Case Report

Opioid-free Anaesthesia and Analgesia in a Sickle Cell Disease Patient with Extensive Orthopaedic Soft-tissue Surgery

Abayomi Kolawole Ojo[1,2], Adedapo Omowonuola Adetoye[1,2], Olanrewaju Ibikunle Ibigbami[1,2], Olumuyiwa Tope Ajayeoba[2], Emmanuel Oladayo Folami[3], Chidozie Uche Ekwem[2], John Olusinmi Ajefolakemi[2]

[1]Obafemi Awolowo University, [2]Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife, [3]UNIOSUN Teaching Hospital, Osogbo, Osun State, Nigeria

Abstract

The provision of anaesthesia through techniques devoid of opioid is referred to as opioid-free anaesthesia. Both pain crisis in sickle cell (SC) disease and poor postoperative pain care worsens patient morbidity. This is a case report of a 22-year-old female SC anaemia patient, who had bilateral quadricepsplasty. Sickle Cell disease is common among individuals of African race and opioids are often abused during the out-of-hospital treatment of pain crisis. We report the case of pentazocine addiction resulting in severe bilateral quadriceps fibrosis. Thus, it was necessary to avoid opioid-based anaesthesia. A combined spinal epidural anaesthesia using magnesium adjunct was applied. The analgesic function of magnesium is linked to the blockade of the N-methyl-D-aspartate receptor. The subarachnoid block was achieved with 3.5 mL of 0.5% heavy bupivacaine (17.5 mg), while epidural anaesthesia was done with 14 mL of 0.25% plain bupivacaine (37.5 mg) and 1 mL of 2 mg/kg of magnesium, (i.e., 120 mg). After the surgery, the surgical sites were infiltrated with 10 mL of 0.25% plain bupivacaine (25 mg) on each limb. Intravenous magnesium-sulfate 5 mg/kg (i.e., 300 mg), was added to 500 mL of crystalloids to run every 4 h. Furthermore, 1 mL of 2 mg/kg magnesium, (i.e., 120 mg,) was added to the 14 mL of 0.125% plain bupivacaine to make 15 mL of magnesium–bupivacaine admixture, every 4 h. These were given for 48 h. The Visual Analog Scale pain scores reduced from 9/10 to 5-6/10 and then to 3/10 over a 6-h period and remained at or lower than 3/10 throughout the postoperative period. Adequate haemodynamics, oxygenation, hydration, warmth, and urine output were ensured. The postoperative period was crisis free.

Keywords: Magnesium-sulfate, opioid addiction, opioid-free anaesthesia, postoperative analgesia, sickle cell anaemia

Introduction

The sickle cell (SC) disease is seen among individuals of Indian, Arabian, and sub-Saharan African descent. The SC trait occurs in 25% of Nigerians, which is probably the world's largest population of SC patients.[1]

The disease is an autosomal recessive genetic disorder of the haemoglobin (Hb), in red cells.[2] Hb S occur when point mutation causes the synthesis of valine, instead of glutamic acid, at the sixth amino acid position of the beta-globin chain.[2,3] The SC disease occurs as either the homozygous inheritance, i.e., SC anaemia, or a heterozygous co-inheritance with another variant.[3]

Repeated hemolytic anaemia and vaso-occlusion produce the clinical features of the SC anaemia.[3] Fever, stress, infections, vascular stasis, viscosity, dehydration, acidosis, and hypoxia are the crisis-triggering factors.[2-4] Red cell polymerization occurs. The resulting pro-coagulation, fibrin deposition, and smooth muscle hyperplasia induce vessel occlusion,[4] which produces pain crisis in the abdomen, limbs, and hips.[4,5]

The stress of surgical trauma, fluid, haemodynamic, and metabolic disturbance may activate pain crisis, and worsen perioperative morbidity in SC disease patients.[6] Effective postoperative analgesia care enhances rapid recovery, reduce hospital cost, and improve patient satisfaction.[2,6]

Address for correspondence: Dr. Abayomi Kolawole Ojo, Obafemi Awolowo University, Ile-Ife, Nigeria. Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife, Nigeria.
E-mail: abayomiojo2002@gmail.com; abayomiojo@oauthc.com

Access this article online

Quick Response Code:

Website: http://journals.lww.com/NJOM

DOI: 10.4103/NJM.NJM_68_23

How to cite this article: Ojo AK, Adetoye AO, Ibigbami OI, Ajayeoba OT, Folami EO, Ekwem CU, *et al.* Opioid-free anaesthesia and analgesia in a sickle cell disease patient with extensive orthopaedic soft-tissue surgery. Niger J Med 2023;32:438-41.

