

Post-operative Pain Management of Orthotopic Liver Transplantation: Retrospective Study

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Abstract

Introduction: Orthotopic liver transplantation (OLT) is one of the most extensive of all abdominal surgeries. The main focus of perioperative management for these patients has been to reduce mortality and morbidity, with little attention to postoperative pain management. This has resulted in a paucity of data on pain and its management in OLT.

Method: This is a descriptive, retrospective study of OLT recipients at the London Health Sciences Centre, Western University, over five years (January 2011-December 2016). In addition to demographic information, we collected data regarding pain management modalities, specific opioid analgesics, route of administration and opioid-related serious side effects.

Results: Data for 200 patients were included in this analysis. The mean visual analogue scores were: day one: 3.40 ± 1.71 , day two: 4.99 ± 0.11 and day three: 4.75 ± 0.12 . During their stay in the intensive care unit (ICU), 178 patients received intermittent boluses of an opioid (89%), nine patients received a continuous infusion of opioid (4.5%) and 13 patients received patient-controlled analgesia (PCA) (6.5%). There was no significant difference in mean pain scores between the three groups on day 1 ($P=0.234$). There was no respiratory depression/arrest observed related to opioid usage.

Discussion: This study demonstrates that OLT patients experience moderate pain during the first three days following extubation. The data obtained from this investigation will help to formulate a better understanding of post OLT pain and optimize a pain management protocol that is both efficient and effective.

Keywords: Orthotopic liver transplantation; Abdominal surgeries; Patient-controlled analgesia

we conducted a retrospective study to evaluate the pain experience and its management for liver transplant recipients at our centre.

Introduction

Orthotopic Liver transplant (OLT) is the most effective treatment for patients suffering from chronic and acute liver disease [1-3]. Compared to other major abdominal surgeries, OLT is one of the most extensive procedures in terms of duration, the complexity of the surgery and the surgical stress [1,3]. However, in recent years, better recipient selection, improvement in surgical techniques and advances in anesthesia and perioperative care have significantly decreased the perioperative morbidity and mortality in this patient population [3-5]. Adequate pain control is an important factor in patient recovery and satisfaction in the immediate postoperative period with shorter hospital stays and improved patient survival [3,4]. Pharmacodynamics and pharmacokinetics of many pain medications are altered in this population due to the change in drug distribution, metabolism and elimination. These factors may predispose post OLT patients to over-sedation and unnecessary prolonged mechanical ventilation [6-9]. Additionally, early extubation and fast-tracking after OLT is gaining popularity [11]. Adequate analgesia is an important aspect of postoperative care; however, it is a clinical challenge to the team involved in the preoperative management of these patients [12]. There is a paucity of information on pain management after OLT. Therefore,

Patients and Methods

After receiving institutional research ethics board approval, we conducted a descriptive, retrospective study on OLT recipients at our centre (London Health Science Centre, Western University, London, Ontario, Canada). The study period was five years, from January 2011 to December 2016. All adult patients undergoing OLT with no history of preoperative chronic pain and were extubated within 48 hours after the surgery were included in the study. The exclusion criteria included postoperative intubation for more than 48 hours, more than one organ transplant, return to the operating room for a second-look surgery, graft failure and subsequent death, history of chronic pain, inability to assess pain scores and incomplete charting. Data were obtained from the hospital's Electronic Medical records (EMR) and patients' charts. The data included patients' demographics, preoperative pain scores, length of hospital stay and pain scores. Pain scores were recorded after extubation and during their stay in the ICU and Multi-Organ Transplant Unit (MOTU). Additionally, data regarding pain management modalities, type and doses of opioid analgesics, route of administration and opioid-related side effects were collected. Descriptive statistical analysis (mean and standard deviation) and analysis of variance were used to analyze the data.

Results

A total of 300 patient records were reviewed. After excluding the patients that did not meet the inclusion criteria, data of 200 patients was analyzed. Male patients represented 72% (144 patients). The mean duration of the surgical procedure was 6.635 hours (± 1.65). The mean duration of intubation in the ICU was 9.93 hours (± 0.54), while the mean duration of stay in the ICU was 2.32 days (± 2.47). The mean length of hospital stay was 14.86 days (± 8.60) (Table 1).

Age (years)	53.34 \pm 11.72
Weight (kg)	78.24 \pm 18.12
Sex (male/female)	144 (72%)/56 (28%)
Data are means \pm SD	

Table 1: Patient demographics.

During their stay in the ICU (post-extubation), 178 patients received intermittent boluses of opioids by the ICU nurses (89%), 9 patients were given a continuous infusion of opioids (4.5%) and 13 patients (6.5%) received patient-controlled analgesia (PCA). Analysis of variance test showed no difference in mean pain scores between the three groups on day 1 ($P=0.234$). During the patients' stay in the Multi-organ Transplant Unit (MOTU) on day 3, 194 patients (97%) received oral rather than IV analgesia. Regarding the type of opioids, 130 patients (65%) received intravenous hydromorphone, while pain in 63 recipients was managed with fentanyl. Morphine was used in 7 patients (3.5%). The mean visual analogue scores (VAS) were: day 1 (3.40 \pm 1.71), day 2 (4.99 \pm 0.11) and day 3 (4.75 \pm 0.12) (Figure 1). There were no opioid-related serious side effects such as respiratory depression.

