DOI: 10.7860/JCDR/2018/29288.11330

Case Report

Anaesthesia Section

Near Fatal Anaphylactoid Reaction Due to Bupivacaine Spinal Anaesthesia

SHRUTI SINGH[1], PRASHANT KUMAR SINGH[2]

ABSTRACT

Cardiorespiratory collapse in perioperative scenario-a dreaded occurrence, can have multiple aetiologies. Among them hypersensitivity reactions although rare, contribute significantly to patient mortality. The incidence of hypersensitivity reactions during anaesthesia have been reported to a range from 1 in 4000 to 1 in 25,000. Latex gloves and skeletal muscle relaxants are quite renowned in causing allergic reactions during perioperative period. The needle points less towards local anaesthetics, due to the rarity of such reports in literature. Also, the use of amide linked local anaesthetics for spinal anaesthesia reduces the chances of any such allergies occurring. Here, we report a case of severe anaphylactoid reaction occurring due to Bupivacaine given as a spinal anaesthetic. The extreme rarity of such reports implicating Bupivacaine as the causative agent for perioperative hypersensitivity puts this case in sharp focus. Preventing any such future episodes that are detrimental to a patient's well-being require awareness and skill on the part of the whole team. Exploring all questionable causative agents; however, less likely or farfetched therefore becomes important.

Keywords: Cardiac arrest, Hypersensitivity, Local anaesthetic, Regional anaesthesia

CASE REPORT

A 15-year-old boy presented to the Outpatient Department of Surgery and was diagnosed with a right sided indirect inguinal hernia. He was later planned for surgery on an elective basis under spinal anaesthesia. Relevant blood investigations e.g., complete blood count, blood sugar, serum creatinine and bleeding and coagulation profile were done followed by pre-anaesthetic checkup. He was declared to be fit for surgery. He was admitted one day before surgery, and preoperative preparations were carried out. Lidocaine skin sensitivity and antibiotic sensitivity were done and patient did not have any hypersensitive manifestation. On the day of surgery, patient was taken to the operation theatre and in the preoperative ward Intravenous cannula was put and normal saline drip started. After infusion of about 500 mL of normal saline patient was shifted to the operation theatre. Multipara monitors were attached and all basic parameters found to be within normal limits. Under strict aseptic conditions, with patient in sitting position 2.5 mL of injection Bupivacaine was administered in L3-L4 space using 25-gauge spinal needle. Within five minutes of drug administration, patient started complaining of itching and burning sensation over whole body followed by paroxysmal sneezing and difficulty in breathing. On auscultation, fine expiratory rhonchi were heard all over the lung fields, but more on left side. Patient was given 10 mg Hydrocortisone injection. However, soon after patients' pulse rate dropped to 20/minute and respiratory collapse occurred. Patient was intubated and two cycles of cardiorespiratory resuscitation were given along with intravenous hydrocortisone, atropine and adrenaline. Intratracheal adrenaline was also given to relieve bronchospasm. Following this, cardiac activity returned but some bronchospasm still remained. The surgery was postponed for a later date and after stabilisation, patient was shifted to ICU and put on ventilatory support. Following recovery patients' attendants were unwilling to go for surgery and patient was subsequently discharged.

DISCUSSION

Spinal anaesthesia has been used for more than a century and is considered as a relatively safe and effective alternative to general anesthesia. It has become a key component of several kinds of operative procedures generally located on the lower extremities, perineum, or lower body wall.

Patient safety during spinal anaesthesia demands meticulous pre-anaesthetic evaluation of the patient and vigilant perioperative care. Despite all precautions taken, anaesthetic practice is a potentially dangerous situation requiring a fine balance to be struck between benefit and risk. Comorbid conditions, human errors, faulty equipment and drug related side effects all can have adverse consequences. The patient in this case, did not have any relevant past or present medical history and neither was the technique or equipment faulty to the best of our knowledge.

While being generally safe, spinal anaesthesia may produce several complications. Some appearing only when it is given inappropriately i.e., inappropriate dose or level e.g., a high spinal may cause cardiovascular collapse presenting as either bradycardia or cardiac arrest. Nausea, vomiting and marked dyspnoea are also reported [1]. The dose (based on body weight) and level of anaesthesia were appropriate in this patient.

Even when used appropriately, complications may arise (post dural puncture headache, urinary retention, haematoma formation etc.,) [2].

The drug/local anaesthetic (in this case Bupivacaine) albeit rarely, may impact patient safety through the appearance of adverse drug reactions [3]. This is because sodium channels are located not only in the peripheral nerve fibres but also other organs, such as the brain and the heart. When given in larger doses epileptic fits and cardiac arrest compromise the situation markedly.

