Comparison Between Intravenous Patient Controlled Analgesia And Subcutaneous Morphine In Patients After Gastrectomy
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Citation

Abstract
The Aim of this study was to evaluate the effectiveness on postoperative pain, by intravenous patient-controlled analgesia (PCA) using morphine compared with subcutaneous (s.c) injections of morphine on demand in patients undergoing gastrectomy, so that subcutaneous morphine if found to have comparable efficacy and safety could be used in the setting of developing nations with less manpower and insufficient monitoring equipments. Fifty patients of either sex weighing b/w (56-80) kg & age b/w (60-80) were randomly assigned to two different postoperative analgesic techniques for 24 hrs: i.v. PCA morphine (dose, 1 mg; lockout interval, 10 min; PCA group) or regular s.c. morphine injections (SC group) on demand. Postoperative pain was assessed using a visual analogue scale (VAS). Side-effects were also recorded systematically during the first 24 h after surgery. The PCA group showed lower pain scores than the SC group. However the clinical significance of pain scores was weak. The incidence of side effects was similar in both the group. We conclude that in healthy subjects with ASA I and ASA II status for gastrectomy, the postoperative pain can be managed effectively and safely using subcutaneous route for administration of morphine. This is true especially in a set up where level of nursing care is limited and high dependency units are not available to monitor patients with epidural or intravenous opioids.

INTRODUCTION
Postoperative pain is one of the most feared and probably the most prevalent of all pain conditions, yet in many cases it continues to be inadequately treated. Physicians, nurses, and patients alike fear opioids, even though they remain the mainstay of acute pain treatment. Furthermore, because of the acute and finite nature of postoperative pain, a degree of complacency in treating it sometimes prevails. In 1990, The Royal College of Surgeons (RCS) report ‘pain after surgery’ found 30–70% patients with moderate or worse pain after surgery. A recent review finds that although the incidence of post-operative pain has reduced by ≈2%/year for the last 30 years, 30% of patients still complain of moderate pain and 11% severe pain. Patient-controlled analgesia (PCA) has emerged as a standard technique for management of acute postoperative pain. In addition to being an efficacious analgesia, several advantages such as high patient acceptability, faster postoperative recovery, earlier hospital discharge and reduced nursing time have been ascribed to PCA (reviewed by Macintyre). However, some of the more recent studies comparing the efficacy of PCA with that of conventional methods of opioid analgesia have produced conflicting results. Choiniere and colleagues have demonstrated that PCA is more expensive and does not offer clinical advantages over regular i.m. dosing for pain management after hysterectomy. We performed a prospective randomized study in patients undergoing gastrectomy, to evaluate the effectiveness on postoperative pain, by intravenous patient-controlled analgesia (PCA) using morphine compared with subcutaneous (s.c.) injections of morphine on demand in patients undergoing gastrectomy, so that subcutaneous morphine if found to have comparable efficacy and safety could be used in the setting of developing nations with less manpower and insufficient monitoring equipments.

METHODS
After informed consent a total of 50 patients of either sex weighing between 56-80 kg and age between 60-80 years belonging to ASA-I and ASA-II presenting for elective
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gastrectomy were included in the study.

Patients with history of moderate to severe vomiting in previous operation as a result of opioid use and Patients with developmental disability or cognitive impairment which limit understanding of PCA therapy or limits successful interface with the pump were excluded from the study.

Patients were assigned to two groups:

Group I: 25 patients in whom subcutaneous morphine was given for Postoperative pain relief.

Group II: 25 patients in whom intravenous patient controlled analgesia (PCA) with morphine was given for Postoperative pain relief.

We used a concentration of morphine 1mg/ml in normal saline for PCA pump. Bolus dose of 1mg with lockout interval of 10 minutes without back ground infusion were the settings used for PCA pump. For subcutaneous group we used 0.1mg/kg body weight of morphine on demand through an indwelling 22G venflon sited in right or left arm.

Patients were premedicated with tab. Alprazolam 0.25mg on night before surgery. On arrival to the operating room, after establishing i/v line, patients were connected to datex ohmeda monitor for monitoring of electrocardiography, noninvasive blood pressure & saturation of oxygen.

Anaesthesia was induced with 0.1mg/kg of morphine and 4-7mg/kg of thiopentone sodium and suxamethonium 1.5mg/kg was used to achieve endotracheal intubation and anaesthesia was maintained with N2O 66%, O2 33% supplemented with 0.5-1.5% halothane & muscle relaxation was maintained with pancuronim bromide 0.1mg/kg.

At the end of surgery residual neuromuscular block was antagonized with appropriate dose of neostigmine in atropine. After surgery patients were transferred to the post anaesthesia care unit (PACU) and were asked after every 10 minutes to rate their pain using the visual analogue scale.

