A case report on succinylcholine hypersensitivity presenting as severe bronchospasm

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Abstract
Succinylcholine is a depolarizing neuromuscular blocking agent, useful as an adjunct to general anaesthesia. Hypersensitivity to succinylcholine might lead to flushing, skin rash, bronchospasm, and shock. However, incidence of bronchospasm is less common in man. A 26 years old female patient at our setup, while undergoing dilatation and evacuation procedure, was administered with Injection Scoline (Succinylcholine) 50 milligrams intravenous. Within a minute, patient was gasping and underwent severe bronchospasms. Her SpO2 was 94% along with development of crepitation with tachypnoea and spasms (>30 respirations/minute). She was immediately resuscitated and intubated by the attending anaesthetist, treated for bronchospasm as well as shifted on ventilator. Within few hours, she was taken off the ventilator and extubated. She was stable then and discharged after two days. Hypersensitivity to NMBAs low incidence of 1 in 6000 - 20,000. NMBAs have a direct effect on mast cells thereby causing hypersensitivity reactions. Succinylcholine is considered to have 1% histamine releasing activity of tubocurarine, producing serious hypersensitivity reactions. This histamine released acts on the effector end-receptors in bronchial wall, leading to bronchoconstriction and sometimes a full-blown spasm. If timely management failed, it can result into an anaesthetic disaster. Rechallenge with succinylcholine was avoided due to possibility of fatal consequences. According to WHO UMC criteria & Naranjo Scale for causality assessment, causality was termed as "Probable".

Keywords: Bronchospasm, Hypersensitivity, Life-threatening, Neuromuscular Blocking Agent (NMBA), Suspected adverse drug reaction.

Introduction
Succinylcholine (Brand Name: Scoline), only depolarizing neuromuscular blocking agent (NMBA) currently used;[1] is administered intravenously (I.V.) and used as an adjunct to general anaesthesia for tracheal intubation and skeletal muscle relaxation during surgery or mechanical ventilation.[2] It is listed on 20th WHO Model List of Essential Medicines (March 2017)[3] due to its effectiveness and safety.

Inspite of its unique properties like short duration of action and intense blockade, it may cause few adverse drug reactions (ADRs) like muscle fasciculations, post-operative muscle pain and increased intraocular pressure; which has been encountered in approximately 50% of the patients.[4] Apnoea is noted with its prolonged or repeated administration.

Hypersensitivity is also one of the ADRs induced by succinylcholine. On rapid administration, it causes histamine release. Flushing, skin rash, bronchospasm and shock have been reported with succinylcholine.[4] Bronchospasm is known in experiments on dogs but its incidence in man is less common.[5] Tachycardia and raised blood pressure due to sympathetic ganglia stimulation by succinylcholine has also been reported.[4]

We present a case report on succinylcholine, suspected for inducing life-threatening bronchospasm in an obstetric patient while inducing her for general anaesthesia.

Case History
A 26 years old female patient presented to the obstetrics and gynaecology department at our setup with chief complaints of five months amenorrhoea and absence of foetal movements since two days. On ultra-sonographic examination, intrauterine foetal death was noted. For dilatation and evacuation procedure, routine investigations carried out were within normal limits. Before commencing the procedure, she was administered with pre-anaesthetic medication. She was fully conscious and vitally stable. After painting and draping, she was administered with Injection Ketamine 70 milligrams I.V. Her pulse rate and blood pressure readings were 116 beats/minute and 146/90-millimetre mercury respectively. Fifteen minutes later, she was injected with Injection Scoline (Succinylcholine) 50 milligrams I.V. Within a minute of administering Injection Scoline, the patient was gasping and underwent severe bronchospasms. Her SpO2 was 94% and vital readings showed pulse rate (120 beats/minute); blood pressure (186/84-millimetre mercury) and crepitation with tachypnoea and spasms (>30 respirations/minute). The procedure was withheld and she was immediately resuscitated and intubated by the attending anaesthetist. She was also managed with Injection Dexona (Dexamethasone) 8 milligram I.V.; Injection Effcorlin (Hydrocortisone) 100 milligram I.V.; Injection Dytor (Torsemide) 2 millilitre I.V.; Injection Lasix (Furosemide) 2 millilitre I.V.; Injection Vecuronium 8 milligram I.V.; Injection Nitroglycerin 1 millilitre/hour and Injection Deriphyllin (Theophylline) 2 millilitre I.V. The patient had started to stabilize with the initiation of treatment. She was also nebulized with Duoline (Salbutamol) continuously for one hour. She was then shifted on ventilator and nebulized with Ipravent (Ipratropium Bromide) along with Duoline (Salbutamol) QDS over fifteen minutes. Within few hours, the patient was taken off the ventilator as well as extubated. She was stable with full consciousness and following verbal commands. Her urine output and electrolyte levels were also within the normal range. The patient was kept under observation and discharged after two days.

