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Opioid consumption and pain in gynecological cancer patients treated with interstitial brachytherapy

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ABSTRACT

PURPOSE: Interstitial brachytherapy (ISBT) has advantages over the intracavitary techniques in the treatment of gynecological malignancies. The insertion of catheters into tumor enables higher dose conformality and normal tissue sparing. However ISBT can be associated with pain due its invasiveness. The goal of this study is to assess pain and opioid consumption of patients implanted with a perineal ISBT applicator.

METHODS AND MATERIALS: Forty-eight patients were treated with ISBT from September 2014 to April 2016. Mean age was 63. Malignancies included 18 cervical cancers, 12 vaginal, 14 recurrent endometrial, and four others. Patient characteristics and technical ISBT data were collected. Opioid consumption was quantified as oral morphine equivalent per day (OMEq/day) from postimplant until removal. Pain score levels were collected by using an 11-point scoring system.

RESULTS: Twenty-three patients had a single ISBT implantation, whereas 25 had a second. Twenty-eight patients required IV-patient-controlled analgesia. Mean OMEq/day for the first insertion was 55 mg. In the second insertion, an increase of 22 mg was seen ($p = 0.0004$). Patients with IV-patient-controlled analgesia had higher opioid consumption (OMEq/day 69.8 mg vs 32.1 mg, $p = 0.001$) and maximum pain scores (5.5 vs 3.4, $p = 0.007$) as compared with patients on oral opioids. Higher levels of pain were detected in the first hours postimplant. Previous opioids and age were associated with increased opioid consumption.

CONCLUSIONS: Pain from perineal-ISBT can be managed with oral opioids in a select group of patients. For repeat insertions, there may be an increase in opioid consumption. While age and previous opioids affected opioid requirements, other factors such as number of needles and insertion depth were not associated factors.

Keywords: Interstitial brachytherapy; Gynecologic malignancy; Opioid use; Pain

Introduction

Perineal-based interstitial brachytherapy (ISBT) is an effective treatment for locally advanced gynecological malignancies and has been available for decades in specialized cancer centers. The technique delivers high-dose conformal radiation and has been shown to result in improvements in local control for bulky cervical tumors (1) and other gynecological cancers. The advantages of ISBT together with the advent of three-dimensional (3D) image-based brachytherapy have led to a growing interest in adopting this technique to improve outcomes for patients with advanced gynecological tumors. However, perineal ISBT is perceived as an invasive procedure as it involves the placement of sharp catheter needles directly through the perineum to reach the tumor and target tissue. This perception along with concerns of pain and complications have stagnated the development of expertise in this important technique.

Despite its apparent invasiveness, the impact of ISBT on pain levels in patients undergoing gynecological

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cancer treatment has not been well-characterized. As it is generally felt that the pain experienced is significant, standard ISBT postprocedure protocols typically include patient-controlled analgesic (PCA) pumps or epidural for pain control (2). However, it is generally unknown what dosage of opioids is required postimplant or whether oral analgesics can adequately control pain for ISBT. In addition, due to the complexity of ISBT treatment, a wide variation of practice protocols exist in regard to the number of needles inserted per implant and the number of implants or fractions prescribed each treatment. These factors may affect the experience of the ISBT patient and impact the level of pain and discomfort associated with this treatment.

The goal of this study is to investigate the opioid consumption and pain levels in patients treated with interstitial brachytherapy in a single-institution study. The secondary objective is to determine associated factors to opioid use in ISBT.

Methods and material

Cohort

Forty-eight patients were treated with interstitial brachytherapy from August 2014 to April 2016 at a single institution and retrospectively reviewed. The majority of the ISBT treatments were given as a boost after EBRT for locally advanced cervical and vaginal cancers or as a salvage treatment after recurrence. Eight patients with metastatic disease or previous radiation to the pelvis received ISBT as a single-treatment modality. In general, cervix and bulky vaginal cancers were treated with two insertions, whereas more elderly and fragile patients received brachytherapy with a single insertion. Patients with recurrent endometrial cancer in the vagina were also treated with a single insertion.

Implant procedure

A preassessment MRI with a vaginal cylinder inserted is done 1−2 weeks before the procedure to aid in preplanning of needle depth and location. Our ISBT institutional standard is general anesthesia with intravenous induction agents (propofol) and maintenance with opioids and either propofol infusion or halogenated inhaled anesthetics. For patients with cervical cancers and an intact uterus, an intracavitary tandem is used along with a vaginal obturator. For patients with vaginal tumors, the vaginal obturator alone is used (no tandem). A disposal perineal template applicator (Best Medical Systems, Inc, Springfield VA) is placed over the obturator. With the template positioned against the perineum, plastic catheters (6F 24 cm) containing metal stylets are inserted through the template holes and obturator grooves, piercing the perineum and vagina respectively. The number, position, and depth of the inserted needles are based on intraprocedural physical evaluation and on preplanning based on the preassessment MRI. The mean procedure time is 75 minutes. After anesthesia recovery, patients are imaged with CT and/or MRI scans for treatment planning. For treatments completely delivered with one single insertion, the goal is to deliver 2−3 fractions of radiotherapy with a minimum 6 hours interval between each fraction. This requires another day of inpatient admission after the procedure day.

After applicator insertion, treatment planning takes place while the patient is in bed with a urinary catheter in place. Subcutaneous low molecular weight heparin and antiembolic stockings are used for deep venous thrombosis prophylaxis during this period of immobilization. Low residue diet and diphenoxylate hydrochloride 2.5 mg plus atropine sulfate 0.025 mg tablets are prescribed to reduce gastro-intestinal motility while the ISBT applicator is in situ. Antiemetics and anxiolytics are provided, if necessary. The patient is turned to her side every 2 h to decrease risk of pressure ulcers. Routine vitals and pain scores are monitored.

All ISBT were implanted in the early morning of day one and the majority of the applicators were removed in the following day (day 2) at late afternoon/early evening with a mean implant time of 32 hours. One patient had the applicator removed after day 2 (on day 5) due to a different fractionation schema. To address pain during the postoperative period, pain levels are scored by the nursing staff using the standardized verbal rating score for pain (VRS), an 11-point Likert scale (3, 4), every 10 minutes immediately after the procedure and then every 4 to 8 h until applicator is removed. Analgesia is prescribed in the form of oral opioids (commonly hydromorphone 4−6 mg every 2 hours) as needed or through intravenous patient-controlled analgesia pump (IV-PCA) in the recovery room after the procedure. Patients prescribed with IV-PCA also received low-dose controlled release opioids and non-opioid analgesics were not contraindicated (acetaminophen, NSAID, pregabalin). Pain pump prescription was determined by the oncologist and/or anesthetist during preoperative assessment or during the postoperative recovery period. No formal criteria was used to guide pain pump prescription, but this decision was commonly tailored by patient's pain level throughout external radiation therapy, preprocedural anxiety level and baseline opioid consumption. The initial IV-PCA regimen prescribed was hydromorphone 0.2 mg intravenous with a lockout of 5 minutes. The PCA dose was increased, to a maximum of 0.4 mg, if the patient experienced inadequate analgesia (VRS $>$ 5). Different opioids medications (hydromorphone, morphine, oxycodone, and fentanyl) were prescribed for pain control, in this cohort of patients.

The implant removal was performed without general anesthesia or conscious sedation. Some patients requested prophylactic opioid medication before applicator removal.