Patients assigned to the s.c group received 1st injection of morphine 0.1 mg/kg four hours after the study started or earlier if they reported inadequate pain relief (pain score > 30). The injections were repeated whenever patient reported pain (VAS > 30). Patients assigned to the PCA group received bolus doses of morphine 2mg IV, repeated after every 15 minutes till their VAS was less than 30, then they were attached to PCA pump and received bolus doses of morphine on demand, lock out interval of 10 minutes and no background infusion.

Side effects of the analgesic procedure like arterial hypotension (systolicBP< 90mmHg), respiratory depression (respiratory rate < or = 8 b/min.), sedation score (0= awake, 1 = sleepy but awakened by oral order, 2 = sleepy but awakened by tactile stimulation, 3 = not awakened), urinary retention (inability to urinate, requiring a urinary catheter to empty the bladder, Nausea & vomiting (yes or no) & pruritis (yes or no) were recorded. The amount of morphine used was recorded for 24 hours after surgery.

Finally all study observations were documented and tabulated, they were analyzed statistically and results were recorded.

The statistical analysis of the data was done by using statistic student’s t-test for difference of means for quantitative data analysis.

For nominal data chi-square test (χ²-test) and fisher’s exact test were used.

All these tests were two sided and were referred for p-values for their significance. Any p-value less than 0.05 i.e. (p< 0.05) were taken to be statistically significant.

The analysis of the data was performed on statistical package for social sciences (SPSS ner 10.0), Chicago, USA for windows.

RESULTS

Age, sex, weight, height and ASA physical status were comparable between the two groups. Mean age of the patients in sc group and PCA group was 64.08 and 63.8 years respectively (table 1.)

Mean duration of anaesthesia was 147 minutes and 150 minutes in sc group and PCA group respectively, the comparison was statistically non significant,

Mean intraoperative morphine requirement in the two groups was 4.8 and 4.7mg respectively with a statistically non significant comparison. Similarly morphine given in the recovery room before the study started was same in both the groups (3.5± 0.0mg at the time before the study period time started).

Mean morphine consumption of subcutaneous group in 24 hours was 11.68 with standard deviation of 1.46 and mean morphine consumption of PCA group in 24 hours was 12.64
with standard deviation of 1.35. The relationship between the two groups was significant (p 0.028) thereby implying that consumption of morphine was more in PCA group (Table 2).

VAS scores were lower in the PCA group than in the SC group at most of test times as shown in fig.1. VAS was more in SC group then in PCA group at 1, 2, 3 and at 4hour that was statistically significant (p < 0.05) but for rest of the study period it remained statistically non significant. However throughout the study period VAS in both the groups remained below 35 which is an indicator of good postoperative pain relief (Fig 1).

In Sc group 8% cases had vomiting as compared to 10% in PCA group. As all the patients were catheterized before surgery, so there was no question of urinary retention. 8% cases in SC group had hypotension as compared to 10% in PCA group, hypotension was treated with fluids and bolus of 0.5mg ephedrine only. Similarly 10% cases had prurites in both the groups and were treated with diphenhydramine 25–50 mg IV 6 hourly. Incidentally all the side effects mentioned above were statistically non significant (Table 3).

**DISCUSSION**

Postoperative pain leads to higher morbidity, increased hospital stay and delayed recovery after major surgical procedure. Failure to recognise the extent of pain and fear of precipitating respiratory depression may lead to analgesia being with held, resulting in irregular administration, fluctuating plasma levels and hence inadequate pain relief. Continuous opioid infusion and epidural analgesia may provide superior pain relief in this regard. After gastrectomy PCA and s.c morphine provided an effective analgesia during the first 24 h after surgery. Despite PCA group had lower VAS score than s.c during most of the time still both the groups had better pain relief. Monitoring of the patient after surgery was not performed in a blinded fashion because of the clinical conditions of the study. It is technically difficult to achieve true double blinding in comparisons of PCA and conventional analgesia (s.c. injections). Rayburn and colleagues abandoned a double-blind trial after finding that patients could distinguish placebo from genuine PCA infusions.

