Letter to the Editor

Does multimodal analgesia premedication improve the management of carcinoma cervix brachytherapy?

To the Editor:

We report a retrospective study of premedication with multimodal analgesia for the management of outpatient carcinoma cervix brachytherapy performed under sedation. High-dose-rate (HDR) brachytherapy is a radiation treatment technique that involves the application of localized internal radiation to the cervix. After the initial external radiation treatment, each patient usually receives three HDR brachytherapy treatments that are administered at weekly intervals. The HDR brachytherapy procedure itself lasts for approximately 2 h and is performed under sedation, with regional or general anesthesia (1-4).

When HDR brachytherapy was initiated at the Ottawa Hospital (Ottawa, Ontario) in July 2008, the first six patients completed their course of treatment under intravenous sedation alone. The seventh patient required a large amount of intravenous sedation and analgesia for the first two treatments; a multimodal analgesia protocol was instituted for the patient’s third treatment and has been continued since. This premedication protocol consisted of two tablets of Tramadol (37.5 mg tramadol and 325 mg acetaminophen, Janssen-Ortho Inc, Canada) and 75 mg pregabalin, administered orally on arrival to the brachytherapy unit approximately 2 h before the procedure.

The present retrospective study was undertaken following approval by the Research and Ethics Board of the Ottawa Hospital. The charts of 18 consecutive patients treated at the centre from July 2008 to March 2010 were reviewed. Each patient underwent three HDR brachytherapy treatments. Excluding incomplete or missing records, a total of 39 treatments were analyzed. The study group consisted of 22 HDR brachytherapy treatments that included premedication with orally administered multimodal analgesia. This group was compared with a control group consisting of the preceding 17 treatments, which did not include premedication. No significant difference in demographic variables between the study and control groups was observed. Patients in the study group received a significantly lower mean dose of midazolam (Table 1). Although multimodal premedication also resulted in decreased analgesic requirements, decreased pain scores and a shorter duration of procedure with increased total recovery score and duration of stay, none of these differences were statistically significant. No operative or treatment complications were reported in either group.

We have found that cervical carcinoma is a unique situation in which the patient is often a middle-aged healthy woman with a recent treatment of a genitourinary malignancy with external radiation. There is, therefore, an expected increase in anxiety, distress and discomfort in this patient population, especially when positioned in lithotomy for the HDR brachytherapy procedure (5). The procedure itself is associated with pain that is described as mild to moderate in intensity, burning in quality and well localized to the pelvis and perineum (5,6). In this acute pain model, which neuropathic pain and hyperalgesia may be present, poor response to opioids and benzodiazepines may be expected (3,7). The multimodal analgesia protocol for HDR brachytherapy used in the present study was designed to address the nature and character of this particular pain model (moderate intensity with hyperalgesia). Pregabalin is not only known to decrease neuropathic pain and hyperalgesia; it also has sedative, anxiolytic and sleep restorative properties that, in our opinion, give tramadol a unique effectiveness in treating moderately severe acute pain that is associated with hyperalgesia, while maintaining an excellent safety and side-effect profile.

For patients undergoing radiation therapy, remaining pain free and comfortable during the treatment may allow for the procedure to be completed effectively in a short time. No significant changes in sedation, level of consciousness or oxygen saturation that may occur in some patients receiving pregabalin (9) were observed in the study group. The increased duration of stay may suggest a prolonged recovery period in the study group administered premedication, although the study was not powered to demonstrate this difference. Nevertheless, the present retrospective quality assurance study contributes to our experience of safety with ‘out of operating room sedation’ reflected in the smaller dose ranges of intravenously administered drugs during the procedure. We hypothesize that this may be due, in part, as previously explained, to a ‘normalization’ of the hyperalgesia in some of the patients undergoing radiation therapy (9).

The drawbacks of the present retrospective study include the small sample size, its retrospective design, and lack of blinding or control for other variables. While the present study suggests that premedication with multimodal analgesia may improve the management of HDR brachytherapy, further research is required in this area.

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Table 1: Outcomes in study variables in control and study groups

<table>
<thead>
<tr>
<th>Study variable</th>
<th>Control group (n=17)</th>
<th>Study group (n=22)</th>
<th>Estimate of difference</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Midazolam, mg</td>
<td>3.4±2.8</td>
<td>2.6±0.9</td>
<td>−1.49±0.73</td>
<td>0.0485</td>
</tr>
<tr>
<td>Morphine equivalents, mg</td>
<td>11.9±4.5</td>
<td>9.9±3.4</td>
<td>−2.65±3.96</td>
<td>0.2513</td>
</tr>
<tr>
<td>Pain, 0 to 2</td>
<td>1.8±0.2</td>
<td>1.7±0.2</td>
<td>−0.008±0.10</td>
<td>0.9392</td>
</tr>
<tr>
<td>Duration of procedure, min</td>
<td>153.6±36.2</td>
<td>147.9±43.1</td>
<td>−11.47±19.37</td>
<td>0.5615</td>
</tr>
<tr>
<td>Duration of stay, min</td>
<td>202.4±76.7</td>
<td>242.2±62</td>
<td>27.7±33.93</td>
<td>0.4255</td>
</tr>
<tr>
<td>Total recovery score, 0 to 12</td>
<td>11.7±0.3</td>
<td>11.6±0.4</td>
<td>0.015±0.15</td>
<td>0.9193</td>
</tr>
</tbody>
</table>

Data presented as mean ± SD unless otherwise indicated. Differences between groups were estimated by mixed-model analysis for each variable, demonstrating the impact of pre-emptive treatment.
REFERENCES

Poster Presentation: Canadian Anesthesiologists Society, Toronto (June 2011) and International Anesthesia Research Society, Boston (May 2012).

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