Post-operative pain therapy with controlled release oxycodone or controlled release tramadol following orthopedic surgery: A prospective, randomized, double-blind investigation

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Post-operative pain therapy with controlled release oxycodone or controlled release tramadol following orthopedic surgery: A prospective, randomized, double-blind investigation

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Summary
Background and objective: The purpose of this trial was to compare the efficacy, safety and side effects of post-operative pain therapy using oral controlled release formulations of tramadol and oxycodone.

Methods: In a prospective, randomized, double-blind investigation, we observed the post-operative course of 57 patients scheduled for orthopedic surgery. We assessed pain at rest and during exercise, vital signs and side effects using direct measuring and Numerical Rating Scales over a period of three post-operative days. We used chi-squared or Fisher's exact test for categorical variables and the Mann–Whitney U-test for numerical variables (p < 0.05).

Results: Demographic medical data and pain levels did not differ between the two treatments. Parameters for vital signs remained stable. Nausea and emesis occurred significantly more frequently with tramadol (p = 0.011, p = 0.013). Despite insignificance, central effects such as sedation, insomnia, myoclonus or nightmares were more frequent with tramadol. During the post-operative period, dizziness and sedation were attenuated significantly in the tramadol group (p = 0.031, p = 0.015) as was dry mouth in the oxycodone group (p = 0.041).

Conclusion: Our findings underline the efficacy of oral controlled release formulations of tramadol and oxycodone for post-operative pain therapy. Controlled release oxycodone was shown to cause less nausea and emesis than controlled release tramadol. Further investigation is needed in order to confirm these results.

Key words: Emesis; nausea; oxycodone; post-operative pain therapy; side effects; tramadol.

Introduction
In recent years the use of tramadol and oxycodone has been established for post-operative pain therapy. The centrally acting weak synthetic μ agonist tramadol possesses two complementary mechanisms: binding to μ-opioid receptors and a weak inhibition of the reuptake of norepinephrine and serotonin. Because of its safety it has found widespread oral or intravenous use in Patient Controlled Analgesia (PCA)1,2, but several studies reveal an incidence of side effects that restrict the use of the drug.3–6

Oxycodone is a strong semisynthetic opioid. Its oral and intravenous formulations have proved to be efficient and safe in post-operative pain therapy, comparable to tramadol.7–13 In some countries oxycodone has

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become one of the most frequently used opioids for post-operative pain therapy.\textsuperscript{14}

Few data are available on the comparative efficacy, safety and side effects of tramadol and oxycodone for post-operative pain therapy.\textsuperscript{15,16} In post-operative pain therapy, oral controlled release (CR) formulations of both drugs caused fewer side effects than the immediate release formulations.\textsuperscript{8,12,20} Prior references on the safety of tramadol reported less frequent adverse events, whereas literature on oxycodone remains contradictory.\textsuperscript{2-4,16}

Comparative studies on the oral CR administration of both substances are lacking. For that reason we investigated the efficacy and safety of orally administered CR formulations of oxycodone and tramadol with special regard to side effects.

**Patients and methods**

**Patients**

After approval of the study design by the local Ethics Committee and written informed consent was obtained from the subjects, 62 patients older than 18 and younger than 65 years of age (American Society of Anesthesiologists classification I–II) scheduled for elective orthopedic surgery of the lower extremities were enrolled in the study. Criteria for exclusion were known or suspected cardiovascular, pulmonary, renal, neurological, psychiatric or allergic diseases, lactation or pregnancy, drug dependency, alcoholism, opioid tolerance, history of abuse or history of treatment with any opioids, and current treatment with analgesics other than the study medications.

During surgery the patients underwent a standardized general anesthesia including the use of propofol as an induction agent, rocuronium as a non-depolarizing neuromuscular blocking drug, remifentanil as an opioid, and isoflurane/air/oxygen mix as anesthetic. The administration of long-acting benzodiazepines, local, regional or epidural and spinal blocks, was not allowed in the peri-operative period. The administration of piritramide was permitted immediately before or after surgery but, after the patient was transferred to the ward, no substance other than the oral study medications was given.