The minimal difference in opioid requirements and the comparable side-effects in both groups are in agreement as reported by H. Keïta and etal. Our data support the view that s.c morphine is equally effective than PCA morphine administration in reducing pain. Opioid self-administration has also been shown to be effective using s.c. route. Although the VAS scores were significantly different between the groups at certain interval of time, the clinical relevance of these results has to be discussed. It could be argued that the median score in the PCA and s.c group was 30 mm or less at 24 hours, which is commonly considered as good and effective analgesia. H. Keïta and etal has reported that PCA and s.c morphine both are effective for postoperative pain relief. Preoperative patient selection allowed us to identify patients with preexisting cognitive impairment, who were subsequently excluded from the study. The incidence of side-effects was similar in the PCA and SC groups. This is supported by the study done by H. Keïta and colleagues. However Choiniere and colleagues observed no differences between two groups of patients (PCA compared with regular i.m. injections of morphine) after hysterectomy in terms of opioid side-effects and analgesia, others have reported a lower incidence of side-effects withPCA. The incidence of respiratory depression with conventional methods of opioid administration is reported to be in the range of 0.2±0.9%, and an incidence of 0.1±0.8% has been reported with PCA. Increased incidences of 1.1±3.9% have been found when a concurrent background infusion is used. We did not use any background infusion with the PCA in our study, and we did not observe any respiratory depression in either group. Regardless of the route of administration of morphine, we reported a low incidence of nausea and vomiting (10% and 8% for the PCA and SC groups, respectively). Such results (or lower incidences) were found because of use of antiemetics after the end of surgery.

Costs involved in the provision of analgesia, including the direct costs of drugs, consumables, equipment, and labour, are important when considering whether or not to use a particular method of pain relief, even if it is more effective. Jacox and colleagues reviewed seven studies published from 1984 to 1995 which compared costs related to PCA and i.m. opioid analgesia. They concluded that while PCA may provide superior analgesia and patient satisfaction, it does so at a higher cost. Similar results have been reported by other authors.

A significant part of the cost of PCA is the cost of equipment, drugs, and consumables. Therefore, in a busy general hospital ward like ours where the number of appropriately qualified nurses are limited and few PCA...
pumps are available, it is possible that the use of sc morphine in post operative patients may allow more time to attend to other duties.

In summary, the current study indicates that in healthy subjects with ASA I and ASA II status for gastrectomy, the postoperative pain can be managed effectively and safely using subcutaneous route for administration of morphine. This is true especially in a set up where level of nursing care is limited, high dependency units are not available to monitor patients with epidural or intravenous opioids and PCA pumps are not available in sufficient number because of cost, so this route of administration will be more cost effective.

As compared to intravenous injections which are painful, subcutaneous route is associated with least discomfort to the patients as the cannula is sited subcutaneously during surgery and subsequent injections are given through this cannula in the postoperative ward.

We recommend the subcutaneous route to be used for administration of morphine in patients for gastrectomy and other upper abdominal surgical procedure.

Figure 1
Table 1 Patient characteristics, surgical variables in the two groups. Data are median (25th±75th percentiles) [range], number of patients or actual number(%)..

<table>
<thead>
<tr>
<th>SC group</th>
<th>PCA group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>68 (60-80)</td>
</tr>
<tr>
<td>Male/female</td>
<td>18/7</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>63 (55-75)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>160 (155-165)</td>
</tr>
<tr>
<td>ASA physical status I/II</td>
<td>19/6</td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>130 (110-150)</td>
</tr>
<tr>
<td>Duration of anaesthesia (min)</td>
<td>147 (140-165)</td>
</tr>
<tr>
<td>Halothane (%)</td>
<td>1.1 (0.4-1.5)</td>
</tr>
<tr>
<td>Intrathecal morphine (mg)</td>
<td>4.8 (4.5-6)</td>
</tr>
<tr>
<td>Morphine (mg) in recovery</td>
<td>3.5 (3.5-3.5)</td>
</tr>
</tbody>
</table>

Figure 2
Comparison of visual analogue scale(VAS) for the two groups at various intervals.

Figure 3
Table 2 Postoperative morphine consumption in mg in the two groups.

<table>
<thead>
<tr>
<th>Morphine consumption</th>
<th>Mean ± S.D</th>
<th>t-value</th>
<th>p-value</th>
<th>result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>11.68 ± 1.46</td>
<td>2.34</td>
<td>0.028</td>
<td>sig.</td>
</tr>
<tr>
<td>Group II</td>
<td>12.64 ± 1.35</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 4
Table 3 Frequency of principal side-effects in the two groups. Values are percentages. There were no statistically significant differences between the groups.

<table>
<thead>
<tr>
<th>SC group</th>
<th>PCA group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypotension</td>
<td>(Systolic pressure &lt;90 mm Hg)</td>
</tr>
<tr>
<td>Respiratory depression</td>
<td>0</td>
</tr>
<tr>
<td>(ventilatory frequency&gt;8 bpm)</td>
<td>0</td>
</tr>
<tr>
<td>Sedation &gt;2</td>
<td>0</td>
</tr>
<tr>
<td>Urinary retention</td>
<td>0</td>
</tr>
<tr>
<td>Nausea and vomiting</td>
<td>8</td>
</tr>
<tr>
<td>Pruritus</td>
<td>10</td>
</tr>
</tbody>
</table>

References
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