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RESEARCH ARTICLE

SUGAMMADEX: A NOVEL APPROACH IN THE MANAGEMENT OF ROCURONIUM-INDUCED ANAPHYLAXIS DURING ANESTHESIA INDUCTION

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Abstract

Anaphylaxisis a rapid-onset, potentially life-threateningsystemichypersensitivityreaction, with an estimated incidence of 1 in 20,000 anesthetic administrations. Neuromuscularblocking agents (NMBAs), particularlyrocuronium and succinylcholine, are implicatedin 60–70% of anestheticanaphylaxis cases. Prompt recognition and intervention are critical in these emergencies. Sugammadex, a selectiveantagonist of rocuronium, offers a noveltherapeuticapproach due to itsability to rapidlyencapsulaterocuroniummolecules, effectivelymitigating the immunologicalprocessesdrivinganaphylaxis. This report presents a 46-year-old womanwhodevelopedrocuronium-inducedanaphylaxisduringcholecystectomy. Manifesting as severe hypotension and urticarialerythemashortlyafter induction, her condition wasunresponsive to initial resuscitativemeasures. Administration of sugammadexpromptlyreversed the reaction, restoringhemodynamicstability and resolvingsymptoms. Allergytestingsubsequentlyconfirmedrocuronium as the causative agent. The discussion explores the pathophysiology, diagnostic challenges, and biochemical investigations pertinent to NMBA-inducedanaphylaxis. A review of the literature supports sugammadex as an emergingtherapeutic option, particularly in refractory cases. This case underscores the necessity of timelydiagnosis and intervention, emphasizingsugammadex'srole in enhancing patient safetyduringanesthesia. Furtherresearch and clinical vigilance are essential to optimizeoutcomes in NMBA-inducedanaphylaxis.

Introduction:-

Anaphylaxisisdefined as a severe, potentially life-threatening, generalized or systemichypersensitivityreactionthatoccursrapidly [1]. Although rare, with an incidence of approximately 1 case per 20,000 anesthetics, anaphylaxisduringanesthetic induction represents a criticalmedical emergency thatcanbe life-threatening [2]. Among the causative agents, neuromuscularblocking agents (NMBAs), particularlyrocuronium and succinylcholine, are the mostcommonpharmacological causes, accounting for about 60 to 70% of cases [3, 4].

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The first line of treatment for anaphylaxis in the anestheticcontextinvolves the immediate cessation of the offending agent and the administration of medicationsaimedatstabilizing the patient'shemodynamicstatus [3]. Sugammadex, a selectiveantagonist of rocuronium, isparticularly effective in thiscontext due to itsability to rapidly reverse rocuronium-inducedneuromuscularblockade [5]. This pharmacologicalcharacteristic of sugammadexpromotesits use in the treatment of rocuronium-inducedanaphylaxis [3].

The incidence of perioperativeanaphylaxis ranges from 1 in 385 to 1 in 20,000 [6]. The worstoutcomesincludemortality (3% to 9%) and severemorbiditysuch as anoxicbraininjury. Neuromuscularblocking agents have been implicatedin 33% to 63% of cases, and 57% to 86% duringanesthesia induction [6]. The mostfrequentsymptomsincludecardiovascularsymptoms (78.6%), cutaneoussymptoms (66.4%), and respiratorysymptoms, withbronchospasmbeing the main symptom in the case of respiratoryinvolvement (39.9%) [6]. However, severe, isolatedcardiovascular collapse and severebronchospasm are the mostcommonsymptomsthathinderdiagnosis [6].

Sugammadex (Bridion; Merck, Madrid, Spain) is a modified gamma-cyclodextrinthatirreversiblybindsrocuroniummolecules in a 1:1 ratio. By binding to rocuronium, it blocks or attenuates the immunologicalprocessesresponsible for rocuronium-inducedanaphylaxis [7]. The ability of sugammadex to selectivelyencapsulaterocuroniummolecules and rapidly reverse neuromuscularblockadesuggestsitspotentialeffectivenessagainstrocuronium-inducedanaphylaxis [5,]. McDonnell et al. reported the first clinical case of successful management of severerocuronium-inducedanaphylaxiswithsugammadex[3].

