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Review

Patient controlled epidural *vs* intravenous analgesia in gynecologic oncology: A systematic review

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Abstract

Background: Gynecologic oncology surgery includes a large variety of procedures which are mainly characterized as major abdominal operations. To date, the effectiveness of patient-controlled epidural analgesia (PCEA) has not been comparedto patient-controlled intravenous analgesia(PCA) for postoperative pain management in patients undergoing these procedures.

Objective: The purpose of the present systematic review is to evaluate the effectiveness of PCEA compared to traditional PCA analgesia.

Methods: We conducted a systematic review searching the Medline (1966-2016), Scopus (2004-2016), Clinical Trials.gov (2008-2016), Cochrane Central Register of Controlled Trials CENTRAL (1999-2016) and Google Scholar (2004-2016) databases together with reference lists from included studies. All prospective and retrospective observational cohort studies were included.

Results: Four studies were finally included in our review which involved 512 women. Two studies reported that PCEA is superior to PCA in terms of postoperative VAS pain scores ($p<.05$). The remaining two did not support these findings. The two methods seem to be comparable in terms of side effects, including nausea and postoperative ileus.

Discussion: According to our systematic review there seem to be evidence which support the use of PCEA in gynecologic oncology patients. However, given the small number of published studies and the increased costs of the later method for postoperative pain management further research is needed to corroborate our findings.

Key words: epidural; PCEA; PCA; gynecologic oncology

Introduction

Gynecologic oncology surgery includes a large variety of procedures which are mainly characterized as major abdominal operations[1-3].They are complicated by various adverse effects including gastrointestinal paralysis, nausea, vomiting, pain and cardiopulmonary complications.

