Multimodal anesthesia for kidney retransplantation in patients with advanced renal osteodystrophy.

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Abstract

End-stage renal failure is a chronic, progressive, debilitating disease that causes disability and high mortality, and the incidence and prevalence have increased in the world population. Among the chronic diseases, dialysis chronic kidney disease is among those that generate the greatest impact on the patient's quality of life, such as living with an incurable disease, dependence on a dialysis machine to survive, rigorous therapeutic regimen, changes in body image and dietary and water restrictions. Dialysis therapy does not completely replaces renal functions and, for this reason, prolonged stay on hemodialysis causes bone complications (ostedystrophy due to secondary hyperparathyroidism), cardiovascular (left ventricular hypertrophy, vascular calcification), brain (advanced arteriosclerosis). The chance of death among hemodialysis patients is 20 times greater than that of the general population. Kidney transplantation is the best treatment for patients with end-stage renal disease. Anesthesia requires an understanding of these metabolic and systemic abnormalities. In addition, associated comorbidities increase perioperative morbidity and mortality, so for a better outcome, multidisciplinary collaboration with well-planned anesthetic strategies is necessary, with individualization of cases.

Keywords: Renal osteodystrophy, Anesthesia, Outcome, Kidney retransplantation.

Introduction

Chronic Kidney Disease (CKD) is a worldwide health problem, with an increasing prevalence and adverse outcomes [1,2]. Mineral and bone disorders are important complications of this disease, which can result in numerous consequences, such as bone pain, skeletal deformities, bone fractures, vascular calcification, cardiovascular disease and even death [3,4]. Levels of calcium, phosphorus and intact PTH (PTHi) should be determined in all patients with CKD in which the Glomerular Filtration Rate (GFR) is below 60 mL/min/1.73 m2. [5]. These measures should be even more frequent in renal transplant patients or in any patient with CKD who is being treated for disorders of calcium and phosphorus metabolism. In CKD, hyperphosphatemia and hypocalcemia occur due to loss of renal function, deficit of active vitamin D, and imbalance in the maintenance of the calcium-phosphorus product. As a consequence of hypocalcemia, there is an increase in the secretion of parathormone, responsible for the reabsorption of bone salts, increasing the levels of Ca++ in the extracellular fluid. The resulting trend is the establishment of a picture of HPTS, which can cause pathological fractures, bone deformities and decrease in patients' survival [6].

Case report

A 35 year-old, female patient, weighing 50 kg and measuring 1.50 meter tall, with a history of nephrotic syndrome onset at age 15, was diagnosed with post-biopsy glomerulonephritis [7]. At the age of 20, she presented anasarca, systemic arterial hypertension, dialysis was initiated and she was submitted to her first kidney transplant, which evolved with immediate loss due to thrombosis [8]. New transplant was performed at age 23, with new graft loss, but now without a clear cause.

Medicines in use: Losartan, Atenolol, Renagel, AC F, Hemax, Complex B, $CACO_3$. Previous Surgeries: Kidney Transplantation, Parathyroidectomy. Main etiology of Chronic Kidney Disease: Glomerulopathy. Comorbidities: Systemic Arterial Hypertension. Echocardiography: Concentric left ventricular hypertrophy, 66% ejection fraction, Grade 2

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diastolic dysfunction, mild mitral insufficiency [9]. ECG: Sinus Bradycardia. Chest: Bell. Chest X-ray: dextroconvex thoracic scoliosis and morph structural alteration of the costal arches, dorsal spondyloarthrosis; Elongated and atheromatous aorta; Free Costophrenic sinuses. Computed Tomography: Infra-renal Vein Hypoplasia. Two previous renal implants in right and left iliac arteries [10]. Anesthesia: Monitoring performed with cardioscopy, pulse oximeter, invasive blood pressure with catheterization of the right radial artery, Bispectral Index (BIS), capnography and gas analyzer. Pre-induction sedation: dexmedetomidine 40 mcg, magnesium sulfate 2 grams, midazolam 5 mg. Epidural Puncture was performed at T8, with the passage of an Epi Dural Catheter (EDC). Anesthetic induction in rapid sequence: lidocaine 100 mg, fentanyl 100 mcg, propofol 100 mg, and rocuronium 60 mg [11]. Orotracheal intubation was performed with the aid of a video laryngoscope. During the surgery, 5 ml of 0.5% ropivacaine + 1% lidocaine were administered through the epidural catheter to maintain analgesia. Heparinization was performed with 2500 IU intravenous heparin and guided by Activated Clotting Time (ACT) and was not reversed at the end of the procedure.

