</td>
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<tr>
<td>Weight (kg)</td>
</tr>
<tr>
<td>Height (cm)</td>
</tr>
<tr>
<td>Sex ratio (M/F)</td>
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<tr>
<td>Duration of surgery (min)</td>
</tr>
</tbody>
</table>

(*) Mean ± Standard deviation.

During the study period, the pain intensity score (assessed by VAS) was not significantly different between the 2 groups, except 3 and 4 hours after the end of surgery where it was higher in group P than in group S (Fig. 1).

![Cumulative narcotic consumption during 24 hours postsurgery](image)

*Fig. 1. — Cumulative narcotic consumption during 24 hours postsurgery (mean values ± s.e. mean) in both groups (○: placebo group, ●: propacetamol group). Asterisks indicate significant difference between groups (p < 0.05).*
The cumulative consumption of piritramide was significantly higher in group P than in group S from 6 hours till 9 hours after the end of surgery (Fig. 2). However, no significant difference was observed between the two groups in the narcotic consumption per patient cumulated over 24 hours (mean ± SEM: P = 9.5 ± 2.0 mg; S = 14.75 ± 2.4 mg). The time elapsed (mean ± SEM) between the end of surgery and the first piritramide injection was longer in group P (323.6 ± 64.9 min) than in group S (200 ± 36.2 min) but the difference did not reach the statistical level. The number of patients who required piritramide at any time of the study was lower in group P (11/20 over 24 h) than in group S (15/20 over 24 h) as shown in Table II but not significantly different between the two groups.

Piritramide administration was associated with a significant reduction in VAS score in group P and in group S. Propacetamol administration did not change VAS score 6 hours after surgery but decreased it significantly when given 12 hours postoperatively.

**DISCUSSION**

Non-opioid analgesics are important in the management of postoperative pain (2). Among them, non-steroidal anti-inflammatory drugs are especially beneficial by providing pain relief and reducing opioid consumption (3, 9). However, many of these drugs have well-known side effects such as gastric ulceration, impaired coagulation and alteration of renal function. Propacetamol is a non-opioid analgesic devoid of any major contra-indications. A single dose of propacetamol (2 g) given intramuscularly within 24 hours following lower limb orthopedic surgery has a similar maximum effect and a similar duration of action than 30 mg of pentozacine (1). However, its role in postoperative analgesia has not been extensively studied.

The results of the present study indicate that systematic i.v. administration of 2 g of propacetamol every 6 hours, starting at the end of surgery, does not improve analgesia until the twelfth hour after surgery. It is well known that i.v. administration of 2 g of propacetamol hydrochlorid gives rise to 1 g of paracetamol, a dose often used for pain relief in comparative trials after orthopedic surgery (8, 10). In the present study, most patients did not score above 3 on the VAS one hour after the end of surgery. This low pain intensity can be explained by a residual analgesic effect of general anesthesia and by the fact that routine lumbar disc surgery does not yield to severe postoperative pain. The analgesic efficiency of propacetamol and piritramide was assessed by comparing the VAS scores before and one hour after the drug administration in each

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**Table II**
Rescue analgesic

<table>
<thead>
<tr>
<th>Number of patients</th>
<th>Group P</th>
<th>Group S</th>
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<tbody>
<tr>
<td>Piritramide +</td>
<td>11</td>
<td>15</td>
</tr>
<tr>
<td>Piritramide -</td>
<td>9</td>
<td>5</td>
</tr>
</tbody>
</table>