Submitted: 02-Jul-2023 **Revised:** 24-Jul-2023
Accepted: 31-Jul-2023 **Published:** 08-Dec-2023

Case Report

A 22-year-old SC anaemia female patient was scheduled for surgery for bilateral Quadriceps fibrosis, at the Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife, Nigeria, in May 2023.

The patient presented with several months' history of extensive bilateral Quadriceps fibrosis, which had affected sitting, standing, walking and other basic functions. This was due to repeated self-injection of intramuscular pentazocine (agonist-antagonist opioid). The patient was initially managed for opioid addiction, for several months, by the psychiatric unit of our institution.

A preoperative assessment revealed a patient with no other comorbid condition. The patient had a Hb concentration of 11 g/dL, which is a stable value. The airway assessment was adequate and the back was normal. The full blood count, serum electrolytes, urea and creatinine, and the chest radiograph were unremarkable. The patient weighed 60 kg. Informed consent was taken. The anaesthesia plan was explained to the patient and the patient was taught the Visual Analog Scale (VAS) pain score.

The anaesthesia and analgesia care plan included an opioid-free regimen. The patient was planned for a combined spinal epidural anaesthesia.

In the theatre, baseline pulse rate, saturation, electrocardiogram (ECG), and noninvasive blood pressure were recorded. Difficult venous cannulation necessitated the siting of 14G venous cannulation at the right external jugular vein. Cleaning was done with povidone-iodine and the patient was draped. Using the landmark method, and Tuffier's line, the Touhy needle was used to gain access to the epidural space at the L3/4 interspace, using the loss of resistance-to-air technique. A 25G Quincke needle was used to facilitate a sub-arachnoid block, with 3.5 mL of 0.5% heavy bupivacaine (17.5 mg), following a free-flowing cerebrospinal fluid (CSF), via a needle-through-needle technique. About 3–4 cm of the epidural catheter was inserted into the space. Neither blood nor CSF was seen. The catheter was taped. The patient was then positioned supine and sensory block was assessed ensuring it was fixed at T8, and the motor block was graded as modified Bromage score 1.

The surgery lasted for about 5 h. A Quadricepsplasty and V-Y tendon elongation was done on both lower limbs. About 2 h into the surgery, epidural anaesthesia was activated using 14 mL of 0.25% plain bupivacaine (37.5 mg) and 1 mL of 2 mg/kg of magnesium-sulfate ($MgSO_4$), (i.e., 120 mg). This was repeated about 3½ h into the surgery. Sedation was achieved with intravenous (IV) midazolam 1–2 mg and IV ketamine 10 mg in aliquots. Both drugs were given in boluses in alternate turns every 30–60 min. A total of 5 mg of midazolam and 80 mg of ketamine were given. Prophylactic antibiotics were given. Blood pressure was kept above 90/60 mmHg. Haemodynamics, respiratory rate, oxygen saturation, 5-lead ECG, and urine output were all monitored. The patient had 2 L of 0.9% normal saline and three units of whole blood transfused. Intranasal oxygen was given through a nasal cannula at 2–4 L/min to supplement oxygenation. The patient made about 900 mL of urine.

At the end of the surgery, the surgical sites were infiltrated with 10 mL of 0.25% plain Bupivacaine (25 mg) in each limb. The patient was transferred to the recovery room and then ward. At the ward, the postoperative pain was disturbingly severe. The VAS pain score was 8–9/10. A possibility of compartmental syndrome was considered and the bilateral Plaster of Paris cast was released under bolus low dose ketamine 40 mg, and magnesium 50 mg.

Thereafter, IV $MgSO_4$ 5 mg/kg, i.e., 300 mg was added to 500 mL of crystalloid to run 4 hourly. In addition, 1 mL of 2 mg/kg of $MgSO_4$ (i.e., 120 mg) was added to the 14 mL of 0.125% plain bupivacaine to make 15 mL of magnesium–bupivacaine admixture, which was given every 4 h. Furthermore, IV paracetamol 1 g was given every 6 h. All medications were given for 48 h.