At the end of the surgery, 2 mg of morphine was administered by EDC [12]. Dipyrone 2 grams and ondansetron 8mg were given intravenously.

Surgery was performed by a xipho-pubic incision with transperitoneal access and organ implantation in vena cava at the level of the renal veins, arterial implantation in the right common iliac artery and ureter implantation of intraperitoneal vesical graft [13,14].

The patient maintained hemodynamic stability throughout the procedure, maintaining mean arterial pressure above 90 mmHg, heart rate around 60 bpm and BIS between 40-60 [15,16]. At the end of the surgery, she was extubated in the room and taken to the ICU, stable and ventilated on room air, without pain complaints.

Discussion

In surgery for kidney transplantation, modified Gibson incisions are made. However, in this specific case, the patient was undergoing her third kidney transplant due to the loss of the previous two grafts [17]. Therefore it was necessary to enlarge the surgical incision to a midline xipho-pubic access to gain intraperitoneal access for implantation in both vena cava and common iliac artery [18-20]. Thus resulting in greater pain stimulation and surgical complexity. Multimodal anesthesia aims to maximize analgesic efficacy and minimize side effects of a single medication. The choice of neuraxial block combined with general multimodal anesthesia in this case, despite the great technical difficulty of the chest with bone deformity helped to maintain analgesia and with greater hemodynamic stability in this case, in addition to analgesic maintenance in the postoperative period [21-23].

Vasodilation can be induced by lidocaine doses higher than 40 µg/ml. And it has been demonstrated that a better diuresis in time zero and within three days after transplantation (early polyuria) is associated with a better graft function [24,25].

Dexmedetomidine is a short acting selective alpha 2 agonist and has a stabilizing effect on hemodynamics mediated by reducing sympathetic tone, decreasing inflammatory response, alleviating I/R injury, inhibiting renin release, increasing glomerular filtration rate, increasing secretion of sodium and water by the kidneys, and decreasing insulin secretion [26,27]. Additionally, in renal cells, Dexmedetomidine can also decrease apoptosis and downregulate monocyte chemo-attractant protein-1 through suppressing injury-induced activation of the Janus kinase/signal transducer and activator of transcription signaling pathways during renal I/R injury [28-30]. These immune modulatory effects may underlie an organ protective effect of Dexmedetomidine from I/R injury. Considering the importance of inflammation and apoptosis, as well as potential anti-inflammation and apoptosis effects.

Dexmedetomidine has emerged as an effective organ protective agent. Gu and colleagues suggested that Dexmedetomidine activated Akt signaling *via* α2 adrenoceptor-dependent and independent-PI3K coupling to improve kidney cell survival [31-33]. Apart from its cytoprotection, Dexmedetomidine might inhibit HMGB1 release and suppress subsequently toll-like receptor 4-mediated inflammatory actions in the setting of renal ischemia. Studies in vivo have reported that the reno-protective property of Dexmedetomidine could be related to modulating vasoreactivity, presented as improved renal blood flow, preserved glomerular filtration, elevated secretion of water and sodium, as well as suppression of renin release [34,35]. Moreover, Dexmedetomidine could induce diuresis through the inhibition of arginine vasopressin in the collecting duct and aquaporin expression.

Epidural analgesia blocks the stress response, either by relieving pain or by blocking sympathetic activity. Epidural analgesia, with the association of local anesthetics and opioids, promotes better quality analgesia than the use of isolated opioids, either *via* epidural route or systemic administration [36-39]. Also, it is superior to the isolated epidural use of local anesthetics. This association allowed to reduce, not only the concentration of the local anesthetic in the epidural analgesic solution, but also the necessary doses of opioid for a better quality postoperative analgesia, with less adverse effects than that obtained when either one of the aforementioned agents are used alone [40-42].

The combination of these factors, along with other measures, such as active postoperative mobilization and early return to oral feeding [43-45] led to the proposal that epidural analgesia would improve the evolution of these patients and could reduce morbidity and mortality.

