

Hypertensive Crisis Associated with Methylphenidate Use During Total Intravenous Anaesthesia for Orthognathic Surgery: A Case Report

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ABSTRACT

Background: Methylphenidate is a central nervous system stimulant prescribed as a first-line treatment for attention deficit hyperactivity disorder. Its primary pharmacological mechanism involves the inhibition of presynaptic dopamine and norepinephrine transporters, effectively increasing catecholamine availability within the synaptic cleft in the prefrontal cortex. This report aimed at presenting a case represents a hypertensive crisis associated with methylphenidate use during total intravenous anesthesia, necessitating the suspension of surgery.

Case Report: A 34-year-old female was scheduled for elective orthognathic surgery. Her medical history included attention-deficit/hyperactivity disorder, depressive illness, and an unspecified anxiety condition, managed with methylphenidate (for the past 18 years) and sertraline. A hypertensive crisis developed 10 minutes after the induction of general anesthesia, prior to any surgical or painful stimulation. After 30 minutes without a reduction in blood pressure levels, intravenous anaesthesia was withdrawn, and the surgery was aborted.

Conclusion: Interactions between methylphenidate and/or sertraline with general anesthesia are documented in the patient package insert. Although these medications are widely used worldwide, adverse events to be very rare. This case demonstrated the interaction of drugs with hypertensive crisis, leading to the surgery being postponed.

Keywords: Attention deficit disorder; Drugs interactions; Methylphenidate; Sertraline; Total intravenous anesthesia; Orthognathic Surgery.

Abbreviations: TIVA: Total Intravenous Anesthesia; ADHD: Attention-Deficit/Hyperactivity Disorder; OR: Operating Room; ADRs: Adverse Drug Reactions

Introduction

An epidemiological study of 3,199 individuals aged 18 to 44 years, using clinical interviews, showed that the estimated prevalence of Attention-Deficit/Hyperactivity Disorder (ADHD) was 4.4% [1]. Current literature does not allow us to say that there is a single universally

“best” medication for all adults; however, psychostimulants present the most consistent evidence of effectiveness in reducing the core symptoms of ADHD. There are now hundreds of systematic reviews on ADHD, there is strong evidence for the efficacy of pharmacological treatment on symptom reduction in the short term, particularly

for stimulants [2]. Evidence supports the use of extended-release methylphenidate and amphetamine formulations, atomoxetine, and extended-release guanfacine to improve symptoms of ADHD in adolescents [3].

While FDA committee members list concerns for its use - acknowledging the growing trend in prescription rates and the potential long-term risk of adverse events, particularly on the cardiovascular system [4]. In a retrospective study starting in 1986 at 1 site and ending in 2005 at all sites, with additional covariate assessment using 2007 survey data, showed that among young and middle-aged adults, current or new use of ADHD medications, compared with nonuse or remote use, was not associated with an increased risk of serious cardiovascular events [5]. Furthermore, classic and rigorously conducted studies in literature provide evidence that methylphenidate can promote earlier emergence from isoflurane and propofol anaesthesia in rats; an experimental model, of course, but it appears to suggest an antagonistic mechanism between methylphenidate and general anaesthesia [6]. The interaction between methylphenidate and anaesthesia is that concomitant use of halogenated anesthetics and methylphenidate may increase the risk of sudden blood pressure and heart rate increase during surgery [7]. To avoid this risk, it is recommended to avoid use of methylphenidate on the day of surgery when halogenated anesthetics are being used [7]. We will report one case of severe hypertension during Total Intravenous Anesthesia (TIVA), which led to the cancellation of the initiated procedure for the patient's safety.

Case Report

This case report was registered in the Plataforma Brasil and approved by the CEP/CONEP of the Hospital São Lucas FAG, Cascavel, PR, Brazil, and the Free and Informed Consent Form was signed by the patient after the explanation of the entire anesthetic procedure to be performed and authorized for publication in an indexed medical journal. A 34-year-old female patient, ASA II, BMI 23.8 kg.m⁻² was scheduled for orthognathic surgery. Previous anesthetic history: adenoidectomy and vaginal delivery, with no reported complications. ADHD, depressive/unspecified anxiety disorder, and no history of hy-

pertension or other cardiovascular system diseases. For the past 18 years, she has been taking methylphenidate 10 mg twice daily (last dose approximately 12 hours before scheduled surgery time), and sertraline. Additionally, she had used bupropion for two months as a smoking cessation aid, which was discontinued one month prior to the surgical procedure. She also reported the nightly use of melatonin gummies.

Routine laboratories were within normal limits. Physical examination, blood pressure and heart rate were at normal values. During the pre-anesthetic consultation, it was deemed unnecessary to suspend the patient's ongoing medication. The patient was referred to in the Operating Room (OR) very calmly without pre-anesthetic medication. She was monitored with cardioscopy (ECG), pulse oximetry, and non-invasive blood pressure control every 5 minutes. The initial levels of blood pressure were 120/70 mmHg and heart rate 68 bpm, and saturation O2 97%. After intravenous access with a 20G catheter, the patient was positioned in the supine position, after pre-oxygenation, lidocaine (60 mg) and sufentanil (15 µg) were administered intravenously and continuous infusions were started: propofol at a target effect-site concentration of 4 µg.ml⁻¹, and remifentanil at 0.25 µg.kg⁻¹.min⁻¹. Rocuronium was administered at a dose 0,8 mg.kg⁻¹. Nasotracheal intubation was performed using a video laryngoscope.

