Journal of Anesthesia & Clinical Research

Pacheco et al., J Anesth Clin Res 2017, 8:11
DOI: 10.4172/2155-6148.1000782

Case Report Open Access

Opioid Sparing Anaesthesia for Living-Donor Renal Transplantation-A Case Report

Marta Pacheco[1], **Cristina Pereira**[1], **Manuela Casal**[1] **and Humberto S Machado**[1,2*]

[1]*Serviço de Anestesiologia, Centro Hospitalar do Porto, Porto, Portugal*

[2]*Instituto Ciências Biomédicas Abel Salazar, Universidade do Porto, Portugal*

[*]**Corresponding author:**Humberto S Machado, Serviço de Anestesiologia, Centro Hospitalar Universitário do Porto, Porto, Portugal, Tel: +351935848475; Fax: +351 222 009483; E-mail: hjs.machado@gmail.com

Received date: October 27, 2017; **Accepted date:** November 20, 2017; **Published date:** November 28, 2017

Abstract

Introduction: Opioids have been the mainstay for perioperative analgesia. Non-opioid drugs with analgesic properties improve intraoperative multimodal analgesia and lead to a decrease in analgesic consumption, reduction in pain scores, postoperative rescue analgesia and in postoperative nausea and vomiting. We report a case of a patient with Alport Syndrome and End Stage Renal Disease (ESRD) proposed for elective Living-Donor Renal Transplantation, with reported allergies/intolerance to opioids.

Case report: 30-year-old male patient, American Society of Anesthesiologists physical status IV, medical history of Alport Syndrome, ESRD treated with peritoneal dialysis, allergy to tramadol and morphine intolerance. A general intravenous anaesthesia and TAP block was performed. Remifentanil and propofol were used until loss of consciousness. Propofol infusion was then started for effect-site concentration. Maintenance of anaesthesia was achieved with remifentanil infusion to target effect-site, dexmedetomidine infusion and a bolus of ketamine. An ultrasound guided TAP block was performed, using ropivacaine. Analgesia was complemented with paracetamol. Surgical procedure lasted 2 h during which patient was stable, with no record of any adverse events. Emergence of anaesthesia was smooth and painless, and there were no analgesic needs during the time-spent in the recovery unit. Postoperative analgesia plan was PCA pump of morphine with ketamine, and paracetamol every 6 h. During the first 48 h, acute pain team reported no PCA pump requirements, no important discomfort and no complications. Patient improved uneventfully, with a total length of hospital stay of 8 days.

Discussion and learning points: Patients proposed for renal transplantation surgery, with ESRD, present significant challenges for the anaesthesiologist and alternatives to use of opioids could be an option. An opioid sparing technique using regional anaesthesia combined with several drugs with analgesic properties was performed and good analgesic control was accomplished, with no adverse effects, providing a good and fast recovery after a renal transplantation.

Introduction

Perioperative pain management is important for successful outcome of any surgery. Opioids have been the mainstay for both intraoperative and postoperative analgesia. Meanwhile, the analgesic properties of non-opioid drugs increased the practice of intraoperative multimodal analgesia leading to a global decrease in the consumption of analgesics in the postoperative period. The better knowledge of pain mechanisms and chronic pain treatments is useful to anaesthesiologists when faced with patients who are intolerant to opioid drugs [1].

Classically, opioids were used to control the intraoperative response to nociception. A high intraoperative opioid consumption is largely associated with higher analgesic consumption in the postoperative period, prolonged sedation, ileus, urinary retention and prolonged length of hospital stay. With the emergence of newer non-opioid analgesics and the practice of multimodal analgesia, opioid therapy could be complemented and, in some cases, replaced by these drugs [2].

Several studies have been reporting encouraging results regarding reduction of pain scores, postoperative rescue analgesic consumption and postoperative nausea and vomiting with the use of non-opioid analgesic drugs, namely dexmedetomidine, lidocaine and ketamine, associated with regional anaesthesia [2,3]. Renal transplantation is the ideal treatment for end stage renal disease (ESRD) which is the last stage of chronic kidney disease (CKD) caused most frequently by glomerulonephritis, chronic interstitial nephritis or obstructive syndromes, hereditary or cystic disease [1,4].

Postoperative pain for renal transplantation is classified as mild to moderate. Inadequately controlled pain can lead to agitation, tachycardia, hypertension and increased risk of pulmonary complications [4]. Non-steroidal anti-inflammatory drugs inhibit prostaglandins synthesis, which are important for autoregulation of renal blood flow and glomerular filtration rate, therefore, these drugs are contraindicated in such clinical situations [5,6]. Local anaesthetic infiltration is not the most effective treatment in relieving deep muscle pain [5]. Epidural analgesia could be a choice, but it causes excessive analgesia, since the incision is in the lower abdomen and causes mild to moderate pain, and there is the risk of neuroaxial complications [4,5].