**Drug administration**

Since there are no recommendations concerning the direct conversion factor of oral tramadol and oxycodone dosage, we referred to other references on the conversion factors to morphine\textsuperscript{2-4,6,9,14,15,18,19} and, thereby, calculated a conversion factor of 10/1. Post-operative pain treatment using the study medication started in the evening of the day of the surgical procedure. Times of administration were fixed at 6.00 and 18.00 h. Using a computerized randomization program, patients received a CR formulation of either a tablet of 100 mg tramadol or of 10 mg oxycodone. In order to preserve the blindness of the investigator and the patient, a study nurse packaged the study drugs identically and another nurse administered them to the patients, both unaware of their contents. A single use of an additional rescue medication for treating acute exacerbation of pain with either 100 mg tramadol or 10 mg oxycodone p.o. was allowed. If pain therapy was still insufficient (numeric rating scales > 50), then the use of additional non-steroidal anti inflammatory drugs (NSAIDs) was allowed.

**Pain and symptom assessment, safety evaluation**

To collect data, an investigator observed the patients enrolled in this study, beginning on the day of surgery. The variables — drug dosage, pain, symptoms, and vital signs — were recorded over 3 days following surgery.
Data were collected daily at each of 4 time points (7.00, 14.00, 19.00, 22.00 h).

Dosage of the study medication, especially the use of the rescue medication, was registered daily. Numeric rating scales (NRS: 0 denotes no pain, 100 worst pain imaginable) were used to assess pain during rest and exercise. Additionally, patients could communicate freely about their satisfaction with the post-operative pain management.

Symptoms such as nausea, sedation, dizziness, dry mouth or pruritus were assessed by the NRS. The incidence of vomiting was additionally recorded. Non-numerical symptoms, such as the occurrence of sleep disturbances (sleep onset and sleep maintenance-insomnia), nightmares and myoclonus, were assessed on a two-step scale (no–yes).

The safety of the post-operative study medication was assessed using vital parameters such as blood pressure (100/60 to 140/90 mmHg), heart rate (60–90 beats per minute), respiratory rate (respiratory depression < 10 breaths per minute), and peripheral oxygen saturation (>95% saturation).

**Statistics**

*Descriptive statistics.* Distinct statistical parameters — mean value (mv), median, standard deviation (sd), minimum and maximum — were used for descriptive purposes. The data obtained at different times of the day were analyzed by means of detailed statistics (e.g. on day 1 at 7.00 h) and by means of summarized statistics (e.g. on day 1, on days 1–3).

*Confirmatory statistics.* Appropriate non-parametric test procedures were applied, depending on the data characteristics. Either the chi-squared or Fisher’s exact test was used for categorical variables to detect group differences on the need for an additional rescue medication, the use of non-opioids and the occurrence of side effects measured by categorical assessments (such as vomiting, sleep disorders, etc.). The Mann–Whitney U-test was used to compare quantitative numerical variables of both groups from day 1 to 3, such as pain intensity (measured by NRS at rest at different given times and during exercise), or the intensity of several symptoms assessed by NRS (such as nausea, dizziness, etc.). A p-value < 0.05 was considered statistically significant for all applied test procedures.

**results**

All patients suffered from acute nociceptive post-operative pain. 57 patients completed the study. Five patients receiving oxycodone did not complete the investigation because of an early discharge after minor surgery, 31 patients received tramadol and 26 oxycodone. Demographic and surgical-medical data were comparable in both treatment groups (Table I).

No severe adverse effects were seen in either group. Vital signs remained stable and within the normal ranges mentioned above. Especially, no respiratory rate lower than 10 breaths per minute or oxygen saturation lower than 95% was observed.

Given the opportunity to communicate complaints about the post-operative pain therapy, two patients in both groups each expressed their dissatisfaction, mainly due to insufficient pain therapy. The mv for NRS of pain at rest (day one to three) were 25, 35, 40, and 59 for these patients.

**Group analysis**

Differences for pain both at rest and with exercise were not significant between the two groups. The number of patients who used the rescue medication (i.e. additional study medication: tramadol: n = 8, oxycodone:
Table I.
Demographic and medical data, pain, n = 57

<table>
<thead>
<tr>
<th></th>
<th>Tramadol (n)</th>
<th>Oxycodone (n)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total</strong></td>
<td>31</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>Age (years) mv ± sd</td>
<td>46.85 ± 18.2</td>
<td>48.35 ± 16.67</td>
<td>0.694</td>
</tr>
<tr>
<td>med-min-max</td>
<td>43-18-64</td>
<td>46-20-64</td>
<td></td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>24/4</td>
<td>21/5</td>
<td>0.757</td>
</tr>
<tr>
<td>Surgical procedure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fractures</td>
<td>9</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Surgery of ligaments of the ankle or knee</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Mesh graft</td>
<td>4</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Removal of material</td>
<td>7</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Other type of surgery</td>
<td>7</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

NRS = numeric rating scales.