Several factors of postoperative care have been

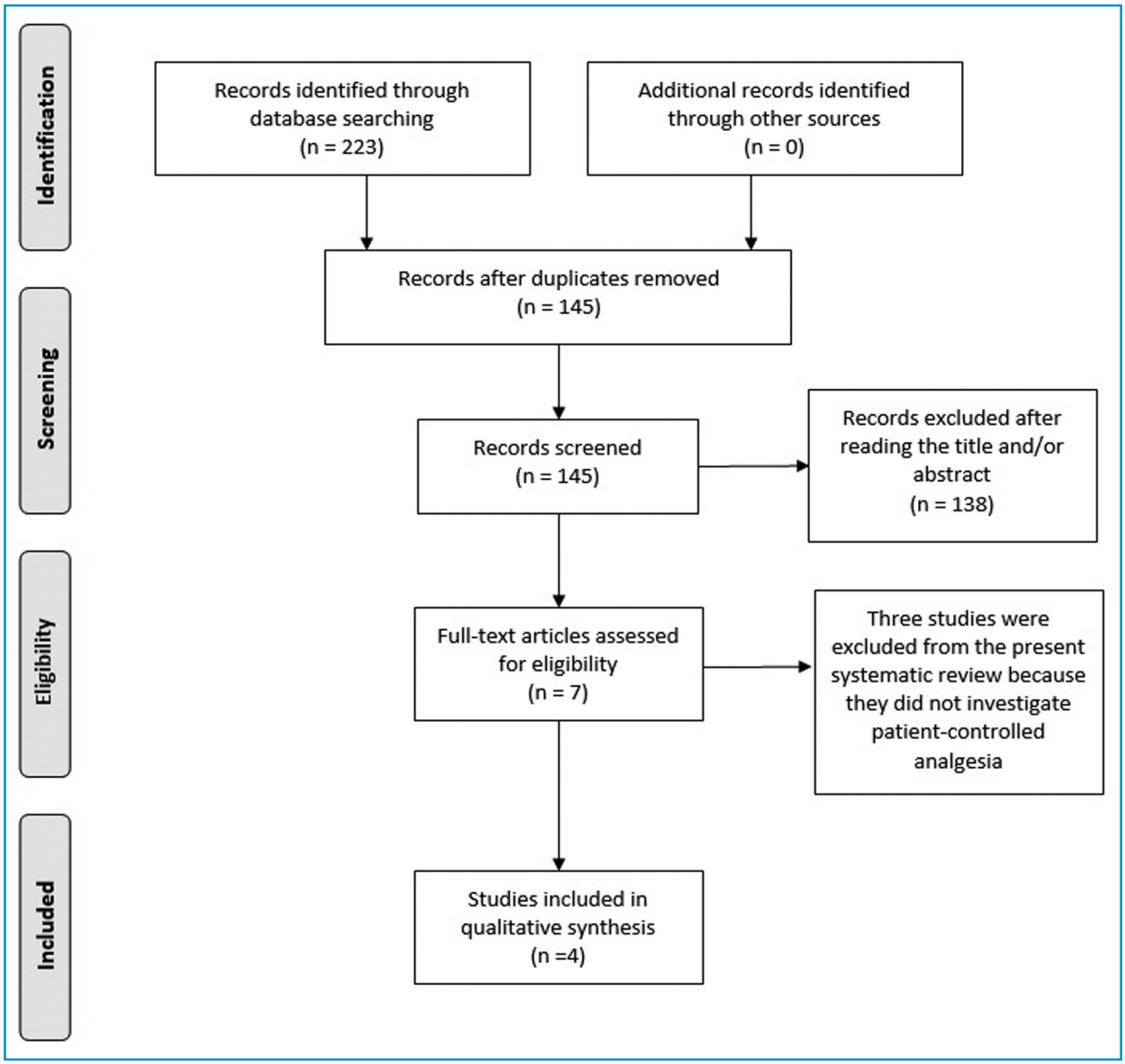

Figure 1. Search plot diagram

found to improve recovery, morbidity and need for hospitalizationfor hospitalization[4]. Among them,sufficient pain relief seems to playa critical role. To date, several techniques are used to manage postoperative pain in the field of surgery including patient- controlled analgesia (PCA) with intravenous opioids, epidural analgesia and non-steroidal anti-inflammatory drugs (NSAIDs)[5,6]. For years,patient controlled analgesia has been considered as an efficient alternative to conventional systemic analgesia[7]. Current evidence has proven lately, thatthoracic patient controlled epidural (PCEA)which uses a combination of opioid and local anesthetics offers superior postoperative pain control[8-10].

To date, however, these evidence have not been introduced in the field of gynecologic. Furthermore, the findings of previous studies, whose references focus on analgesia and restoration of bowel function, are contradicting each other[1]. The purpose of this systematic review is to compare the effective-

Table 1. Study characteristics (epidural *vs* iv)

Date; author	Type of study (OLE)	Inclusion criteria	Epidural analgesia
2015; Moslemi	RCT (1b)	Women with ASA physical status of I, II or III, aged 40 to 60 years, undergoing major gynecologic oncologic surgeries without contraindications to epidural catheter placement, history of anaphylaxis or contraindication to bupivacaine or fentanyl	0.5% bupivacaine and 1.5 µg/mlfentanyl *vs* 300 µg (6 mL) fentanyl, 200 mg (4 mL) pethidine and 8 mg (2 mL) ondansetron in 0.9% normal saline with a total volume of 100 mL
2015; Courtney-Brooks	Retrospective (2b)	Women without a history of chronic narcotic use, defined asdaily narcotic use in the 30 days prior to surgery, known voidingproblems, and known ambulation difficulties	N/A
2009; Ferguson	RCT (1b)	Women 18 years and older undergoingabdominal surgery by laparotomy for a gynecologic disorder without contraindications to epidural catheterplacement, history of anaphylaxis or contraindication to bupivacaineor morphine, planned total pelvic exenteration, planned laparoscopicsurgery only, palliative surgery for malignant bowel obstruction,emergency surgery, inability to take oral intake, and current history ofchronic (within last three months) opioid use or known active alcohol	0.05% bupivacaine with morphine 100 µg/mL *vs* 1 mg/h with morphine rescueboluses of 1 mg every 10 min
2009; Chen	Prospective (2b)	Gynecologiconcology patients undergoing laparotomy who were not taking opiate painmedications in the month prior to surgery	0.125%ropivicaine and 2 µg/ml fentanyl at 6–8 ml/h *vs* hydromorphone 0.2 mg
2014; Rivard	Retrospective (2b)	Gynecologiconcology patients undergoing laparotomy via a vertical midline abdominal incisionfor a known or suspected gynecologic malignancy	0.125% or 0.0625% bupivacaine with dilaudid 3-6 mcg/ml