In this case, attending anaesthetist considered acute left ventricular failure as a differential diagnosis for bronchospasm due to pregnancy and precipitated by lithotomy position. However, her ECG and two-D ECHO were perfectly normal. She also responded well to anti-allergic treatment in short time period. Thus, considering shorter duration of action as well; Succinylcholine Hypersensitivity looks like the most appropriate diagnosis.

Discussion

ADRs can be broadly classified into two types: Type A (Augmented or Predictable) and Type B (Hypersensitivity or Unpredictable). Hypersensitivity to NMBAs is a dreadful complication but difficult to analyse. This is due to the fact that it has a low incidence (1 in 6000 - 20,000 administrations of NMBA).[6]

NMBAs have a direct effect on mast cells thereby causing hypersensitivity reaction. All NMBAs can elicit anaphylaxis and there is an agreement that the short-acting depolarizing succinylcholine poses greatest risk, despite its close structural homology to acetylcholine.[7] Succinylcholine is considered to have only 1% of the histamine releasing activity of tubocurarine (potent agent for histamine release) that is likely to produce serious hypersensitivity reactions.[4] Clinical responses owing to histamine release are bronchospasm, hypotension, excessive bronchial and salivary secretion.[1]

Bronchospasm is an exacerbated airway hyper-reactivity. It is characterised by prolonged expiration, wheeze and increased peak airway pressures during Intermittent Positive Pressure Ventilation (IPPV).[8] The prevalence of bronchial hyper-reactivity is approximately 10% and this condition is an important risk factor for perioperative bronchospasm, a potentially life-threatening event whose incidence in anaesthesia practice varies from relatively low rates of 0.17% or 4.2% to higher ones of about 7% or 20%.[7] Thus, if we fail to provide timely management, it can result into an anaesthetic disaster.

The first case of a bronchospasm induced by succinylcholine was reported by Fellini and his co-workers in 1963.[5] Bronchospasm can either be allergic (IgE) mediated or non-allergic (mechanically) mediated. Here with reference to this case, mechanical factor like intubation was absent prior to manifestation of bronchospasm. On eliciting patient's history, it was noted that she had undergone caesarean sections twice in the past. Therefore, prior sensitization to NMBA is also a possibility. Thus, by ruling out other mechanism for bronchospasm, a diagnosis of pharmacologically induced hypersensitivity (bronchospasm) was made. Once histamine is released, it acts on the effector end-receptors localised in the bronchial wall, leading to bronchoconstriction and sometimes to a full-blown spasm.[5] Also, this hyperreactivity of bronchi is IgE-dependent with the quaternary ammonium (NH4 +) structures as main antigenic epitope. Cross-reactivity between NMBA is also said to be common because of this ubiquitous ammonium groups in these drugs. The estimated prevalence of cross-reactivity between NMBA is about 65% by skin tests and 80% by radioimmuno assay (RIA) inhibition tests.[7] In recent years, newer studies from allergists, mainly considering positive skin test as a proof for IgE-mediated type B ADR, indicated that for safety reasons, re-exposure to the culprit drug and to cross-reactive drugs needs to be avoided.[9]

Here NMBA, succinylcholine, is suspected as the etiological agent for hypersensitivity. This is because bronchospasm manifested within few minutes of I.V. administration of succinylcholine and subsided with the discontinuation of succinylcholine (dechallenge), immediate resuscitation and intubation, treatment with parenteral corticosteroids and vecuronium. Another drug administered prior to succinylcholine was Ketamine. This parenteral anaesthetic agent has unique properties that makes it useful for anesthetizing patients at risk for hypotension and bronchospasm. It is a potent bronchodilator due to its indirect sympathomimetic activity and some direct bronchodilator activity.[10] Hence, ketamine was excluded as the causative agent for bronchospasm.

Now, stimulation of sympathetic ganglia by succinylcholine may result into tachycardia and hypertension as mentioned above. Succinylcholine stimulates autonomic cholinoceptors, including the nicotinic receptors at both sympathetic and parasympathetic ganglia and muscarinic receptors in the heart (e.g. sinus node).[11] Thus, when nicotinic receptors get stimulated, it can produce tachycardia and hypertension. With large doses of succinylcholine, positive inotropic and chronotropic effects may also be observed.[11] With respect to this case, the pulse rate and blood pressure readings varied slightly after I.V. administration of succinylcholine.