![Figure 1](image)

**Figure 1.** Symptom assessment: NRS of nausea, dizziness, sedation, pruritus, and dry mouth for tramadol and oxycodone, during the post-operative period (day 1 to day 3), n = 57 (NRS 0–100, mv, sd of several symptoms for each group)

n = 11, p = 0.707, chi-squared test) or additional NSAIDs (tramadol: n = 4, oxycodone: 2, p = 0.523, Fisher’s exact test) did not differ significantly. Additional NSAIDs were administered in cases where the rescue medication was considered insufficient (tramadol: 2, oxycodone: 1) and where there was no need for further rescue medication (tramadol: 2, oxycodone: 1). It involved dipyrone, rofecoxib, or celecoxib. Cumulative doses of dipyrone were 3500 mg (130 drops), 1200 mg celecoxib (6 capsules) and 75 mg rofecoxib (3 tablets).

During the postoperative period significant differences between the two groups emerged for nausea and emesis. Additionally, differences were significant for sleep maintenance-insomnia at day 3 (Fig. 1, Fig. 2, Table II). Nightmares occurred in the tramadol group only. Although these results lacked significance, myoclonus, sleep onset insomnia and sedation were more severe or frequent with tramadol, while dryness of the mouth was more severe with oxycodone. No group differences were seen for pruritus.

An additional detailed analysis of the NRS for pain at different given times over of the 3 days yielded no significant differences, except for the first morning of the observation with a significant higher NRS for oxycodone than for tramadol (oxycodone: mv, sd 27.88 ± 16.74; tramadol: mv, sd 19.03 ± 14.69; p = 0.044).
Comparison of controlled release oxycodone and tramadol

Figure 2. Symptom assessment: cumulative frequency of the symptoms emesis, sleep onset insomnia, sleep maintenance insomnia, nightmares, and myoclonus, for tramadol and oxycodone, during post-operative day 1 to day 3, \( n = 57 \) (\( n = \) cumulative number of patients with symptoms during the post-operative period).

Table II.
Pain scores, \( n = 57 \)

<table>
<thead>
<tr>
<th></th>
<th>Tramadol</th>
<th>Oxycodone</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain (rest) day 1</td>
<td>22.83 ± 17.03–20</td>
<td>27.93 ± 18.01–26</td>
<td>0.290</td>
</tr>
<tr>
<td>Pain (rest) day 2</td>
<td>17.10 ± 14.51–10</td>
<td>20.96 ± 16.38–20</td>
<td>0.316</td>
</tr>
<tr>
<td>Pain (rest) day 3</td>
<td>10.65 ± 13.88–5</td>
<td>16.30 ± 15.37–15</td>
<td>0.161</td>
</tr>
<tr>
<td>Pain (rest) day 1–3</td>
<td>16.67 ± 14.29–13</td>
<td>21.73 ± 15.40–20</td>
<td>0.209</td>
</tr>
<tr>
<td>Pain (exercise) day 1–3</td>
<td>16.96 ± 17.76–8.33</td>
<td>9.58 ± 7.98–10</td>
<td>0.649</td>
</tr>
<tr>
<td>Pain (rest) day 1 vs. 3</td>
<td>0.000</td>
<td>0.000</td>
<td>Ø</td>
</tr>
<tr>
<td>Pain (exercise) day 1 vs. 3</td>
<td>0.102</td>
<td>0.256</td>
<td>Ø</td>
</tr>
<tr>
<td>Need for rescue medication</td>
<td>11</td>
<td>8</td>
<td>0.707</td>
</tr>
<tr>
<td>Mean dosage rescue medication (mg/d/patient)</td>
<td>11.83</td>
<td>1.03</td>
<td>Ø</td>
</tr>
<tr>
<td>Mean daily dosage (mg/d/patient)</td>
<td>211.83</td>
<td>21.03</td>
<td>Ø</td>
</tr>
<tr>
<td>Additional use of NSAID</td>
<td>4</td>
<td>2</td>
<td>0.523</td>
</tr>
</tbody>
</table>

Differences between day one and day three

During the three-day observational period, NRS for pain at rest decreased significantly in both groups. Changes of pain levels (pain at rest) were all significant for each given time (\( p \)-values 7.00/14.00/19.00/22.00 h: oxycodone day 1 vs. day 3: 0.001/0.001/0.000/0.001; tramadol day 1 vs. day 3: 0.021/0.001/0.001/0.001). By contrast, pain during exercise on day 1 did not differ significantly from day 3 in either group (Table II).