After an initial 10-minute hypotensive phase, when the surgical team was still performing antisepsis (causing no nociceptive stimulus) she developed a hypertensive crisis with maximum blood pressure level was 192/107 mmHg (Table I). Blood pressure decreased slightly following the readjustment of propofol (4.8 µg.mL⁻¹) and remifentanil (0.4 µg.kg⁻¹.min⁻¹). The patient exhibited no clinical signs of inadequate anesthetic plan at any moment. Heart rate was close to 50 bpm and marked miosis was observed. Concurrently, generalized piloerection was observed. Another anesthesiologist and a nurse helped rule out the possibility of a medication mix-up. Anesthetic infusion pumps and venous access were fully operational. Blood pressure was also measured using a manual device, which showed a reading of 160/110 mmHg.

Table 1: Monitoring (vital signs) vs. elapsed time during the anaesthetic procedure.

VITAL SIGN	T0	T1	T2	T3	T4	T5	T6
NIBP (mmHg)	120/70	90/50	192/107	180/89	138/88	138/88	124/82
HR (bpm)	68	68	52	52	52	52	68
SpO2 (%)	98	98	98	98	98	98	98

T0: pre induction; T1: 5 minutes after induction; T2: 10 minutes after induction;
T3: 20 minutes after induction; T4: 30 minutes after induction; T5: 60 minutes after induction;
T6: 90 minutes after induction.

This hypertensive episode lasted for approximately 30 minutes, during which the surgical and anesthetic teams analyzed the adverse event and agreed that an inexplicable phenomenon had occurred. Furthermore, given the extensive expected operative time of around 6 hours, there was a substantial risk of subsequent blood pressure fluctuations, particularly during emergence from anesthesia. The decision was made to withdraw TIVA medications and abort the surgical procedure. No medication with a hypotensive purpose was administered. Thirty minutes following sugammadex administration, the patient emerged from anesthesia. Blood pressure levels returned directly to her preoperative baseline values. The generalized piloerection resolved completely. At the post-anesthesia care unit, no pharmacological anti-hypertensive support was required. The patient was admitted to a room within 30 minutes and discharged home the same day. The clinical team decided to reschedule the orthognathic procedure, with the condition of methylphenidate suspension, for 7 days.

Discussion

During the pre-anesthetic consultation, the anesthesiologist informed the patient and her family, and noted in the medical record, that it was not necessary to discontinue the use of the two medications for the treatment of ADHD (methylphenidate and sertraline). However, the surgical procedure was performed by another anesthesiologist who preferred TIVA as the anesthetic technique, because of understanding the relationship between halogenated compounds and methylphenidate. Following the induction and normal hypotension of the TIVA technique, the patient developed a hypertensive crisis despite increased medication, with blood pressure readings of 192/107 mmHg. Because the hypertensive crisis persisted for 30 minutes, the surgical team and anesthesiologist decided to discontinue anesthesia and postpone the surgery. During general anesthesia in clinical practice there is no single bedside “test” that detects all drug interactions [8]. Interactions are generally identified through prior pharmacological analysis and, during anesthesia, by observing pharmacodynamic effects and objective monitoring. Perioperative drug-drug interaction associated with intraoperative hypertension is defined as a phenomenon in which the combination of medications used chronically by the patient and drugs administered in the perioperative period produces a higher than expected blood pressure response, usually due to increased sympathetic/catecholaminergic activity, altered reuptake or metabolism of neurotransmitters, or abrupt withdrawal of drugs that normally inhibit the sympathetic system [9].

Both methylphenidate and sertraline have documented relevant interactions with medications/anesthetics used in the perioperative period, and there are published case reports specifically in anesthesia [10,11]. However, there is an important difference: for methylphenidate, the classic concern is hypertension/tachycardia with halogenated anesthetics and sedation antagonism; for sertraline, the most documented interaction is serotonin syndrome, especially when associated with certain opioids. Since a hypertensive

crisis occurred, the diagnosis that guided us was based on methylphenidate and not sertraline, which led us to suspend the procedure at that time. The initial course of action by the anesthetic-surgical team was to suspend methylphenidate for 7 days, maintaining sertraline. In the immediate postoperative period, the course of action decided by the anesthesiology-surgical team was communicated to the doctor and the patient’s family, and the surgery was subsequently scheduled. Thus, the surgical procedure was postponed for 49 days pending the discontinuation of methylphenidate with the maintenance of sertraline, then completed within normal parameters with the same anesthetic technique (TIVA) and the same anesthetic-surgical team. The surgery was performed only 49 days later, with methylphenidate being discontinued during this time and sertraline maintained by the same anesthetic-surgical team and using the same anesthetic technique (TIVA), without any cardiocirculatory changes or hypertension. The surgery lasted 6 hours without any complications, and the patient was extubated in the operating room and transferred to the PACU, for subsequent transfer to his room.

Conclusion

The estimation of the probability that a drug caused an adverse clinical event is usually based on clinical judgment [12]. Using conventional definitions of Adverse Drug Reactions (ADRs), two physicians and four pharmacists evaluated 63 ADRs, and the concordance index ranged from 0.21 to 0.40, and the intraclass correlation coefficient of reliability was 0.49 [12]. As methylphenidate was withdrawn while sertraline remained in use, the absence of recurrence suggests that methylphenidate may have been a contributing factor to the event. This observation repositions the central pathophysiological hypothesis: rather than an obligatory synergism between the two drugs, the presentation appears to have critically depended on the indirect sympathomimetic action of methylphenidate on an adrenergic system chronically sensitized by 18 years of use, with sertraline possibly acting as a factor potentiating the magnitude of the response, without, however, constituting an isolated determinant of the event.

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