The magnesium/bupivacaine regimen reduced the VAS pain scores from 9/10 to 5-6/10, and then to 3/10 over a 6-h period. The VAS pain score remained at or lower than 3/10 throughout the postoperative period. Supplemental oxygen was continued. Adequate haemodynamics, oxygenation, hydration, warmth, and urine output were ensured. The postoperative period was crisis free. The epidural catheter was removed after 48 h.

Discussion

Effective postoperative analgesia is one of the primary concerns of the anaesthesia care provider. The possibility of both perioperative vaso-occlusive (painful) crisis and postoperative pain constitute a peculiar bi-modal pain management challenge to the anaesthetist, during the care of a surgical patient with SC disease.[6]

On the one hand, ineffective postoperative pain care produces poor ventilatory effort, a reduction in effective cardiac function; nausea and vomiting, ileus, and urinary retention. A negative effect on immune function, coagulation, and wound healing has been described.[6,7] On the other hand, a perioperative SC pain crisis worsens the patient's overall morbidity. The provision of postoperative analgesia is still poor in Africa.[7] Another remarkable challenge is the fact that opioids (considered the mainstay potent postoperative analgesia drug) have caused opioid addiction in the index patient, in addition, opioid also promotes ventilatory depression, nausea and vomiting, urinary retention, delirium and ileus.[8] Therefore, it was necessary to avoid opioid-based anaesthesia.

Opioid-free anaesthesia has emerged as a practical, viable and effective alternative in recent times.[9] It reduces the chances of opioid-induced life-threatening problems such as hypoventilation and is beneficial in varied groups of patients.[10] Various combinations and dosages of drugs

such as magnesium, acetaminophen, alpha-2 agonist, (for example, dexmedetomidine), beta-blockers, (for example, labetalol), ketamine, lidocaine, corticosteroids, (for example, dexamethasone), gabapentinoids, with or without nerve block have been used.[9,10]

Anaesthesia without opioids has been described as a viable alternative to remifentanil.[11] Both clonidine and dexmedetomidine provide effective analgesia in bariatric surgery compared to opioids.[12] Lidocaine, dexmedetomidine and ketamine admixture produce a better pain score in pancreatic surgeries.[13] Similar findings were recorded in a meta-analysis of gastrointestinal, gynaecological and breast surgeries.[14]

In this patient, we used a magnesium-based regimen to facilitate perioperative pain care and prevent pain crisis in a SC disease patient. The understanding of pain in SC disease is evolving.[15] Inflammatory cytokines and bradykinin activate peripheral nerve endings. The A δ-and C-fibers send afferents to the spinal cord. Glutamate, interleukin-1 and N-methyl-d-aspartate (NMDA) receptors exacerbate pain sensation.[15,16]

The analgesic properties of magnesium have been linked to the blockade of the NMDA receptor. It blocks both calcium and sodium ion influx, in voltage-gated channels. It enhances anaesthesia and prolongs analgesia.[15,16] Xiang *et al*.[17] and El-Hussein *et al*.[18] reported a positive postoperative anti-nociceptive effects of magnesium adjunct in limb procedures. Magnesium adjunct reduces pain scores after mastectomy[19] and in bariatric abdominoplasty.[20] A meta-analysis has shown consistent postoperative analgesia efficacy.[21] In our patient, the use of magnesium significantly reduced postoperative pain scores.

Magnesium's use may be complicated by headache, flushing, and hypoventilation. Loss of tendon reflexes, oliguria, and even cardiac arrest may occur. A continuous surveillance and usage of 10 mL of 10% calcium gluconate, among other standard guidelines would have been used to treat complications.[22] However, toxicity signs were not seen in this patient.

Conclusion

The double trouble of preventing perioperative SC disease pain crisis and managing postoperative pain is disturbing to anaesthesia care providers. The search for the optimal regimen continues. Magnesium adjunct, an NMDA receptor antagonist shows a great positive potential in managing this complication.

Strength of the study

Neuraxial magnesium adjunct and infusions enhance the provision of postoperative analgesia to surgical patients. This can serve as a viable alternative in low-resource settings, most especially in peculiar cases like the SC disease patient.