Between day 1 and day 3, the severity of sedation and dizziness decreased significantly with tramadol, while with oxycodone, dryness of the mouth, and dizziness did, though not significantly. In both groups, changes of the NRS for sleep onset and maintenance-insomnia, nightmares, and myoclonus were either not significant or parameters remained constant.
Emesis and the use of anti-emetics

In the tramadol group, the number of patients who vomited remained constant but with an increasing frequency of vomiting. On day 1, all five patients vomited just once; on day two, three of five once and two twice; and on day three, three of five patients once, two twice and one three times. In both groups, the frequency of the use of antiemetics was not significantly different (oxycodone: n = 2, tramadol: n = 4; p = 0.523). Even though dosages of metoclopramide did not differ significantly, consumption in the tramadol group distinctly exceeded that in the oxycodone group (cumulative doses were in tramadol group: 131.2 mg in metoclopramide group 410 drops, in oxycodone group: 100 drops; p = 0.48). Additionally, one patient in the tramadol group received 210 mg of dimenhydrinate (3 suppositories). Side effects are shown in Table III.

discussion

Study design, patients, substances and formulation

In this prospective, controlled, randomized, double-blind trial, both treatment groups had a comparable background in terms of demographic and medical data or surgical procedure. We assume no major significant influences by the peri-operative agents because of a 'wash out' period of at least one night and their short half-time of metabolism and elimination. Post-operative pain therapy was acceptable with both CR tramadol and oxycodone, since no drop-outs due to side effects, excessive doses of rescue medication or changes of methods were registered. We could not discriminate possible influences on the premature discharge of five patients, as a better efficacy of oxycodone or the kind of the surgical procedure.

Most prior studies have analyzed CR oxycodone for cancer pain therapy, but few for post-operative analgesia. Previous comparisons of oral CR oxycodone and tramadol have not been reported for post-operative pain therapy after orthopedic surgical procedures, whereas in most studies oral oxycodone is compared with other substances and not with tramadol or else intravenous administration is studied.

In contrast to other studies, the combination with NSAIDs was restricted in this trial in order to assess distinctly the side effects of tramadol or oxycodone. Indirectly, our results might demonstrate the potential for a mono therapy with oral CR µ-agonists as an alternative to NSAIDs, in case of contraindications.

We used comparable CR formulations of tramadol and oxycodone. There is controversy as to whether CR formulations might have lower side effects than immediate release formulations. The attenuation of some symptoms agreed with results of another trial.

Dosage, efficacy, conversion ratio

The dosage of the study medication was effective for post-operative pain therapy after the chosen surgical procedures. The significantly higher pain level for oxycodone at the first recorded time in the investigation remains unclear. As we did not investigate plasma levels, we could not relate this neither to different pharmacokinetic parameters of both CR formulations, nor did we find a correlation to influences of different surgical procedures. Nevertheless, it was a short-term phenomenon, as no further differences of pain levels and the use of the rescue medication were observed at any other point in time.

Despite significantly decreasing pain levels at rest, improvement of pain during exercise from day one to three was poor in both groups, pointing to the need to improve post-operative pain therapy. Other authors used
Comparison of controlled release oxycodone and tramadol

Table III.
Daily assessment of symptoms, differences between the both opioids and between day one and three: \( n = 57 \) (NRS, \( n = \text{patients} \)) \# tramadol vs. oxycodone