Adverse drug reactions to local anaesthetics appear in two ways: 1) Local reactions-trauma, contact dermatitis; and 2) systemic reactions-psychosomatic (anxiety, vasovagal), toxic reactions (CNS, cardiovascular), idiosyncratic, anaphylactoid, anaphylactic (usually on re-exposure) [4]. Allergic reactions to local anaesthetics do occur, but true IgE-mediated allergy is not so common, estimated to occur in less than 1% of all reported reactions [5,6]. Most of the reports of allergic reactions have been to ester-bonded agents since they are derivatives of PABA, a known allergen. The preservatives methylparaben and metabisulphite, are the second most likely culprit in local anaesthetic anaphylaxis [7]. Allergy to amide local anaesthetics is extremely rare, still conflicting reports keep coming up [8]. Rae SM et al., reported anaphylaxis associated with extradural bupivacaine [9]. Hosahally JS et al., have documented an anaesthetic death most likely due to bupivacaine toxicity [3]. Cross reactivity among amides has been suggested by a few recent

cases [10]. Amide-bonded local anaesthetics are not immunologically cross-reactive with their ester-bonded cousins [11]. However, there is one report of a 33-year-old woman who had urticaria and shortness of breath during spinal anaesthesia with lidocaine. Later, she was found to be reactive to both lidocaine and procaine during her skin testing [12]. More studies are needed to fully evaluate the problem.

The two primary causes of true anaphylaxis in patients under anaesthesia are skeletal muscle relaxants (60% to 70%) and latex allergy [13]. Premedication with sedatives and the use of skeletal muscle relaxants was not present in our patient as they are not required during spinal anaesthesia. Latex gloves were used for a considerable period, both before and after the administration of bupivacaine with no signs suggesting hypersensitivity prior to or subsequent to use of bupivacaine. All manifestations clustered closely around the time of bupivacaine administration.

Two distinct types of allergic reactions to local anaesthetics have been described:

- Contact dermatitis and oedema at site of administration-several reports
- Urticaria and anaphylaxis-Rare with limited case reports [14,15].

The diagnosis of anaphylaxis becomes easy when manifestations are immediate associated with cutaneous signs-itching, rash, erythema (appearing in about 65% cases), burning sensations, bronchospasm and/or cardiovascular collapse-hypotension, cardiac arrest. Bronchospasm, cardiovascular collapse and asphyxiation from upper airway oedema may lead to death of the patient. Respiratory tract involvement, shortness of breath and wheezing are present in 50% patients [16]. Whole body itching and sneezing were possibly the first symptoms and signs found in this patient followed by cardiorespiratory collapse.

Respiratory failure may occur due to airflow obstruction, cardiogenic or non cardiogenic pulmonary oedema or Acute Respiratory Distress Syndrome (ARDS). Pulmonary oedema was consistently present in our patient also. At the onset, anaphylactic reactions are usually diagnosed on clinical grounds; however, retrospectively they must be confirmed via skin testing and serology. None of which were done in our patient. The increase in serum tryptase is considered a reliable indicator of mast cell degranulation, not of an anaphylactic reaction as such. Diagnostic levels are reached within 30 minutes of the onset of a reaction. Half-life of the enzyme is only two hours; hence serum should be collected as early as possible. Unfortunately, its diagnostic efficacy is decreased due to the fact that tryptase levels rise with drugs causing non immune mediated mast cell degranulation also [17].

Irrespective of aetiology treatment remains the same; adequate oxygenation, sympathomimetic drugs, IV fluids. Termination of exposure and administration of antagonists in the setting of anaphylaxis are vital. A comprehensive drug and personal history and avoidance of suspected agents is the surest way to prevent perioperative anaphylaxis.

If patients on β blockers and asthma medications develop anaphylaxis, they are usually refractory to the standard treatments. In such patients, resistance to the effects of adrenaline, requires glucagon administration (1-5 mg) for controlling the anaphylaxis [18]. Histamine (H) 1 or 2 receptor antagonists or glucocorticoids should be avoided during pre-medication, as it blunts the initial onset and delays diagnosis of anaphylaxis [19]. These drugs should be reserved for early treatment of the anaphylactic/anaphylactoid event.

CONCLUSION

In the context of allergic reactions and hypersensitivity, spinal anaesthesia represents a potentially fatal situation. The rapidity of cardiovascular and respiratory compromise, inability to recognise early cutaneous manifestations due to surgical drapes, multifactorial causes for hypotension and impaired ventilation, administration of multiple drugs, disinfectants and use of instruments over a short period of time; all confound the aetiology drastically. It is difficult to differentiate between local anaesthetic hypersensitivity and other causes of adverse reactions as symptoms such as dyspnoea, swelling, and light-headedness may occur by multiple mechanisms. Still, it is imperative that the entire episode be studied in detail and steps taken to avoid any future calamity. Challenge testing (skin prick testing) with all proposed culprit agents along with appropriate safeguards as suggested by the recently published Association of Anaesthetists may help in preventing further episodes.

