

Diphenhydramine for Acute Extrapyramidal Symptoms After Propofol Administration

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Extrapyramidal symptoms are an uncommon but well-recognized side effect after the administration of general anesthesia in patients without a significant neurologic history. Several case reports implicate propofol as the likely causative agent producing these symptoms, which include ballismus, dystonia, choreoathetosis, and opisthotonus. Currently, there is no clear consensus on first-line treatment of these symptoms. In each of the published cases, anticholinergic medications and benzodiazepines were central to initial management, although the speed and extent of symptom resolution were variable. Here we present a case of a 17-year-old boy with ulcerative colitis who presented with ballismus, torticollis, tongue thrusting, and oculogyric movements after colonoscopy under general anesthesia with propofol. The patient responded promptly to treatment with diphenhydramine. This is the first reported case in which diphenhydramine was successfully used as the primary treatment of severe extrapyramidal symptoms in a pediatric patient after propofol administration.

An intravenous anesthetic agent commonly used in the pediatric population, propofol is approved by the US Food and Drug Administration for anesthesia maintenance in patients >2 months old and for anesthesia induction in patients >3 years old.¹ With wide clinical use, propofol is considered invaluable by many physicians, given its overall safety and efficacy in patients of all ages.² However, propofol may cause a number of well-recognized adverse reactions, including hypotension, injection site burning, apnea, and central nervous system (CNS) effects.³ The CNS effects of propofol are varied and well documented, ranging from prolonged unresponsiveness to abnormal movements.³ Treatment of the CNS side effects of propofol has traditionally consisted of a cocktail of benzodiazepines, although it has

been effective in only a minority of cases.⁴ Our case demonstrates how a regimen of diphenhydramine followed by benzotropine may be an effective treatment for relief of extrapyramidal symptoms caused by propofol.

CASE

A 17-year-old boy with ulcerative colitis presented with severe extrapyramidal symptoms after a colonoscopy under general anesthesia. At home, the patient took mercaptopurine 75 mg and 100 mg on alternating days, mesalamine 2.4 mg daily, omeprazole 20 mg twice daily, and a multivitamin daily. The patient had never experienced an adverse reaction to any medication, and there was no family history of anesthesia problems. The procedure was performed with propofol 200 mg,

abstract

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Mr Sherer performed the literature review, drafted the original case report, edited the finalized case report, and coordinated with co-authors; Mr Salazar reviewed the details of the case and aided in drafting the original case report; Mr Schesing reviewed the literature and aided in drafting the original case report; Ms McPartland reviewed the literature, aided in drafting the original case report, and edited the finalized case report; Dr Kornitzer diagnosed and treated the patient discussed in the case report, conceptualized the original case report, and edited and critically reviewed the case report; and all authors approved the final manuscript as submitted.

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lidocaine 60 mg, and sevoflurane 2%. To reduce the risk of aspiration during the procedure, given vomiting and gastroesophageal reflux in the days leading up to the colonoscopy, the anesthesiologist used rapid induction with succinylcholine 100 mg, followed by uncomplicated intubation. The patient did not receive ondansetron, metoclopramide, or any other antiemetic medication, because he did not complain of nausea or vomiting the morning of the colonoscopy. The procedure lasted for 1 hour. Shortly after regaining consciousness, the patient experienced violent, uncontrolled bilateral ballismus involving all 4 extremities. Additionally, he had torticollis, intermittent tongue thrusting, and sporadic oculogyric crises. Despite the movements, he remained awake and communicative throughout these events, stating that he was unable to control his arms, legs, neck, and eyes. During this time the patient's cardiopulmonary status remained stable, he had no tongue biting, and he did not exhibit bladder or bowel incontinence.

Midazolam 2 mg was administered intravenously without relief of symptoms, and the patient was transferred to the postanesthesia care unit. Because of continuing symptoms, he received 1 mg intravenous lorazepam and an additional 2 mg midazolam. When the patient did not respond to these medications, the neurology team was consulted. After determining him to be having an extrapyramidal reaction to propofol, the neurology team gave the patient diphenhydramine 50 mg intravenously. Within several minutes, there was near complete cessation of all extrapyramidal movements. Some lingering, intermittent, athetoid movements were completely halted by 2 mg benztropine administered 30 minutes after diphenhydramine was given. To ensure that these symptoms would

not recur, the patient was maintained on intravenous diphenhydramine for the next 2 days, with the dosage tapered from 25 mg every 6 hours the first day to 12.5 mg every 6 hours the second day. He had no more abnormal movements.

DISCUSSION

In addition to propofol, many anesthetics, including sevoflurane, thiopentone, and etomidate, have been associated with extrapyramidal movements. Propofol is of particular interest because of its widespread use for anesthesia induction and maintenance in the pediatric population. Although there are a number of reports of abnormal movements associated with propofol,⁵⁻¹¹ no clear treatment has been developed. Reported reactions to propofol include opisthotonus, a state of spine and extremity hyperextension.⁵ Dystonic reactions, such as intermittent or sustained contractions of muscles in the face, larynx, trunk, pelvis, and extremities, have also been detailed in the literature.⁶⁻⁸ Our patient experienced oculogyric crisis (with prolonged upward deviation of the eyes), a rare side effect previously reported in association with propofol.¹² Although the neuroexcitatory mechanisms of propofol are not well understood,¹³ it is hypothesized that the potential extrapyramidal effects of propofol result from activation of excitatory pathways in the subcortical region, extended refractory periods in inhibitory pathways in the brainstem and spinal cord, or a combination of both.¹⁴

Recent therapeutic attempts aimed at alleviating extrapyramidal symptoms associated with propofol have included anticholinergics and benzodiazepines, but these interventions have led to suboptimal outcomes.⁴ In the literature to date, there is no clear consensus on treatment of these symptoms. One

literature review describes the use of benzodiazepines as treatment in 7 reported cases.⁴ In 5 of these cases, there was no response to treatment, and the remaining 2 cases displayed only partial remission of symptoms. The only documented patient to achieve complete remission of extrapyramidal symptoms was treated with biperiden, an anticholinergic agent.⁴ Interestingly, none of the published cases report treatment with diphenhydramine, despite the fact that diphenhydramine is often used as prophylaxis for extrapyramidal symptoms caused by other medications, such as metoclopramide.¹⁵

Our treatment regimen builds on the successful treatment with an anticholinergic described in the literature but uses diphenhydramine rather than biperiden for its anticholinergic properties. Previously, diphenhydramine has been used to aid in the treatment of movement disorders in the pediatric population,¹⁶⁻¹⁸ but it has not specifically been used to treat extrapyramidal symptoms associated with propofol use. In this case, prompt and nearly complete resolution of severe symptoms was achieved with 50 mg diphenhydramine alone, although full resolution required the addition of 2 mg benztropine soon after. Benefits of using diphenhydramine in this way include its widespread availability and limited side effects at low dosages.¹⁹ Although more research is clearly indicated, we suggest that giving diphenhydramine, followed by benztropine for lingering movements, and then a diphenhydramine taper is an effective and safe approach to treating extrapyramidal symptoms associated with propofol use.

ABBREVIATION

CNS: central nervous system

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