<table>
<thead>
<tr>
<th>Symptom Substance</th>
<th>Day 1 (NRS resp. ( n ))</th>
<th>( p ) day 1</th>
<th>Day 2 (NRS resp. ( n ))</th>
<th>( p ) day 2</th>
<th>Day 3 (NRS resp. ( n ))</th>
<th>( p ) day 3</th>
<th>( p ) day 1 vs. day 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nausea</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tramadol (mg mv sd)</td>
<td>15.97 ± 24.58</td>
<td>0.082</td>
<td>15.81 ± 20.25</td>
<td>0.033</td>
<td>12.26 ± 15.86</td>
<td>0.012</td>
<td>0.305</td>
</tr>
<tr>
<td>Oxycodone (mg mv sd)</td>
<td>5.77 ± 15.54</td>
<td></td>
<td>7.69 ± 17.28</td>
<td></td>
<td>4.62 ± 14.21</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Emesis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tramadol (mg mv sd)</td>
<td>5</td>
<td>0.041</td>
<td>5</td>
<td>0.041</td>
<td>5</td>
<td>0.041</td>
<td>constant</td>
</tr>
<tr>
<td>Oxycodone (mg mv sd)</td>
<td>0</td>
<td></td>
<td>0</td>
<td></td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Sleep onset insomnia</strong></td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Tramadol (mg mv sd)</td>
<td>8</td>
<td>0.153</td>
<td>12</td>
<td>0.164</td>
<td>12</td>
<td>0.047</td>
<td>0.277</td>
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<td></td>
<td>6</td>
<td></td>
<td>4</td>
<td></td>
<td>0.685</td>
</tr>
<tr>
<td><strong>Sleep maintenance insomnia</strong></td>
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<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Tramadol (mg mv sd)</td>
<td>19</td>
<td>0.278</td>
<td>22</td>
<td>0.145</td>
<td>22</td>
<td>0.221</td>
<td>0.421</td>
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<tr>
<td>Oxycodone (mg mv sd)</td>
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<td>14</td>
<td></td>
<td>15</td>
<td></td>
<td>0.578</td>
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<tr>
<td><strong>Nightmares</strong></td>
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<tr>
<td>Tramadol (mg mv sd)</td>
<td>2</td>
<td>0.291</td>
<td>2</td>
<td>0.544</td>
<td>1</td>
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<tr>
<td>Oxycodone (mg mv sd)</td>
<td>0</td>
<td></td>
<td>0</td>
<td></td>
<td>0</td>
<td></td>
<td>constant</td>
</tr>
<tr>
<td><strong>Sedation</strong></td>
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<tr>
<td>Tramadol (mg mv sd)</td>
<td>22.90 ± 22.685</td>
<td>0.132</td>
<td>21.94 ± 18.52</td>
<td>0.146</td>
<td>15.16 ± 15.89</td>
<td>0.877</td>
<td>0.031</td>
</tr>
<tr>
<td>Oxycodone (mg mv sd)</td>
<td>13.85 ± 16.27</td>
<td></td>
<td>15.00 ± 17.94</td>
<td></td>
<td>15.38 ± 16.79</td>
<td></td>
<td>0.285</td>
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<tr>
<td><strong>Dizziness</strong></td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Tramadol (mg mv sd)</td>
<td>10.00 ± 17.51</td>
<td>0.446</td>
<td>9.03 ± 15.78</td>
<td>0.446</td>
<td>6.45 ± 13.55</td>
<td>0.844</td>
<td>0.015</td>
</tr>
<tr>
<td>Oxycodone (mg mv sd)</td>
<td>11.73 ± 16.79</td>
<td></td>
<td>10.38 ± 18.65</td>
<td></td>
<td>8.46 ± 16.90</td>
<td></td>
<td>0.173</td>
</tr>
<tr>
<td><strong>Myoclonus</strong></td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Tramadol (mg mv sd)</td>
<td>9</td>
<td>0.098</td>
<td>7</td>
<td>0.120</td>
<td>5</td>
<td>0.291</td>
<td>0.224</td>
</tr>
<tr>
<td>Oxycodone (mg mv sd)</td>
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<td>2</td>
<td></td>
<td>2</td>
<td></td>
<td>0.638</td>
</tr>
<tr>
<td><strong>Pruritus</strong></td>
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<td></td>
</tr>
<tr>
<td>Tramadol (mg mv sd)</td>
<td>4.19 ± 11.19</td>
<td>0.642</td>
<td>3.87 ± 10.86</td>
<td>0.662</td>
<td>3.55 ± 10.82</td>
<td>0.801</td>
<td>0.157</td>
</tr>
<tr>
<td>Oxycodone (mg mv sd)</td>
<td>3.46 ± 10.93</td>
<td></td>
<td>3.85 ± 12.35</td>
<td></td>
<td>4.23 ± 12.39</td>
<td></td>
<td>0.157</td>
</tr>
<tr>
<td><strong>Dry mouth</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tramadol (mg mv sd)</td>
<td>15.16 ± 18.23</td>
<td>0.140</td>
<td>13.55 ± 17.23</td>
<td>0.323</td>
<td>13.55 ± 17.43</td>
<td>0.291</td>
<td>0.493</td>
</tr>
<tr>
<td>Oxycodone (mg mv sd)</td>
<td>21.92 ± 17.89</td>
<td></td>
<td>18.08 ± 17.89</td>
<td></td>
<td>18.08 ± 17.89</td>
<td></td>
<td>0.041</td>
</tr>
</tbody>
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TIRS = numeric rating scales.
higher doses or the intravenous administration and demonstrated improvements of pain at exercise, function or mobilization for both oxycodone and tramadol.\textsuperscript{1,2,9,15,22,23} Due to the heterogeneity of the surgical procedures we did not evaluate functional improvement.