Here, we report a case of rocuronium-inducedanaphylaxiseffectivelytreatedwith the administration of sugammadex, illustrating the relevance of thisinnovativetherapeuticapproach.

Case Report:
A 46-year-old woman, weighing 64 kg and standing at 168 cm, was scheduled for a cholecystectomy. Her medical history included two cesarean sections performed over two years ago and a diagnosis of allergic rhinitis. Preoperative assessment did not reveal any airway abnormalities. The patient was premedicated with hydroxyzine, 75 mg, administered both the day before and on the morning of the surgery.

Anesthesia induction was initiated with propofol (170 mg) and fentanyl (200 µg). Rocuronium (40 mg) was administered to achieve neuromuscular blockade, and orotracheal intubation was performed successfully. Shortly after intubation, the patient developed intense urticarial erythema and severe hypotension, with systolic blood pressure dropping to 50-30 mmHg and heart rate fluctuating between 70 and 90 bpm. No signs of bronchospasm were noted, indicating a grade II anaphylactic reaction.

Initial treatment included intravenous ephedrine (4 mg) and rapid infusion of Ringer's acetate solution; however, the patient's hemodynamic instability persisted, with systolic blood pressure remaining below 70/40 mmHg. Given the lack of response to these interventions, epinephrine was considered but ultimately not administered. Instead, 1000 mg of sugammadex was given to reverse the effects of rocuronium. Shortly after administration of sugammadex, the patient's skin symptoms resolved, and blood pressure spontaneously returned to preinduction levels.

Following the successful resolution of the anaphylactic reaction, the surgical procedure continued without further complications. No additional doses of muscle relaxant were administered. Anesthesia was maintained using propofol and remifentanil, with no recurrence of anaphylactic reactions. The operation was completed in one hour and 50 minutes, and tracheal extubation was performed in the recovery room. The patient's postoperative recovery course was uneventful.

On postoperative day 1, the patient was transferred from the ICU to a general ward. She was subsequently referred to an allergologist for further evaluation. One month after surgery, allergy testing revealed a positive reaction only to rocuronium, the muscle relaxant used during anesthesia.

Discussion:-

Clinical Aspects:

Allergicreactions to neuromuscularblocking agents (NMBAs) pose a significantconcern in anesthesia, with up to 75% of suchreactionsoccurringupon the first knownexposure to an NMBA. Studies on structure and activity have establishedthat the substituted ammonium groups are part of the allergenicdeterminant structure, suggestingpotentialprevioussensitization to NMBAs [8].

In our patient, the diagnosiswasinitiallydelayed due to the presence of isolatedrespiratorysymptoms and the sustained trauma. Whenbronchospasmoccurs, itis essential to exclude causes such as inadequateanestheticdepth, muscle relaxation, and aspiration of gastric contents or blood.

Biochemical Investigations :

Combiningserum tryptase and plasma histamine levelsincreases the diagnostic accuracy of immediatehypersensitivityreactions, although normal levels do not exclude the diagnosis due to their short half-lives [9]. Whilehistamine'shalf-life isimpractical for diagnosis, tryptaselevelsremaindetectable for a longer period, with multiple samplesimprovingdetection due to the narrowwindow for elevation and effects of hemodilution [9].

Detection of specificIgEantibodiesplays a crucial role in diagnosing NMBA-inducedhypersensitivity. Rouzaire et al. [10] demonstrated the utility of specificIgEagainstsubstitutedtertiary ammonium structures over individual NMBA molecules. Skin prick and intradermal tests, performedat least 4–6 weeksafter the reaction to avoid false negatives, exhibithighspecificity and adequatenegativepredictive value [11,12].