ACKNOWLEDGEMENTS

I sincerely acknowledge the help provided to me by staff and juniors of the Department of Pharmacology and Surgery.

REFERENCES

[1] Javed S, Hamid S, Amin F, Mahmood KT. Spinal Anaesthesia induced complications in caesarean section-A review. Journal of Pharmaceutical Sciences and Reasearch. 2011;3(10):1530-38.
[2] Agarwal A, Kishore K. Complications and controversies of regional anaesthesia: a review. Indian Journal of Anaesthesia. 2009;53(5):543-53.
[3] Hosahally JS, Chandra YPG, Ramkumar J. Anaesthetic death. A case report. European Journal of Forensic Sciences. 2015;2(3):24-27.
[4] Phillips JF, Yates AB, Deshazo RD. Approach to Patients with Suspected Hypersensitivity to Local Anaesthetics. Am J Med Sci. 2007;334(3):190-96.
[5] Wasserfallen JB, Frei PC. Long-term evaluation of usefulness of skin and incremental challenge tests in patients with history of adverse reaction to local anaesthetics. Allergy. 1995;50:162-65.
[6] Gall H, Kaufmann R, Kalveram CM. Adverse reactions to local anaesthetics: analysis of 197 cases. J Allergy Clin Immunol. 1996;97:933-37.
[7] Soto-Aguilar MC, deShazo RD, Dawson ES. Approach to the patient with suspected local anaesthetic sensitivity. Immunol Allergy Clin North Am. 1998;4:851-65.
[8] Brown BT, Beamish D, Wildsmith JAW. Allergic reactions to an amide local anaesthetic. British Journal of Anaesthesia. 1981;53:435-37.
[9] Rae SM, Milne MK, Wildsmith JAW. Anaphylaxis associated with but not caused by extradural bupivacaine. British Journal of Anaesthesia. 1997;78:224-26.
[10] Delgado PG, Antón R, Soriano V, Zapater P, Niveiro E. Cross-reactivity among amide-type local anesthetics in a case of allergy to mepivacaine. J Investig Allergol Clin Immunol. 2006;16(5):311-13.
[11] Kastrup EK. Facts and Comparisons., St. Louis: Facts and Comparisons Division: J.B. Lippincott Co; 2002.
[12] Seng GF, Kraus K, Cartwright G. Confirmed allergic reactions to amide local anaesthetics. Gen Dent. 1996;44:52-54.
[13] Brown V, Brandner B, Brook J, Adiseshiah M. Cardiac arrest after administration of Omnipaqueradiocontrast medium during endoluminal repair of abdominal aortic aneurysm. Br J Anaesth. 2002;88:133-35.
[14] Allergic Reactions to Local Anaesthetics. Available from: https://www.uptodate.com/contents/allergic-reactions-to-local-anesthetics. [Last accessed on 2017 June 19].
[15] Lane CG, Luikart R. Dermatitis from local anesthetics with a review of one hundred and seven cases from the literature. Journal of the American Medical Association. 1951;146(8):717-20.
[16] Shankar A, Puri R, Singh Y. Cardiovascular collapse under spinal anaesthesia. South Asian Fed of Obs & Gynae. 2009;1(3):67-69.
[17] Drug allergy: diagnosis and management of drug allergy in adults, children and young people. London: National Institute for Health and Care Excellence (UK); 2014 Sep. (NICE Clinical Guidelines, No. 183.) 7, Measuring serum tryptase after suspected anaphylaxis. Available from: https://www.ncbi.nlm.nih.gov/books/NBK274147/. [Last accessed on 2017 June 19].
[18] Mertes PM, Tajima K, Regnier-Kimmoun MA. Perioperative anaphylaxis. Med Clin North Am. 2010;94:761-89.
[19] Setlock MA, Cotter TP, Rosner D. Latex allergy: failure of prophylaxis to prevent a severe reaction. Anesth Analg. 1993;76:650-52.

PARTICULARS OF CONTRIBUTORS:
1. Senior Resident, Department of Pharmacology, All India Institutes of Medical Science, Patna, Bihar, India.
2. Assistant Professor, Department of Surgery, All India Institutes of Medical Science, Patna, Bihar, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Prasant Kumar Singh,
Assistant Professor, Department of Surgery, All India Institutes of Medical Science, Patna-801507, Bihar, India.
E-mail: pras_doc@yahoo.com

FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Submission: **Apr 13, 2017**
Date of Peer Review: **Jun 17, 2017**
Date of Acceptance: **Aug 24, 2017**
Date of Publishing: **Mar 01, 2018**