Comparable pain levels and the use of further medication in both groups support the calculated conversion factor of tramadol/oxycodone = 10/1,\textsuperscript{2,4,6,9,14,15,18,19,24-26} but further pharmacokinetic studies are needed to confirm the result by titration.

\textbf{Safety}

According to prior studies, neither substance generated any serious adverse effects on vital signs.\textsuperscript{2-4,7,14} Possibly, this might be related to the exclusion criteria. However, studies enrolling patients with organ malfunctions are difficult to execute owing to ethical restrictions. None of the CR formulations of either drug produced respiratory depression, contradictory to a publication on the intravenous administration reporting a significant higher incidence with oxycodone than with tramadol.\textsuperscript{16}

\textbf{Side effects}

\textit{Nausea, emesis.} Sunshine and Reuben found a lower frequency of nausea and vomiting with CR oxycodone than with oral immediate release oxycodone.\textsuperscript{8,12} Comparisons of analogous formulations of tramadol have not yet been published.

Comparisons of oxycodone with morphine reported no differences in the rates of nausea and emesis during the post-operative period,\textsuperscript{9,14,23} but reports on the use in cancer pain are ambiguous.\textsuperscript{18,19,21-25} Prior trials on tramadol showed varying incidences of nausea and emesis in comparison with other opioids.\textsuperscript{2-6,26}

The significant results of our trial on the oral CR formulation agree with Silvasti \textit{et al.}'s findings, which report a lower incidence of nausea and emesis for intravenous oxycodone than for intravenous tramadol. The higher consumption of anti-emetics with post-operative oral tramadol had also been demonstrated for intravenous administration.\textsuperscript{15}

\textit{Central symptoms.} While Silvasti found comparable central effects for tramadol and oxycodone,\textsuperscript{15} in this comparative trial we found that central effects such as sedation, sleep onset and maintenance-insomnia, and nightmares tended to be more frequent with tramadol. Prior studies comparing either oxycodone or tramadol with morphine showed diverging incidences of sedation, dizziness, impairment of mental state, sleep disturbances and nightmares.\textsuperscript{2,3,6,9,14,18,19,21,25,26} However, the attenuation of sedation and dizziness and the increase in sleep disorders in the tramadol group might correlate to central nervous effects of this substance and, from that, underline the impact of the noradrenaline and serotonin reuptake inhibition of this drug.\textsuperscript{4,26}

In the patients of our investigation, myoclonus emerged more frequently with tramadol than with oxycodone. Overall, the higher frequency of myoclonus contrasts with the findings of other authors.\textsuperscript{25,26} Nor did our patients suffer from organ impairment with the risk of the accumulation of \(\mu\)-agonists or their metabolites, nor were high dosages applied. Possibly, this symptom has been underestimated so far.

\textit{Pruritus, dry mouth.} The fact that no significant differences in the incidence of pruritus emerged agrees with other references.\textsuperscript{9,12,24} In general, this symptom was not severe with only low NRS.
Comparison of controlled release oxycodone and tramadol

Prior investigations comparing oxycodone or tramadol with morphine yield contradicting results on the incidence of dry mouth.\(^{3,24-26}\) Although autonomic nervous system effects such as dry mouth are principal symptoms of tramadol,\(^4\) the results of our trial indicate a higher rate with oxycodone, especially at the beginning of a therapy, although it decreased significantly over a three-day period.

conclusions

This trial demonstrates that the oral controlled release administration of oxycodone and tramadol for therapy of post-operative pain is effective, safe, and convenient, even as a mono treatment. Although oxycodone is a highly potent opioid, its side-effect profile seems to be more favorable than that of the less potent \(\mu\)-agonist tramadol. Because of a reduced frequency and severity of the symptoms of nausea and vomiting, the use of oxycodone should replace the recent practice of using tramadol for the management of post-operative pain therapy.

references