Effect of Propofol on Anal Sphincter Pressure During Anorectal Manometry

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ABSTRACT

We evaluated the effect of propofol on resting anal sphincter pressure (RP) during anorectal manometry performed under general anesthesia in 20 children with chronic constipation. After propofol bolus administration, there was a significant decrease in the RP in 95% of children from a mean of 51.5 ± 15.3 to a mean nadir of 21.7 ± 10.5 mmHg ($P < 0.001$). The new postpropofol RP of 47.0 ± 12.4 mmHg was significantly lower compared with prepropofol RP ($P < 0.0001$). Propofol should be used with caution as an anesthetic agent for anorectal manometry, given the potential for confounding RP measurements.

Key Words: anal sphincter pressure, anorectal manometry, constipation, propofol

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An anorectal manometry (ARM) is a valuable tool to evaluate children with disorders of defecation. In addition to assessing the rectoanal inhibitory reflex (RAIR), an ARM can measure resting anal sphincter pressure (RP). Ideal testing conditions involve an awake and cooperative patient; however, in young children, ARM testing often requires general anesthesia (GA) for patient comfort and compliance. The choice of anesthesia for ARM varies from center to center and includes the use of ketamine, inhalation agents, propofol, and preanesthetics such as midazolam. The use of GA raises the concern that some anesthetic agents can interfere with assessment of RAIR, although studies have not shown that to be the case (1–3); however, with the increasing use of the anesthetic propofol for pediatric procedures, we have anecdotally observed a potential for the RP to be affected, leading to a falsely lower RP measurement. The aim of this study was to prospectively investigate the effect of propofol on RP during an ARM performed under GA.

METHODS

This prospective study was approved by the Massachusetts General Hospital institutional review board. Written informed consent was obtained from at least 1 parent. Children between 2 and 6 years old with chronic constipation scheduled for ARM under GA were candidates for the study. GA was administered by pediatric anesthesiologists and followed the institutional policy of using an inhalation anesthetic combination of sevoflurane and nitrous oxide in oxygen. After induction of anesthesia, an intravenous catheter was placed by the anesthesia team as per routine.

Once an appropriate depth of anesthesia was achieved, the child was positioned in the left lateral position with knees and hips flexed. A lubricated balloon manometry probe was inserted into the rectum and ARM testing commenced. Using station pull-through, the RP was identified. The rectal balloon was then sequentially filled and deflated rapidly to allow for the identification of the RAIR. At this point in the test, the pediatric anesthesiologist stopped inhaled anesthetics and administered a 1-time dose of 1 mg/kg intravenous (IV) bolus of propofol to reduce the likelihood of delirium from anesthesia per institution standard protocol. The manometry probe was maintained in place with continuous measurement of the anal sphincter pressure until a new baseline RP was established up to a maximum of 5 minutes. If the sphincter pressure seemed to have reached a steady state by showing little or no pressure variation for approximately 30 to 60 seconds, the recording was concluded even if the 5 minutes had not been reached. The manometry probe was then removed and any additional procedures, such as suction rectal biopsy or chemical denervation of the internal anal sphincter (IAS) with botulinum toxin, were performed if clinically indicated. Outcome measures included initial prepropofol RP, postpropofol anal sphincter nadir pressure, postpropofol RP, and time to reach postpropofol nadir. Statistical analysis was performed with the use of paired *t* tests. $P < 0.05$ was considered significant.

RESULTS

Twenty children between 2 and 6 years old (mean age 4.2 years) were enrolled. Fourteen (70%) were boys. Two patients had a previous diagnosis of Hirschsprung disease and were repaired surgically. Two children had previously received chemical denervation to the IAS with botulinum toxin, one 6 months before ARM and the other 3 months before ARM. The RAIR was positive in 18 of 20 patients.

Of those with negative RAIR, 1 had known Hirschsprung disease, whereas the other child underwent suction rectal biopsy, which showed the presence of ganglion cells. Internal anal sphincter hypertonicity was observed in 13 of 20 (65%) patients and all of the

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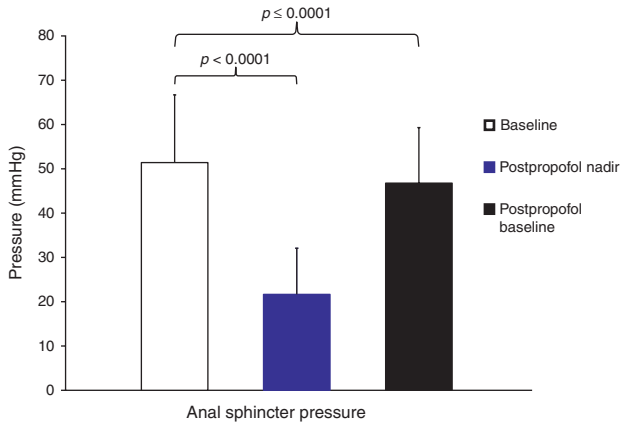

FIGURE 1. The mean anal sphincter pressure (mmHg) at baseline, at the nadir after propofol bolus, and at new postpropofol baseline.

affected patients received botulinum toxin to the IAS. The mean RP was 51.5 ± 15.3 mmHg. After IV propofol bolus, the anal sphincter pressure showed a decrease in 19 of 20 patients to a mean nadir of 21.7 ± 10.5 mmHg, which was significantly lower ($P < 0.005$) compared with mean RP (Figs. 1 and 2). The average reduction in anal sphincter pressure was 58% (29.9 ± 13.8 mmHg). The new postpropofol RP of 47.0 ± 12.4 mmHg was significantly lower compared with prepropofol RP ($P < 0.0001$). Mean time for IAS to reach the nadir was 42 seconds, whereas average time for anal sphincter pressure to recover and establish a new baseline was 170 seconds.