Hypomagnesemia is frequently observed after kidney transplantation, in part to immunosuppressive regimens including CalciNeurin Inhibitors (CNI) that induce Magnesium (Mg) urinary waste. Hypomagnesemia was observed in 6.6% of patients treated with tacrolimus and in 1.5% of patients on cyclosporine [46]. The mechanisms leading to hypomagnesemia are not fully understood, but it has been shown that CNI induce a down-regulation of renal expression of the epidermal growth factor and TRMP6 in the distal collecting tubule, leading to decreased Mg reabsorption.

Sirolimus might induce hypomagnesemia through inhibition of Na-K-Cl co-transporter 2 expression in the thick ascending loop of Henle. Renal Mg wasting has been shown to be similar between rats treated with sirolimus and those treated with cyclosporine or tacrolimus [47]. Many other factors influence Mg levels after kidney transplantation, such as post-transplantation volume expansion, metabolic acidosis, insulin resistance, decreased gastro-intestinal absorption due to diarrhea, low Mg intake and medication such as diuretics or proton pump inhibitors. Post-transplant diabetes mellitus-associated mortality is mainly related to cardiovascular events, which are today the main cause of death in kidney transplant patients. Hypomagnesemia has been shown to play a role in the pathogenesis of arterial hypertension, endothelial dysfunction, dyslipidemia and inflammation, with all these factors contributing to Coronary Heart Disease (CHD) [48].

Conclusion

Kidney transplantation is the gold standard treatment for patients with end-stage kidney disease. These patients have several metabolic changes and associated comorbidities, in which the anesthetic-surgical procedure must be studied and individualized in order to be successful. Multimodal anesthesia with the combination of several drugs in lower doses helps to enhance analgesia quality and hemodynamic performance in the perioperative period. Dexmedetomidine was associated with a reduced incidence of DGF, infection, graft rejection, overall complications, and LOS in patients who undergo renal transplantation. Epidural anesthesia with opioid promotes longer postoperative analgesia, in addition to decreasing the morbidity and mortality of these patients. Lidocaine also demonstrates a positive effect during intraoperative period with vasodilation and improvement of diuresis during the postoperative period. Therefore multimodal anesthesia exerts a positive effect in kidney transplantation surgery when compared to opioid based anesthesia.

References

1. James MT, Hemmelgarn BR, Tonelli M. Early recognition and prevention of chronic kidney disease. The Lancet. 2010;375(9722):1296-309.
2. Parfrey PS, Foley RN. The clinical epidemiology of cardiac disease in chronic renal failure. J Am Soc Nephrol. 1999;10(7):1606-15.
3. Block GA, Klassen PS, Lazarus JM, et al. Mineral metabolism, mortality, and morbidity in maintenance hemodialysis. J Am Soc Nephrol. 2004;15(8):2208-18.
4. Wheeler DC, Winkelmayer WC. KDIGO 2017 clinical practice guideline update for the diagnosis, evaluation, prevention, and treatment of chronic kidney disease-mineral and bone disorder (CKD-MBD) foreword. Kidney Int Suppl. 2017;7(1):1-59.
5. SampaioEDA, Lugon JR, & Barreto FDC. Pathophysiology of secondary hyperparathyroidism. J Bras Nefrol. 2008;30(1):6-10.
6. Baxi V, Jain A, Dasgupta D. Anaesthesia for renal transplantation: an update. Indian J Anaesth. 2009;53(2):139.
7. Johns RA, DiFazio CA, Longnecker DE. Lidocaine constricts or dilates rat arterioles in a dose-dependent manner. The Journal of the American Society of Anesthesiologists. 1984;61(3):A204-A204.
8. Matteucci E, Carmellini M, Bertoni C, et al. Urinary excretion rates of multiple renal indicators after kidney transplantation: clinical significance for early graft outcome. Renal failure. 1998;20(2):325-30.
9. Banasch HL, Dersch-Mills DA, Boulter LL, et al. Dexmedetomidine use in a pediatric intensive care unit: a retrospective cohort study. Annals of Pharmacotherapy. 2018;52(2):133-9.
10. Geng J, Qian J, Cheng H, et al. The influence of perioperative dexmedetomidine on patients undergoing cardiac surgery: a meta-analysis. PLoS One. 2016;11(4):e0152829.
11. Yang YF, Peng K, Liu H, et al. Dexmedetomidine preconditioning for myocardial protection in ischaemia-reperfusion injury in rats by downregulation of the high mobility group box 1-toll-like receptor 4-nuclear factor κB signalling pathway. Clin Exp Pharmacol. 2017;44(3):353-61.
12. Si Y, Bao H, Han L, et al. Dexmedetomidine protects against renal ischemia and reperfusion injury by inhibiting the JAK/STAT signaling activation. J Transl Med. 2013;11(1):1-2.
13. Delano MJ, Ward PA. Sepsis-induced immune dysfunction: can immune therapies reduce mortality?. J Clin Investig. 2016;126(1):23-31.
14. Harjai M, Bogra J, Kohli M, et al. Is suppression of apoptosis a new therapeutic target in sepsis?. Anaesth Intensive Care. 2013;41(2):175-83.
15. Gu J, Sun P, Zhao H, et al. Dexmedetomidine provides renoprotection against ischemia-reperfusion injury in mice. Critical care. 2011;15(3):1-1.
16. Cai YE, Xu H, Yan J, et al. Molecular targetsandmechanism of action of dexmedetomidine in treatment of ischemia/reperfusion injury. Mol Med Rep. 2014;9(5):1542-50.
17. Liu Y, Sheng B, Wang S, et al. Dexmedetomidine prevents acute kidney injury after adult cardiac surgery: a meta-analysis of randomized controlled trials. BMC anesthesiology. 2018;18(1):1-1.
18. Jo YY, Kim JY, Lee JY, et al. The effect of intraoperative dexmedetomidine on acute kidney injury after pediatric congenital heart surgery: a prospective randomized trial. Medicine. 2017;96(28).
19. Carvalho WA, Lemonica L-Central mechanisms of pain transmission and modulation. Therapeutic update. Rev Bras Anestesiol, 1998;48:221-241.

