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Original research

Epidural analgesia for cytoreductive surgery with peritonectomy and heated intraperitoneal chemotherapy

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HIGHLIGHTS

- Epidural analgesia ensures adequate pain relief and is well tolerated after CRS and HIPEC surgery.
- In this context, postoperative hypotensive episodes are frequent in patients with epidural analgesia.
- Intraoperative developed coagulopathy resolves in 3–4 days after CRS and HIPEC.
- Careful epidural catheter management is essential to avoid neuraxial complications.

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ABSTRACT

Purpose: To evaluate epidural analgesia role after cytoreductive surgery with peritonectomy combined with heated intraperitoneal chemotherapy.
Methods: 101 patients were retrospectively studied (between 2008 and 2012) to evaluate epidural analgesia effectiveness, tolerability and safety in this surgical context through the assessment of pain, detection of adverse events (nausea, vomiting, itching), temporary motor block, respiratory failure and coagulation profile in the post-operative period.
Results: The median duration of epidural analgesia was 5 [range 1–10] days. As regards pain relief, the median verbal numerical scale scores at rest and on movement were below 2 and 5 until the fifth post-operative day, respectively. 13% of patients suffered nausea, 4% vomit, and 1% itching. No bradycardia or respiratory failure event was reported. 9.9% of patients had hypotension episodes. Coagulation reached normality only 3–4 days after surgery. 5 risky accidental dislodgments of epidural catheter occurred (prothrombine time INR > 1.5) without neurological complications.
Conclusions: Epidural analgesia ensures adequate pain relief and is well tolerated by patients after cytoreductive surgery with peritonectomy combined with heated intraperitoneal chemotherapy. Hypotension is common in this context and careful monitoring of coagulation parameters, especially in the first 3 days after surgery, is advisable to reduce the risk of neuraxial complications.

1. Introduction

The cytoreductive surgery with peritonectomy (CRS) combined with heated intraperitoneal chemotherapy (HIPEC) has improved the prognosis of patients affected by some types of peritoneal carcinomatosis from colorectal cancer, pseudomyxoma peritoneii and peritoneal mesothelioma [1–7]. Despite the positive results observed in the treatment of oncologic disease, the combined treatment is characterized by a high rate of complications that renders challenging the management of patients during both intra and post-operative periods [8].

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An important aspect to highlight in this kind of surgery is the management of pain in the post-operative period. CRS is considered a much more painful surgery than other major abdominal ones [8], therefore epidural analgesia represents an option of critical importance to manage these patients. Another sensitive issue is the alteration of coagulation profile observed intra-operatively and during the first post-operative days. The coagulopathy raises concerns regarding the role of epidural analgesia as it implies a greater risk of epidural hematoma a few hours after catheter insertion and during its removal.

In literature, there are few available data about this topic: some authors support the use of epidural analgesia [9–11] but only 72% of centres worldwide regularly use epidural analgesia to manage CRS and HIPEC post-operative pain [12]. In 2010 Desgranges published a critic letter emphasising the problems related to the use of epidural analgesia after CRS and HIPEC [13]. In 2012 the same author analyzed the safety of epidural analgesia in patients undergoing HIPEC, but his conclusions did not confirm the safety of this analgesic technique (despite no cases of epidural hematoma) due to poor sample size at disposal (35 patients) [14]. Recently, Owusu-Agyemang published a retrospective review on 215 patients who had undergone CRS and HIPEC with epidural analgesia, suggesting the safety of this analgesic technique in this clinical scenario [15]. In their series, Owusu-Agyemang and co-workers mainly focused their research on the intra-operative and post-operative hemodynamic effect of epidural analgesia. Given these facts, more data are needed to assess the correct role of epidural analgesia after CRS and HIPEC, as suggested by the recent international survey published by Bell and co-workers [12].

We conducted a retrospective observational study to report our experience and preliminarily evaluate the efficacy, tolerability, and safety of epidural analgesia, after CRS and HIPEC. Furthermore, we aimed to describe the per-operative coagulation disorder related to this complex surgical procedure.