Table 2. Pain outcomes (epidural vs iv)

Date; author	Patient No.	VAS 24 hours	VAS 48 hours
2015; Moslemi	45 *vs* 45	1.51±1.14 *vs* 0.69±0.73	0.56±0.01 *vs* 0.20±0.50
2015; Courtney-Brooks	56 *vs* 181	2.6 *vs* 4.0	2.5 *vs* 3.5
2009; Ferguson	67 *vs* 68	5.5 *vs* 6.7	5.0 *vs* 6.5
2009; Chen	107 *vs* 98	2.4 *vs* 2.5	N/A
2014; Rivard	38 *vs* 44	3.3 *vs* 4.1	3.0 *vs* 4.0
Adverse effects (epidural *vs* iv)			
Date;author	**Patient No.**	**Nausea**	**Ileus**
2015; Moslemi	45 *vs* 45	10/45 *vs* 13/45	0/45 *vs* 4/45
2015; Courtney-Brooks	56 *vs* 181	16/56 *vs* 44/181	N/A
2009; Ferguson	67 *vs* 68	41/62 *vs* 35/62	7/67 *vs* 4/68
2009; Chen	107 *vs* 98	N/A	N/A
2014; Rivard	38 *vs* 44	N/A	6/38 *vs* 4 /44

ness of PCEA to PCA for postoperative pain management in gynecologic oncology procedures. In addition, the reported adverse effects of each analgesic method will be evaluated.

Methods

Study design

We designed our study taking in mind the PRISMA guidelines[11]. Eligibility criteria were predetermined by the authors. No language or date restrictions were applied during the literature search. All observational studies, prospective and retrospective were held eligible for inclusion. Case reports were excluded. Two authors abstracted and tabulated predetermined data to a structured form, while the rest reviewed them independently. Discrepancies between the authors during data collection were resolved by the consensus of all authors.

Literature search and data collection

We used the Medline (1966-2016), Scopus (2004-2016), Clinical Trials.gov (2008-2016), Cochrane Central Register of Controlled Trials CENTRAL (1999-2016) and Google Scholar (2004-2016) search engines in our primary search, together with reference lists from included studies. We restricted our search strategy to a minimum number of keywords in order to assess an eligible number that could be hand searched, minimizing the loss of articles. All the articles which met or were presumed to meet the inclusion criteria were retrieved in full text.

We searched the literature using the words "epidural, gynecologic oncology, patient control". The PRISMA flow diagram summarizes the process of article retrieval (Figure 1).

Quality assessment

We assessed the methodological quality of all included studies using the Oxford Level of Evidence (OLE) criteria[12, 13].

Results

We included five studies in our review involving, 749 patients[14-18]. Table 1 summarizes the patient eligibility criteria. Table 2 presents the pain outcomes of PCEA *vs* PCA using the VAS score graded from 1 cm (no pain) to 10 cm (worst imaginable pain) and the principal adverse effects which were observed in the postoperative period.

Three studies reported statistically significant differences in the VAS pain score on postoperative days 1 and 2 between patient controlled epidural analgesia and patient controlled intravenous analgesia[15, 16, 18]. Specifically, Rivard et al.[16] observed observed that the VAS scores in the PCA were significantly higher ($p=0.046$ for postoperative day 1, $p=0.08$ for postoperative day 2). They also reported that the need for morphine-equivalents was more frequent among patients of the PCA group ($p<0.0001$ and $p=0.048$ for postoperative days 1 and 2 respectively). Ferguson et al. confirmed these findings ($p<0.05$ in VAS scores)[15]. They also found that patients who received thoracic epidural analgesia after gynecological surgery had a better control of postoperative pain during coughing. Courtney-Brooks et al. reported that epidural analgesia was more efficient among gynecologic oncology patients during the 1st and 2nd postoperative days and that the proportion of patients experiencing mild pain (VAS <2) was significantly higher among patients receiving an epidural infusion ($p<0.001$)[18].The remaining two studies, however,reported comparable mean pain scores between the two groups [14, 17].