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20. Liu SS, Carpenter RL, Mackey DC, et al. Effects of perioperative analgesic technique on rate of recovery after colon surgery. The Journal of the American Society of Anesthesiologists. 1995;83(4):757-65.

21. Dahl JB, Rosenberg J, Hansen BL, et al. Differential analgesic effects of low-dose epidural morphine and morphine-bupivacaine at rest and during mobilization after major abdominal surgery. Anesth Analg. 1992;74(3):362-5.

22. Boylan JF, Katz J, Kavanagh BP, et al. Epidural bupivacaine-morphine analgesia versus patient-controlled analgesia following abdominal aortic surgery: analgesic, respiratory, and myocardial effects. The Journal of the American Society of Anesthesiologists. 1998;89(3):585-93.

23. Mann C, Pouzeratte Y, Boccara G, et al. Comparison of intravenous or epidural patient-controlled analgesia in the elderly after major abdominal surgery. The Journal of the American Society of Anesthesiologists. 2000;92(2):433.

24. Correll DJ, Viscusi ER, Grunwald Z, et al. Epidural analgesia compared with intravenous morphine patient-controlled analgesia: postoperative outcome measures after mastectomy with immediate TRAM flap breast reconstruction. Reg Anesth Pain Med. 2001;26(5):444-9.

25. Flisberg P, Tornebrandt K, Walther B, et al. Pain relief after esophagectomy: thoracic epidural analgesia is better than parenteral opioids. J Cardiothorac Vasc Anesth. 2001;15(3):282-7.

26. Crews JC, Hord AH, Denson DD, et al. A comparison of the analgesic efficacy of 0.25% levobupivacaine combined with 0.005% morphine, 0.25% levobupivacaine alone, or 0.005% morphine alone for the management of postoperative pain in patients undergoing major abdominal surgery. Anesth Analg. 1999;87(6):1504.

27. Kampe S, Weigand C, Kaufmann J, et al. Postoperative analgesia with no motor block by continuous epidural infusion of ropivacaine 0.1% and sufentanil after total hip replacement. Anesth Analg. 1999;89(2):395-8.

28. Kopacz DJ, Sharrock NE, Allen HW. A comparison of levobupivacaine 0.125%, fentanyl 4 μg/mL, or their combination for patient-controlled epidural analgesia after major orthopedic surgery. Anesth Analg. 1999;87(6):1497.

29. Paech MJ, Westmore MD. Postoperative epidural fentanyl infusion—is the addition of 0.1% bupivacaine of benefit?. Anaesth Intensive Care. 1994;22(1):9-14.

30. Scott DA, Blake D, Buckland M, et al. A Comparison of Epidural Ropivacaine Infusion Alone and in Combination with 1, 2, and 4 [micro sign] g/mL Fentanyl for Seventy-Two Hours of Postoperative Analgesia After Major Abdominal Surgery. Anesth Analg. 1999;88(4):857-64.