Limitation

Alpha-2 agonist and syringe pumps were not used, as it was not readily available in our centre at the time.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understand that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Lee L, Smith-Whitley K, Banks S, Puckrein G. Reducing health care disparities in sickle cell disease: A review. Public Health Rep 2019;134:599-607.
2. Inusa BP, Hsu LL, Kohli N, Patel A, Ominu-Evbota K, Anie KA, *et al.* Sickle cell disease-genetics, pathophysiology, clinical presentation and treatment. Int J Neonatal Screen 2019;5:20.
3. Tebbi CK. Sickle cell disease, a review. Hemato 2022;3:341-66.
4. Ballas SK, Darbari DS. Review/overview of pain in sickle cell disease. Complement Ther Med 2020;49:01-12. doi: 10.1016/j.ctim.2020.102327.
5. Takaoka K, Cyril AC, Jinesh S, Radhakrishnan R. Mechanisms of pain in sickle cell disease. Br J Pain 2021;15:213-20.
6. Walker I, Trompeter S, Howard J, Williams A, Bell R, Bingham R, *et al.* Guideline on the peri-operative management of patients with sickle cell disease: Guideline from the association of anaesthetists. Anaesthesia 2021;76:805-17.
7. Gao L, Mu H, Lin Y, Wen Q, Gao P. Review of the current situation of postoperative pain and causes of inadequate pain management in Africa. J Pain Res 2023;16:1767-78.
8. Butterworth JF. Chapter 10. Analgesic agents. In: Butterworth JF, Mackey DC, Wasnick JD, editors. Clinical Anaesthesiology. 7th ed. New York: Lange McGraw-Hill Education, LLC; 2013. p. 300-12.
9. Beloeil H. Opioid-free anaesthesia. Best Pract Res Clin Anaesthesiol 2019;33:353-60.
10. Kaniyil S, Haley C. Opioid free anaesthesia. Anaesth Tutor Week 2021;461:1-6.
11. Forget P. Opioid-free anaesthesia by total intravenous anaesthesia techniques may be alternative to remifentanil. BMJ 2022;378:o2071.
12. Berlier J, Carabalona JF, Tête H, Bouffard Y, Le-Goff MC, Cerro V, *et al.* Effects of opioid-free anaesthesia on postoperative morphine consumption after bariatric surgery. J Clin Anesth 2022;81:110906.
13. Hublet S, Galland M, Navez J, Loi P, Closset J, Forget P, *et al.* Opioid-free versus opioid-based anaesthesia in pancreatic surgery. BMC Anaesthesiol 2022;22:9.
14. Olausson A, Svensson CJ, Andréll P, Jildenstål P, Thörn SE, Wolf A. Total opioid-free general anaesthesia can improve postoperative outcomes after surgery, without evidence of adverse effects on patient safety and pain management: A systematic review and meta-analysis. Acta Anaesthesiol Scand 2022;66:170-85.
15. Kamel WY, Shoukry AA. Magnesium sulphate within multimodal analgesia, pre-emptive or preventive analgesia. Ain Shams J Anaesthesiol 2022;14:1-9.
16. Shin HJ, Na HS, Do SH. Magnesium and pain. Nutrients 2020;12:2184.
17. Xiang W, Jiang L, Shi L, Jiang C, Zhou Y, Yang C. The effect of magnesium added to bupivacaine for arthroscopy: A meta-analysis of randomised controlled trials. J Orthop Surg Res 2021;16:583.
18. El – Hussein AK, Ahmed MA, Sadek MK. The effect of adding different doses of Magnesium Sulphate to Bupivacaine in the ultrasound-guided supraclavicular brachial plexus block anaesthesia. MJMR

2020;31:28-32. doi: https://dx.doi.org/10.21608/mjmr.2022.217057.
19. El-Aziz RA, ASal MF, Maaly AM. Effectiveness of adding magnesium sulfate to bupivacaine in ultrasound-guided serratus anterior plane block in patients undergoing modified radical mastectomy. Egypt J Anaesth 2022;39:100-6.
20. Silva Filho SE, Sandes CS, Vieira JE, Cavalcanti IL. Analgesic effect of magnesium sulfate during total intravenous anaesthesia: Randomised clinical study. Braz J Anaesthesiol 2021;71:550-7.
21. Choi GJ, Kim YI, Koo YH, Oh HC, Kang H. Perioperative magnesium for postoperative analgesia: An umbrella review of systematic reviews and updated meta-analysis of randomised controlled trials. J Pers Med 2021;11:1273.
22. Eldridge J, Jaffer M. Obstetrics anaesthesia and analgesia. In: Allman KG, Wilson IH, editors. Oxford Handbook of Anaesthesia. 4th ed. Oxford, United Kingdom: Oxford University Press; 2016. p. 758-917.