The frequency of side effects was comparable among studies with the exception of Ferguson et al.[15] who noted a significant difference in the development of pruritus during the first and second postoperative day ($p=0.07$ and $p=0.002$).

Discussion

According to the findings of our systematic review there seems to be evidence to support that PCEA is more effective for postoperative pain management compared to PCAin the field of gynecological cancer. Furthermore, the differences in terms of postoperative complications seem to be insignicant. Previous studies in the field suggested that continuous non-patient controlled analgesia was more effective

than intravenous analgesia in gynecologic oncology patients[19, 20].

The superiority of PCEA compared to PCA has been also investigated in a wide range of patient populations[21]. A Cochrane systematic review comparing the two methods for pain control after intra-abdominal surgery, confirmed the improvedeffectiveness of PCEA[22]. This review included nine studies involving 711 participants and showed that the weighted mean difference in VAS scores of resting pain was significantly increased in patients receiving PCA (1.74, 95% CI 1.30 to 2.19). Moreover, Weinbroum et al. found that ropivacaine and fentanyl via PCEA reduces pain more successfully than IV morphine via PCA, after resection of bone malignancy carried out under combined general and epidural anesthesia (3.0 ± 0.9 *vs* 4.7±0.6, p <0.01)[23]. The same findings were also confirmed in the field of colorectal surgery with PCEA scoring better than PCA[24, 25].

In the field of obstetrics once again PCEA was found superior to PCA in terms of pain intensity scores[26]. However, mean satisfaction scores were similar in both groups (remifentanil 8.1 ± 1.2 *vs* epidural 8.4 ± 1.2).

In our systematic review the superior efficacy reported in the PCEA group was not associated with significant adverse events including pruritus, nausea and ileus. Only one study suggested that PCEA patients had a higher incidence of pruritus in the first two days postoperatively. The same observation was also suggested in the previous Cochrane systematic review on major abdominal surgery (OR 0.27, 95% CI: 0.11 to 0.64)[22]. According to a previous study, intravenous analgesia seems to beassociated with higher incidence of nausea[26]. The small number of enrolled patients may, however, limit the number of patients experiencing side effects, because in an uncontrolled retrospective study in 598 women suffering from gynecological cancer Goodrich et al. observed that the frequency of nausea was as high as 71.4%, followd by pruritus (46.8%) and postoperative hypotension (6.7%)[27].

Strengths and limitations of our study

Our study is the first systematic review that evaluates studies assessing the effectiveness of patient-controlled intravenous analgesia (PCA) to patient-controlled epidural analgesia (PCEA) in the field of postoperative pain management in gynecologic oncology patients. It is based in meticulous review of the literature; hence, the possibility of article loss is minimal.

Nevertheless, certain limitations preclude safe interpretation of our findings. Specifically, the relatively small number of included studies and recruited patients renders impossible the extraction of safe suggestions. Furthermore, most of the studies included did not report the standard deviation of VAS scores, thus, making impossible the meta-analysis of these data.

Implications for future research

According to the current evidence in this field PCEA should be considered by physicians who deal with the postoperative management of gynecologic oncology patients. Despite the fact that the available data are not strong enough to reach firm conclusions, PCEA seems to be associated with minimal (if any) adverse effects. Certain questions arise, however, in this field and these should be assessed by future studies. Specifically, the cost-effectiveness of PCEA (which is traditionally, significantly more expensive than PCA) should be investigated. In this context, it might be useful to also investigate whether PCA combined with NSAID administration might actually reach the VAS scores of PCEA. Furthermore, stratification of patients according to their age, morbidity factors and intraoperative characteristics (such as surgical wound length, operative duration, extensiveness of operation) seems to be needed to identify whether different subgroups are more or less benefited.

Conclusion

Patient controlled epidural analgesia seems to be superior to traditional patient controlled intravenous analgesia during the postoperative management of gynecologic oncology patients. Current evidence support that both treatment modalities are associated with comparable numbers of side effects, includ-

ing nausea and postoperative ileus. Nevertheless, further studies are needed in this field to corroborate our findings, because the relatively small number of recruited patients precludes safe interpretation of our findings.

Conflict of interest

The author declares no conflict of interest.

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