31. Wiebalck A, Brodner G, Van Aken H. The effects of adding sufentanil to bupivacaine for postoperative patient-controlled epidural analgesia. Anesth Analg. 1997;85(1):124-9.

32. Lutti MN, Simoni RF, Cangiani LM, et al. Patient-controlled analgesia with fentanyl and sufentanil in the postoperative period of knee ligament reconstruction: Comparative study. Rev Bras Anestesiol 2000;50:8-13.

33. George KA, Chisakuta AM, Gamble JA, et al. Thoracic epidural infusion for postoperative pain relief following abdominal aortic surgery: bupivacaine, fentanyl or a mixture of both?. Anaesthesia. 1992;47(5):388-94.

34. Cooper DW, Turner G. Patient-controlled extradural analgesia to compare bupivacaine, fentanyl and bupivacaine with fentanyl in the treatment of postoperative pain. British journal of anaesthesia. 1993;70(5):503-7.

35. Breivik H, Niemi G, Haugtomt H, et al. Optimal epidural analgesia: importance of drug combinations and correct segmental site of injection. Bailliere's clinical anaesthesiology. 1995;9(3):493-512.

36. Cooper DW, Ryall DM, McHardy FE, et al. Patient-controlled extradural analgesia with bupivacaine, fentanyl, or a mixture of both, after Caesarean section. Br J Anaesth. 1996;76(5):611-5.

37. Kehlet H. Multimodal approach to control postoperative pathophysiology and rehabilitation. Br J Anaesth. 1997;78(5):606-17.

38. Brodner G, Van Aken H, Hertle L, et al. Multimodal perioperative management combining thoracic epidural analgesia, forced mobilization, and oral nutrition—reduces hormonal and metabolic stress and improves convalescence after major urologic surgery. Anesth Analg. 2001;92(6):1594-600.

39. Carli F, Mayo N, Klubien K, et al. Epidural analgesia enhances functional exercise capacity and health-related quality of life after colonic surgery: results of a randomized trial. The Journal of the American Society of Anesthesiologists. 2002;97(3):540-9.

40. Liu S, Carpenter RL, Neal JM. Epidural anesthesia and analgesia: their role in postoperative outcome. The Journal of the American Society of Anesthesiologists. 1995;82(6):1474-506.

41. Rodgers A, Walker N, Schug S, et al. Reduction of postoperative mortality and morbidity with epidural or spinal anaesthesia: results from overview of randomised trials. Bmj. 2000;321(7275):1493.

42. Buggy DJ, Smith G. Epidural anaesthesia and analgesia: better outcome after major surgery?: Growing evidence suggests so. Bmj. 1999;319(7209):530-1.

43. Margreiter R, European Tacrolimus vs Ciclosporin Microemulsion Renal Transplantation Study Group. Efficacy and safety of tacrolimus compared with ciclosporin microemulsion in renal transplantation: a randomised multicentre study. The lancet. 2002;359(9308):741-6.

44. Ledeganck KJ, De Winter BY, Van den Driessche A, et al. Magnesium loss in cyclosporine-treated patients is related to renal epidermal growth factor downregulation. Nephrol Dial Transplant. 2014;29(5):1097-102.

Citation: *Schons LC, Bersot CDA, Linhares R, et al. Multimodal anesthesia for kidney retransplantation in patients with advanced renal osteodystrophy. J Anesthetic Anesthesiol. 2022;4(3):111*

45. Nijenhuis T, Hoenderop JG, Bindels RJ. Downregulation of Ca2+ and Mg2+ transport proteins in the kidney explains tacrolimus (FK506)-induced hypercalciuria and hypomagnesemia. J Am Soc Nephrol. 2004;15(3):549-57.

46. Alexandre CD, de Bragança AC, Shimizu MH, et al. Rosiglitazone prevents sirolimus-induced hypomagnesemia, hypokalemia, anddownregulation ofNKCC2protein expression. AmJPhysiol Renal Physiol. 2009;297(4):F916-22.

47. Andoh TF, Burdmann EA, Fransechini N, et al. Comparison of acute rapamycin nephrotoxicity with cyclosporine and FK506. Kidney international. 1996;50(4):1110-7.

48. Van Laecke S, Van Biesen W. Hypomagnesaemia in kidney transplantation. Transplantation Reviews. 2015;29(3):154-60.