Recent studies advocate continuous Transverse Abdominis Plane (TAP) block as a safe and effective alternative to epidural [7]. Patient

controlled analgesia (PCA) with opioids, while less effective for pain control than epidural block, is an option. However, for the patient having a renal transplantation surgery, other implications of opioid therapy must be taken into account, specifically the renal excretion of their active metabolites, which might be delayed until the graft, is fully functional [4].

We report a case of a patient with Alport Syndrome and ESRD scheduled for Living-Donor Renal Transplantation, with several documented allergies to drugs, including tramadol. We proposed a balanced intravenous anaesthesia complemented with TAP block and PCA of morphine with ketamine for postoperative pain control.

Case Report

A 30-year-old male patient, classified as ASA (American Society of Anesthesiologists) physical status IV, weighting 66 kg, BMI of 21.6 kg/m^2, had a medical history of Alport Syndrome, with bilateral hearing loss (with hearing aid use), ESRD with proteinuria and residual diuresis of about 200 ml, treated with peritoneal dialysis for 2 years, controlled hypertension, dyslipidaemia, depression, migratory polyarthritis, controlled epilepsy, moderate asthma and multiple known allergies, specifically to blue fish, mites, pollens, animal fur, drug allergies to tramadol, ibuprofen, hydroxychloroquine and morphine intolerance, documented in previous postoperative events as severe dyspnoea and urinary retention. His chronic drug therapy included levetiracetam, trazodone, ramipril, furosemide, simvastatin, prednisolone, sertraline, calcium, oral iron therapy and sevelamer. Lab investigations revealed normochromic normocytic anemia, haemoglobin 9.1 mg/dL and renal function impairment, creatinine 16.10 mg/dL, without further relevant changes.

The patient was admitted for living-donor renal transplantation with an ABO incompatible donor. A balanced anaesthesia technique was chosen combining general intravenous anaesthesia and TAP block. The patient was monitored according to ASA standards. Depth of anaesthesia was monitored with BIS™ (Bispectral Index Monitor) and muscle relaxation with Train-of-Four (TOF). Induction was performed with a bolus of remifentanil (20 μg/mL) 35.8 μg, followed by 40 mg of lidocaine 1% and 100 mg of propofol 1% to loss of consciousness, using a Target-Controlled Infusion (TCI) pump.

A propofol 1% infusion was then started using the Schnider model for effect-site concentration. A bolus of 60 mg of rocuronium was administered for muscle relaxation. The airway was approached with a Macintosh blade number 3, and secured with an orotracheal tube number 7.5. Maintenance of anaesthesia was achieved with remifentanil infusion to target effect-site using the Minto model, dexmedetomidine infusion (4 mcg/mL) 16 mcg/h and a bolus of ketamine 25 mg, followed by antibiotic prophylaxis with cefoxitin. After induction, an ultrasound guided TAP block was performed on the right abdominal wall, using 75 mg of ropivacaine (20 mL).

For nausea and vomiting prophylaxis, dexamethasone 4 mg and droperidol 0.625 mg were administered. Analgesia was completed with 1000 mg of paracetamol. Surgical procedure lasted 2 h, at the end of which all infusions were stopped, and muscle relaxation was reversed with sugammadex according to TOF ratio. The patient was stable during the entire procedure, with no record of instability or events of any sort. Blood loss was 100 mL.

Emergence of anaesthesia was smooth and painless, and there were no analgesic needs during the time-spent in the post-anaesthesia recovery unit. At arrival in this unit, he presented a VAS (visual analogic scale) of 0, and upon leaving the unit he had a VAS scale of 1. Patient's hearing aid was withdrawn after anaesthetic induction and placed at the end of surgery. The patient's postoperative analgesic plan was a PCA pump containing morphine (1 mg/mL) and ketamine (1 mg/mL), associated with paracetamol every 6 h and PRN antiemetic.

The acute pain team visited him for two straight days during the postoperative period, no complications and no important discomfort were reported and he had no PCA pump requirements. During the postoperative follow-up, the patient improved uneventfully, with a total length of hospital stay of 8 days.

Discussion

Intraoperative amnesia, analgesia, and control of autonomic responses, followed by rapid emergence, are primary objectives for surgical anaesthetic management. Balanced anaesthesia using multiple synergistic agents can attain these goals while minimizing the side effects that may result from high doses of a single agent [1,3]. Opioids are fundamental drugs to achieve a balanced anaesthesia, however, there are clinical situations in which their use is relatively contraindicated, such as opioid intolerance and allergy [1].