In order to confirm whether succinylcholine was causally related to bronchospasm, tachycardia and hypertension, a drug rechallenge test could have been performed. But the risk of fatality always stands. Thus, rechallenge was avoided in the present case scenario. Hence, according to WHO UMC criteria[12] & Naranjo Scale[13] for causality assessment, there is a "Probable/Likely" causal relationship between the succinylcholine and bronchospasm. This ADR was also reported to the nearest ADR Monitoring Centre & uploaded via Vigiflow under the Pharmacovigilance Programme of India (PvPI).

Conclusion

Hypersensitivity can lead to severe morbidity and mortality. Proper management of such emergencies is a prime requirement as a healthcare professional. With respect to hypersensitivity reactions like in our study, biological tests (IgE specific assays, plasma histamine, plasma tryptase) and skin tests are considered as the gold standard for diagnosing them.[14] These confirmatory tests should be performed post-operatively to suggest a definite causal relationship between the drug and reaction. This also allows the anaesthetists to decide whether the same NMBA should be used for muscle relaxation in the same patient or not. This may help prevent the future episodes of

succinylcholine hypersensitivity in the patients. Elicitation of past history as well as allergic history of the patient can also help avert such events.

References

1. Personal authors: Hibbs RE, Zambon AC. Agents Acting at the Neuromuscular Junction and Autonomic Ganglia. Goodman and Gilman's: The Pharmacological Basis of Therapeutics.12th Ed:255-276. McGraw Hill; 2011.
2. John P. Cunha. Side-effects Centre. Last reviewed on Rx List 08/01/2017. http://www.rxlist.com/anectine-side-effects-drug-center.htmillilitre.
3. WHO Model List of Essential Medicines (20th List). World Health Organization. March 2017.lkiiiiiiii/
4. Chapter in a book: Suxamethonium chloride. Martindale: The Complete Drug Reference. 36th Ed:1909-1912. Pharmaceutical Press; 2009.
5. BeleBinda N, Valebi F. A Case of Bronchospasm Induced by Succinylcholine. *Canad Anaesth Soc J.* 1971;18(1):116-117.
6. Sadleir PHM, Clarke RC, Bunning DL, Platt PR. Anaphylaxis to neuromuscular blocking drugs: incidence and cross-reactivity in Western Australia from 2002 to 2011. *BJA: Br J Anaesth.* 2013;110(6):981–987. https://doi.org/10.1093/bja/aes506.
7. Mali S. Anaphylaxis during the perioperative period. *Anesth Essays Res.* 2012;6(2):124–133. doi: 10.4103/0259-1162.108286
8. Loosely A, editor. Management of bronchospasm during general anaesthesia. Update in Anaesthesia :17-21. Available from: http://www.anaesthesiologists.org.
9. Spoerl D, Nigolian H, Czarnetzki C, Harr T. Reclassifying Anaphylaxis to Neuromuscular Blocking Agents Based on the Presumed Patho-Mechanism: IgE-Mediated, Pharmacological Adverse Reaction or "Innate Hypersensitivity"? Haybaeck J, Pichler W, eds. *Int J Mol Sci.* 2017;18(6):1223.
10. Personal authors: Patel PM, Patel HH, Roth DM. General Anaesthetics and Therapeutic Gases. Goodman and Gilman's: The Pharmacological Basis of Therapeutics. 12th Ed: 527-564. Mc Graw Hill; 2011.
11. Personal authors: Kruidering-Hall M, Campbell L. Skeletal Muscle Relaxants. Katzungs Basic & Clinical Pharmacology. 13th Ed: 614-637. Mc Graw Hill Education; 2015.
12. Kumar A, Majhee L, Gari M. Causality, severity and preventability assessment of adverse drug reactions in patients received anti-retroviral therapy in a tertiary care hospital: A retrospective study. *Natl J Physiol Pharm Pharmacol* 2017;7(2):178-182.
13. Srinivasan R, Ramya G. Adverse drug reaction-Causality assessment. *IJRPC.* 2011;1(3):606-612.
14. Dorze M; Plaud B; Mebazaa A. A case series of life-threatening succinylcholine-induced anaphylaxis. *Eur J Anaesthesiol*. 2017;34:562–567.

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