Cell-targetedassays, such as the basophil activation test (BAT) by flow cytometry, are consideredunnecessary if skin tests or specificIgEassays are positive. BAT demonstrates good specificity but lowsensitivity, stronglycorrelatingwith skin tests [13]. Provocation testingistypically not performed.

In our case, the subsequent positive test result for Rocuroniumconfirmsitsrole as the causative agent of the anaphylacticreaction. However, wedid not conduct tests for Cisatracurium, as theywere not performed in thisspecific case.

Literature Review:-

The efficacy of sugammadex in managingrocuronium-inducedanaphylaxisissupported by several case reports. Kim et al. [14] presented a case report detailing the successfultreatment of rocuronium-inducedanaphylaxisusingsugammadex. Similarly, TakashiKawano et al [15] reported a case of successful management of rocuronium-inducedanaphylaxiswithsugammadex. De La Cruz et al[16] alsodocumented a case wheresugammadexeffectivelytreatedanaphylaxis to rocuronium, withbronchospasm as the onlysymptom. These cases highlightsugammadex'spotential as a treatment option for rocuronium-inducedanaphylaxis.

Baldo et al. [17] demonstratedthatencapsulatingrocuroniumwithsugammadexcanprevent but not stop NMBA-induced activation. Clarke et al. [18] showedthatsugammadex-boundrocuroniumpreventstriggering type 1 hypersensitivityreactions in sensitizedindividuals but does not modify an alreadytriggeredreaction. Sugammadexwas ineffective in some cases responding to epinephrine and fluidloading, whileotherssuggestrecoverycouldoccurafter 15–20 minutes with standard treatment [19]

The causative agent of the allergicreactionisoftenincorrectlyidentifiedat the time of the reaction in one-third of cases. Theoretically, sugammadex'saffinity for rocuroniumshouldexceed the cell-boundIgEantibodies' affinity, encapsulating the epitoperesponsible for rocuronium-inducedanaphylaxis[17]

In our patient, sugammadexwasadministeredapproximately 15 minutes after the reactionstarted, with no prioradrenalinetreatment, indicatingimprovementwas not due to adrenaline. Additionally, improvementcannotbeattributed to increasedpreload as the only manifestation wasbronchospasm, and reversal of neuromuscularblockadetypicallyworsensrespiratorymechanics. The current guidelines recommendadministeringnebulizedadrenalineafterinhaled beta-2 adrenergicreceptoragonists or an intravenous bolus and infusion of beta-agonist or adrenaline. Corticosteroids are a second-line treatment [20]

Conclusion:-

The presented case underscores the significance of recognizing and effectivelymanagingrocuronium-inducedanaphylaxisduringanesthesia induction. The prompt administration of sugammadexproved instrumental in reversing the neuromuscularblockadeinduced by rocuronium, therebyresolving the life-threateninganaphylacticreaction. This case adds to the growing body of evidencesupportingsugammadex as a crucial therapeutic option in such scenarios. Furthermore, the discussion highlights the importance of biochemical investigations and literaturereview in confirming the diagnosis and guidingtreatmentdecisions. Movingforward, continued vigilance, prompt recognition, and appropriateutilization of sugammadex are essential for optimizing patient outcomes in the management of rocuronium-inducedanaphylaxisduringanesthesia induction.

Author Statement

Conflict of Interest Statement

No authors have competing interests.

Consent

As per international standard or university standard, patient's consent has been collected and preserved by the authors.

Ethical Approval

None.

Methods:-

Use of Large Language Models (LLMs):

In conducting this review, we employed Large Language Models (LLMs), specifically ChatGPT, developed by OpenAI. LLMs were utilized to generate text in sections where comprehensive analysis or discussion was required, such as the introduction, discussion, and conclusion. It's important to note that LLMs function as AI-driven text generation tools and do not constitute traditional authorship. Consequently, the text generated by LLMs was reviewed and edited by the authors to ensure accuracy, coherence, and alignment with the objectives and scope of this review.

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