On the other hand, patients proposed for renal transplantation surgery, with ESRD, present significant challenges for the anaesthesiologist in the perioperative period. Specifically, opioids given during the perioperative period, or their active metabolites, depend on renal excretion and may accumulate depending on the perfusion and function of the new graft [1]. Therefore, alternatives to use of opioids should be used.

In this case report, a patient with allergy to tramadol and previous described morphine intolerance was proposed for renal transplantation, presenting therefore both, intolerance to opioids and an ESRD. For this reason, an opioid sparing technique using regional anaesthesia combined with several drugs with analgesic properties was chosen, to achieve good analgesic control during both, intraoperative and postoperative periods.

TAP block

Renal transplant recipients are ideally suited to gain maximum benefit from TAP block as the incision classically involves the lower abdomen, providing analgesia to the parietal peritoneum as well as the skin and muscles of the anterior abdominal wall. It has a high margin of safety and is technically simple to perform, especially under ultrasound guidance [5,8]. The TAP block decreases the need for intraoperative analgesia, but due to the long duration of surgery, the analgesic effect of the block fades, and it does not reduce morphine requirements postoperatively, according to randomized controlled trials [9,10].

Therefore, it must still be complemented in the postoperative period. For this reason, some authors advocate the use of a continuous infusion of local anaesthetic *via* the TAP catheter, placed preoperatively. This presents some technical problems: difficulty inserting the catheter into the TAP space, low success rate in terms of catheter placement and possible interference with the surgical field [11]. Other studies still advocate that TAP block provides significant pain relief in the first 24 h after operation which, coupled with the ease of performing the block and the good safety profile, makes it an appealing choice for this group of patients [8,12].

Remifentanil and dexmedetomidine perfusions

Perioperative analgesics should be administered with care in ESRD patients undergoing transplantation, given that these agents, or their active metabolites, depend on renal excretion and may accumulate. Morphine is metabolized in the liver to morphine-6-glucuronide (M6G), morphine-3-glucuronide and normorphine, all of which are excreted in the kidneys. M6G is the only active metabolite, which accumulates in renal failure and mediates central nervous system and respiratory depression [6]. Similarly, meperidine is metabolized in liver to normeperidine, also excreted by the kidneys. Fentanyl is metabolized in the liver with only 7% excreted unchanged in urine making it suitable and safe for short-term use during surgery.

However, if used for a long period, the pharmacodynamic effects should be monitored in view of parent compound accumulation. The clearance and half-life of sufentanil are not significantly altered in patients with reduced renal function. The use of rapidly metabolized potent opioids is one common method of achieving a balanced anaesthesia. Remifentanil is mainly metabolized by blood and tissue esterases while its main metabolite is excreted in the kidney [6]. In our case, a bolus of remifentanil 35.8 μg (20 μg/mL) was given, followed by a perfusion using the Minto model in a TCI pump.

A dexmedetomidine perfusion of 4 mL/h (4 μg/mL) was added to the remifentanil perfusion. Dexmedetomidine is a selective alfa-2 adrenoreceptor agonist with analgesic and sedative properties and minimal impact on respiratory parameters, providing effective postoperative analgesia and reducing postoperative morphine requirements without increasing the incidence of side effects, in spite of its less effective analgesic properties when compared with remifentanil [2,13,14].

Ketamine

In addition to remifentanil and dexmedetomidine, a bolus of 25 mg of ketamine was given to the patient after induction of anaesthesia. Ketamine is a unique intravenous anaesthetic with analgesic properties in subanaesthetic doses [15]. Analgesia induce by ketamine alone is not equivalent to the opioid analgesic effects, but its action as a noncompetitive antagonist N-methyl-D-aspartate (NMDA) receptors can reduce hyperalgesia, prevent opioid tolerance and lower morphine consumption [15,16]. This drug appears to have an opioid-sparing effect, and is gaining acceptance both by patients and physicians because of the decreased incidence of side-effects [17]. The opioid-sparing effect of a single dose of ketamine of 0.1-0.15 mg/kg has also been demonstrated after major orthopaedic and intra-abdominal surgeries with no increase in side effects [18,19].

PCA of morphine with Ketamine

In order to minimize the adverse effect of opioids in our patient, ketamine (1 mg/mL) was added to morphine (1 mg/mL) and administered *via* PCA. Clinical trials have found contradictory results regarding the use of ketamine for this purpose. A qualitative review of randomized trials concluded that, for thoracic surgery, adding ketamine to opioid for i.v PCA was superior to i.v PCA opioid alone, but the benefit of this addition remained unclear for abdominal surgery [16]. A 1:1 ratio with a lockout interval of 8 min, such as the one used in this case, has been described with positive effects after major orthopaedic procedures [20].