2. Materials and methods

The Independent Ethics Committee of the Fondazione IRCCS Istituto Nazionale dei Tumori of Milan approved the study protocol on December 17, 2012 (protocol INT150/12). All patients undergoing CRS and HIPEC between November 2008 and December 2012 at the Fondazione IRCCS Istituto Nazionale dei Tumori that received epidural analgesia were reviewed. The only exclusion criterion was the use of other analgesic technique. Data regarding patient characteristics and surgical information were retrieved from a prospectively collected Institutional database. Epidural analgesia details and pain referred at rest and on movement (according to a Verbal Numerical Scale – VNS: 0 = no pain; 10 = intolerable pain) during the first 5 post-operative days (POD) were reviewed from the electronic Acute Pain Service database installed on a pocket-pc device and prospectively maintained by anaesthesiologists in the operative room and in the ward. Similarly, the adverse events data related to epidural analgesia occurred in the first 24 post-operative hours were reviewed (from the above mentioned database). Hypotension, bradycardia and respiratory depression were considered indicative of the technique safety whereas nausea and vomiting, itching and motor block indicated the tolerability of epidural analgesia.

Coagulation profile (prothrombin time – PT-INR, activated partial thromboplastin time - aPTT and platelet count), and blood cell count were obtained by consulting the institutional laboratory test database. The daily amounts of red blood cells (RBCs) units, fresh frozen plasma (FFP) and platelets units transfused were also registered. These data were collected by the Immunohaematology Unit database. All these data were collected from the pre-operative day to the tenth post-operative day.

Table 1
Demographic and surgical variables. Data are numbers, median [range] or mean (95% CI).

Patients; N	101
Age; yrs	60 [23–81]
Gender; M:F	46:55
Weight; kg	69 [42–119]
Heights; cm	167 [150–187]
BMI; kg m^{-2}	23.9 [16.4–42.2]
ASA class	
1	26
2	68
3	7
Tumour entity	
Pseudomixoma peritoneii	47
Mesothelioma	42
Colon cancer	5
Peritoneum primary tumour	4
Ovarian cancer	2
Uterine leiomyosarcoma	1
Peritoneal Cancer Index (PCI)	17 [3–38]
Duration of surgery; min	568 (563–574)

2.1. Anaesthetic and post-operative management

Before entering the operating room, an epidural catheter (Polymedic®, Temena SARL, Bondy, France) was inserted via a 17/18-gauge Rodiera needle between the sixth and the tenth thoracic interspaces. Inadvertent intrathecal or intravascular catheter placement was evaluated by aspiration and administering a test dose of 3 ml 1% mepivacaine with epinephrine 1:200.000.

General anaesthesia was induced with intravenous propofol (2 mg/kg), rocuronium (0.6 mg/kg) or cisatracurium (0.15–0.2 mg/kg) and remifentanil by Target Controlled Infusion system (effect site target concentration: 4–5 ng/ml). After tracheal intubation, anaesthesia was maintained with desflurane (end-tidal 3.0–4.5%) and epidural administration of 0.1–0.2% bupivacaine. Anaesthesia monitoring included electrocardiography, pulse oximetry, capnography, invasive blood pressure via the radial artery, central venous pressure via the right internal jugular vein, cardiac output and stroke volume variation based on pulse wave analysis (Flotrac/Vigileo® – Edwards Lifesciences – Irvine – CA – USA), urine output and esophageal temperature. In addition to epidural analgesia, patient received intravenous ketorolac 30 mg as adjuvant analgesic therapy before the end of surgery.

Cytoreductive surgery was performed according to peritonectomy procedure described by Sugarbaker [7]. HIPEC was conducted using the closed abdomen technique and setting the target intra abdominal temperature at 42.5 °C. The drug schedules were cisplatinum + mitomycin or cisplatinum + doxorubicin. The duration of perfusions were 60 or 90 min.

During surgery, coagulation parameters and platelet count were checked about 5 h after skin incision, after the first FFP administration and at the end of procedure. During and after surgery, RBCs, FFP and platelets were transfused if haemoglobin value fell below 8–8.5 g/dl, PT-INR raised over 1.5 and platelet count fell below $50 \times 10^3/mm^3$, respectively. Following surgery, all patients were transferred intubated to the intensive care unit.

Post-operatively, an elastomeric pump infused bupivacaine 0.1–0.125%. Epidural infusion rate was initially set to 6 ml/h and then adapted to patient pain and hemodynamic status. After intervention, the patients received ketorolac 30 mg iv and acetaminophen 1 gr iv every 8 and 6 h, respectively. The epidural catheter was removed preferentially on the POD 5, when patient pain was mild (VNS at rest < 4) and the PT-INR < 1.5 (which is considered the INR value for a safe catheter removal [16]).