$z^2 = 0.983$ NS.
patients' group. Piritramide injection yielded a significant analgesic effect in both groups. Propacetamol infusion, the maximum analgesic effect of which is observed one hour after administration (1), resulted in a decrease in VAS score 6 hours and 12 hours after surgery. However, this decrease was statistically significant only 12 hours postoperatively. In addition, pain intensity scores did not differ significantly between the two groups during the entire period of study except 3 and 4 hours after surgery when VAS scores were higher in group P than in group S. This paradoxical finding is probably related to the administration of piritramide. Indeed, the time elapsed between the end of surgery and the first piritramide injection was shorter in group S than in group P, although the difference did not reach the significant level. In fact, the opioid consumption was significantly higher in group S from 6 hours till 9 hours after the end of surgery. However at the end of the study, no significant difference was observed between the two groups in the number of patients who required piritramide, neither in the piritramide consumption over 24 hours. Our failure to demonstrate an opioid sparing effect could be explained both by the low pain intensity in the postoperative period, as already mentioned, and by the mode of piritramide administration. The traditional intramuscular administration of opioids involves defined doses and, the most often, dosing interval limitations. On the contrary, intravenous patient-controlled analgesia (PCA) is a dynamic and flexible analgesic modality allowing patients to "titrate" as little or as much opioid as they desire, and allowing to accommodate patients' widely divergent analgesic requirements (5). Our results show only a non significant tendency to the decrease in opioid consumption but we cannot exclude the possibility of a real opioid sparing effect in the P group if opioid analgesia had been administered using a PCA pump. Such a sparing effect has already been demonstrated with propacetamol after repair of bilateral inguinal hernia (7).

In conclusion, propacetamol hydrochloride has minor analgesic properties after lumbar disc surgery. Given I.V. as a bolus of 2 g every 6 hours, it does not affect significantly I.M. opioid consumption and does not improve immediate postoperative analgesia. However, it provides pain relief when administered 12 hours after the end of surgery.

References


Nous avons étudié l'influence de l'administration intraveineuse de propacétamol sur la douleur postopératoire et la consommation de piritramide injecté par voie intra-musculaire. Quarante patients opérés d'une hernie discale lombaire ont été répartis en deux groupes. Ils ont reçu par voie intraveineuse 2 g de propacétamol ou du liquide physiologique (placebo) toutes les 6 heures au cours des 24 premières heures post-opératoires, en commençant dès la fin de l'intervention chirurgicale. Le score de douleur (échelle visuelle analogique) ne différait pas de façon significative entre les deux groupes à l'exception de la 3e et de la 4e heure postopératoire où il était plus élevé dans le groupe Propacétamol. Cette différence est probablement due à l'administration plus précoce de piritramide dans le groupe placebo. La consommation cumulée de piritramide était plus faible dans le groupe placebo. La consommation cumulée de piritramide était plus faible dans le groupe Propacétamol que dans le groupe Placebo mais la différence n'était significative que de la 6e heure à la 9e heure post-opératoire. La piritramide a entraîné une diminution significative du score de douleur dans les deux groupes tandis que le propacétamol n'a provoqué une diminution significative du score de douleur qu'à partir de la 12e heure après l'intervention chirurgicale.


Wij hebben de invloed onderzocht van intraveneus propacetamol op de pijn, na chirurgische ingreep en het verbruik van intramusculair piritramide tijdens dezelfde periode. Veertig patiënten met lumbaire discus hernia werden, voor de ingreep, ondergebracht in twee groepen.

Zij kregen ofwel 2 g propacetamol intraveneus of een placebo (fysiologisch serum) om de zes uur tijdens de eerste 24 uren na de ingreep, te beginnen bij het einde van de operatie. Er was geen relevant verschil in de pijnsschaal (analoge visuele schaal) in beide groepen, met uitzondering van het derde en vierde uur na de ingreep, periode tijdens welke de pijn heviger was in de propacetamol groep. Dit verschil is waarschijnlijk te wijten aan het vroeger inspuiten van piritramide in de placebo groep. Het totale verbruik van piritramide was minder in de propacetamol dan in de placebo groep. Het verschil was enkel relevant van het zesde tot het negende uur na de ingreep.

Het inspuiten van piritramide gaat gepaard met een significante vermindering op de pijnsschaal in de twee groepen, terwijl propacetamol enkel de pijn aanzienlijk verminderde vanaf het twaalfde uur na de ingreep.