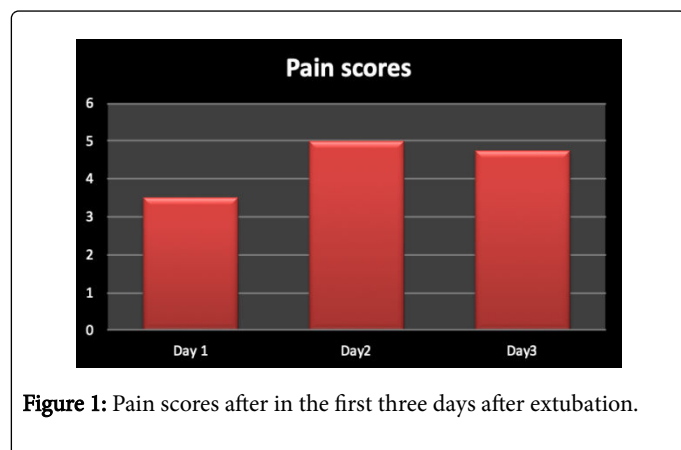


Figure 1: Pain scores after in the first three days after extubation.

Discussion

To the best of our knowledge, this study has the biggest sample population, amongst other retrospective studies available in the literature. Our study revealed that OLT patients experience mild to moderate pain during the first 3 days after extubation despite a somewhat uncomplicated approach to pain management. The highest pain scores were observed on day two post-extubation. Generally, it is assumed that patients undergoing liver transplant surgery require less postoperative analgesia than other abdominal surgeries [2,4,10]. However, current anesthesia management and an interest in early

extubation may result in early awakening from anesthesia and being predisposed to early onset of postoperative pain [3]. A balanced approach to postoperative analgesia can provide satisfactory pain management without causing over-sedation which may delay extubation and ICU discharge [4].

To the best of our knowledge, there are no evidence-based guidelines on the use of analgesics in patients with OLT [6]. Additionally, publications addressing pain management in this patient population are limited to studies with a small sample size.

In a retrospective study by Milan et al., 34 patients who underwent OLT and received subcostal Transversus Abdominus Plane (TAP) block (levobupivacaine 0.5%, 20 mL) and morphine PCA postoperatively were compared to 17 patients as a control group who just received Morphine PCA. They observed a statistically significant reduction in the 24-hour morphine consumption in the TAP block group (45.9 \pm 33.9 mg in the TAP group vs 71.8 \pm 39.9 mg in the control group) ($P<0.005$). There was no statistically significant difference in postoperative pain scores and time to extubation between the two groups. Median pain scores recorded in this study were 1 in the TAP group and 2 in the control group on a pain scale of 0-3.

Eugene et al. retrospectively studied 25 patients undergoing OLT or liver resection surgery. They reported a significant reduction in pain and postoperative morphine consumption in the OLT group despite a more extensive operative procedure. This difference was significant for the first 72 hours after the operation. However, another retrospective study in 2010 compared postoperative morphine requirements in healthy living liver donors, patients with hepatocellular carcinoma undergoing partial hepatectomy, and liver transplant recipients. The study showed no difference in pain scores (VAS) among the three groups. Mean pain scores reported in the liver transplant recipient group on a postoperative day (POD)1, POD2 and POD3 were 3.4 (SD 1.1), 2.6 (SD 1.2) and 2.3 (0.9) respectively. However, the morphine consumption in liver transplant patients was only lower on POD1 compared to living related liver donors and patients undergoing partial hepatectomy due to hepatocellular carcinoma with the mean 24-hour doses of 20 mg (SD 1.2), 35.6 mg (SD 14.5), and 34.6 mg (SD 15.3) respectively. Pharmacodynamic and pharmacokinetic changes of opioids such as morphine in chronic liver disease may contribute to this difference. It may also be attributed to endogenous factors, rather than altered morphine pharmacokinetics, as morphine metabolism is unchanged after liver transplantation if renal function is intact. Additionally, donor's liver has no innervation, so pain due to capsule stretch is less likely [3,10].

Although several studies showed less pain and lower analgesics requirements in liver transplant receipts compared to other major abdominal procedures, a large surgical incision deserves effective analgesia based on patient comfort rather than patient sedation, as unrelieved pain may increase surgical stress responses and organ dysfunction, delayed extubation and prolonged recovery [3].

It is important to note that our study is a retrospective one with its limitations including and not limited to: a variation in anesthesia delivery by different providers, an absence of protocolized intraoperative and postoperative pain management guidelines, no data about total opioid consumption and no control group. Randomized clinical trials need to be conducted to confirm our results. In our centre, most OLT patients received nurse-controlled analgesia in the form of intermittent opioid boluses in the ICU on day one post-extubation rather than PCA which is reported in other studies.

Conclusion

Similar to other published studies on the pain experience of OLT patients, this study showed that OLT patients experience mild to moderate postoperative pain. Our study has the largest sample population amongst other retrospective studies available in the literature. Our findings can be used to develop a methodology to address the effectiveness postoperative pain management. Similarly, the intensity of pain scores of POD 2, identifies a point at which a quality improvement project can improve the current OLT care paths. The global trend of fast-tracking liver transplant recipients also necessitates better pain management in this patient population. Effective management of postoperative pain may improve quality of care, patient satisfaction and decreased length of hospital stay. It is also important to develop guidelines for postoperative analgesia in this patient group. It is time to reassess the type and quantity of analgesics. However, more studies on different pain medications, the role of multimodal analgesia and the safety of regional anesthesia are warranted.

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