Conclusion

Sparing analgesia anaesthetic technique proved to be efficacious in a patient with intolerance to opioids, and proved to have few or no adverse effects, providing a good and fast recovery after a renal transplantation. This case supports the literature regarding the use of different anaesthetics to reduce their cumulative dose, and therefore reducing the patient's analgesic needs and the drugs' side effects.

References

1. Plunkett A, Fahlgren M, McLean B, Mundey D (2009) Opioid-free balanced anesthesia for cervical ganglionectomy subsequent to recent ultra-rapid opioid detoxification. Pain Med 10: 767-770.
2. Bakan M, Umutoglu T, Topuz U, Uysal H, Bayram M, et al. (2015) Opioid-free total intravenous anesthesia with propofol, dexmedetomidine and lidocaine infusions for laparoscopic cholecystectomy: a prospective, randomized, double-blinded study. Rev Bras Anestesiol 65: 191-199.
3. Daccache G, Caspersen E, Pegoix M, Monthé-Sagan K, Berger L, et al. (2017) A targeted remifentanil administration protocol based on the analgesia nociception index during vascular surgery. Anaesth Crit Care Pain Med 36: 229-232.
4. Benjamin S Martinez, Irina Gasanova, Adebola O Adesanya (2013) Anesthesia for Kidney Transplantation-A Review. J Anesth Clin Res 4: 1-6.
5. Parikh BK, Waghmare V, Shah VR, Modi P, Rizvi S, et al. (2015) The analgesic efficacy of continuous transversus abdominis plane block in renal transplant recipients. J Anaesthesiol Clin Pharmacol 31: 531-534.
6. Baxi V, Jain A (2009) Anaesthesia for Renal Transplantation: An Update. Indian J Anaesth 53: 139-147.
7. Bugada D, Nicola FG, Carboni V, Allegri M (2013) TAP block for opioid-free postoperative analgesia in obese surgery. Minerva Anestesiol 79: 1447-1448.
8. Young MJ, Gorlin AW, Modest VE, Quraishi SA (2012) Clinical Implications of the Transversus Abdominis Plane Block in Adults. Anesthesiol Res Pract 2012: 731645.
9. Kuruba SMG, Mukhtar K, Singh SK (2014) A randomised controlled trial of ultrasound-guided transversus abdominis plane block for renal transplantation. Anaesthesia 69: 1222-1226.
10. Freir NM, Murphy C, Mugawar M, Linnane A, Cunningham AJ (2012) Transversus Abdominis Plane Block for Analgesia in Renal Transplantation. Anesth Analg 115: 953.
11. Jankovic ZB, Pollard SG, Nachiappan MM (2009) Continuous transversus abdominis plane block for renal transplant recipients. Anesth Analg 109: 1710-1711.
12. Mohammadi SS, Dabir A, Shoeibi G (2013) Efficacy of transversus abdominis plane block for acute postoperative pain relief in kidney recipients: a double-blinded clinical trial. Pain Med 15: 460-464.
13. Arain SR, Ruehlow RM, Uhrich TD, Ebert TJ (2003) The efficacy of dexmedetomidine versus morphine for postoperative analgesia after major inpatient surgery. Anesth Analg 98: 153-158.
14. Gurbet A, Basagan-Mogol E, Turker G, Ugun F, Kaya FN, et al. (2006) Intraoperative infusion of dexmedetomidine reduces perioperative analgesic requirements. Can J Anaesth 53: 646-652.
15. Subramaniam K, Subramaniam B, Steinbrook RA (2004) Ketamine as adjuvant analgesic to opioids: a quantitative and qualitative systematic review. Anesth Analg 99: 482-495.
16. Carstensen M, Moller AM (2010) Adding ketamine to morphine for intravenous patient-controlled analgesia for acute postoperative pain: a qualitative review of randomized trials. Br J Anaesth 104: 401-406.
17. Kohrs R, Durieux ME (1998) Ketamine: teaching an old drug new tricks. Anesth Analg 87: 1186-1193.
18. Menigaux C, Fletcher D, Dupont X, Guignard B, Guirimand F, et al. (2009) The benefits of intraoperative small-dose ketamine on

postoperative pain after anterior cruciate ligament repair. Anesth Analg 90: 129-135.

19. Fu ES, Miguel R, Scharf JE (1997) Preemptive ketamine decreases postoperative narcotic requirements in patients undergoing abdominal surgery. Anesth Analg 84: 1086-1090.

20. Sveticic G, Gentilini A, Eichenberger U, Luginbühl M, Curatolo M (2003) Combinations of morphine with ketamine for patient-controlled analgesia: a new optimization method. Anesthesiology. 98: 1195-1205.