DISCUSSION

This prospective study of young children with constipation undergoing an ARM under GA determined that an IV propofol bolus leads to a significant decrease in the RP in 95% of patients. Liu et al (4) demonstrated similar reduction in RP in healthy adults undergoing an ARM under propofol conscious sedation. The anal sphincter consists of 2 muscular components, an external and an internal anal sphincter, with the latter composed primarily of smooth muscle. Studies have demonstrated that internal anal sphincter is responsible for 70% to 85% of the RP (5,6). With smooth muscle accounting for a large component of the RP, our findings are consistent with previous observations on propofol; it is known have a relaxing effect on various smooth muscle components throughout the body, including esophageal sphincters and bronchial airway (7–9). The exact mechanism by which

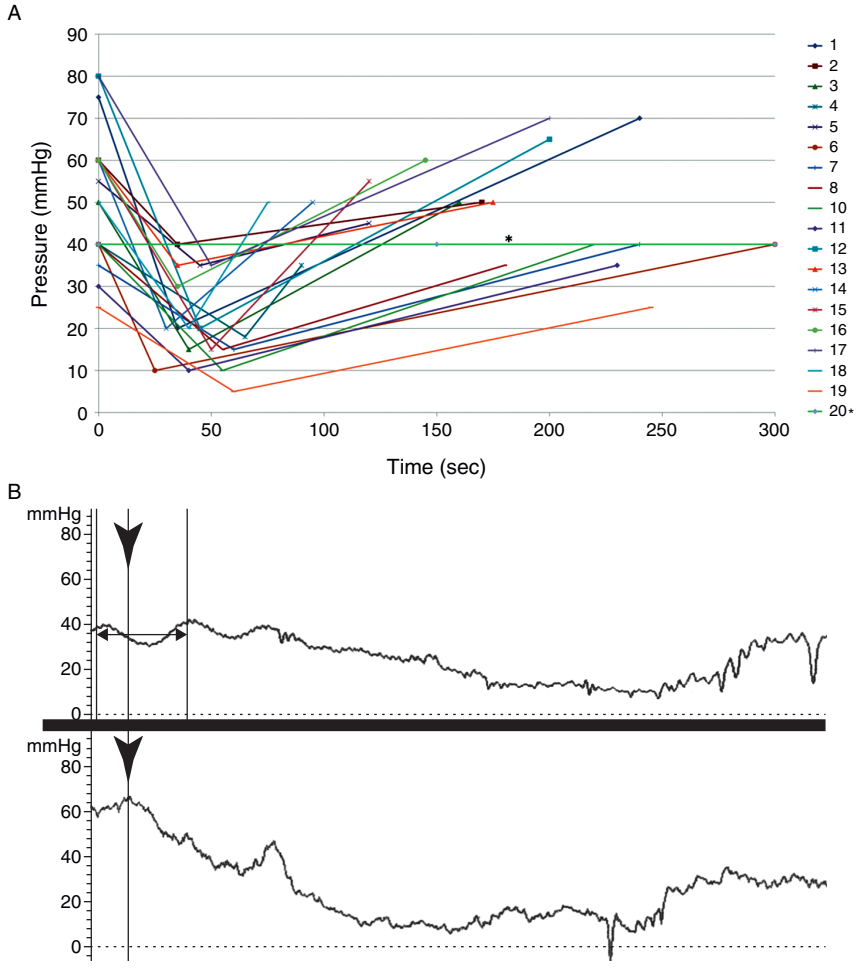

FIGURE 2. A, Anal sphincter pressure changes over time for each study participant after intravenous (IV) bolus of propofol (1 mg/kg). ∗Represents lone patient who did not have a decrease in anal sphincter pressure. B, Representative actual tracings from 2 sample cases (arrows point to initiation of IV propofol push dose).

propofol leads to relaxation of anal sphincter smooth muscle is unknown, but studies on other smooth muscle tissues in the body suggest that its mechanism of action is on calcium channels (9–12).

The relaxing effect of propofol on the anal sphincter is transient, which is consistent with the pharmacodynamics of propofol such as the ultrashort onset of action and short half-life; however, although the RP recovered from the propofol-induced nadir, the new baseline RP was significantly lower than that before the propofol bolus. This finding suggests that although propofol has a short recovery time, there is a lingering effect of propofol on the anal sphincters that leads to the development of the new, lower baseline RP. It should be noted that the maximum time of monitoring was 5 minutes after propofol bolus, so it is possible that the RP would have continued to rise further to its previous baseline past our monitoring stop point.

Because RP is one of the key measurable parameters of an ARM, the use of propofol as an anesthetic agent in young children should be cautioned given the potential for confounding RP measurements. An RP value that is artificially decreased secondary to propofol increases the possibility of missing a diagnosis of anal achalasia or internal sphincter hypertonicity, which can only be definitively made by ARM. Because children undergoing ARM often have constipation, the detection of anal achalasia is important because it opens up treatment modalities. For these conditions, surgical myectomy has had success (13,14); however, chemical denervation with *Clostridium botulinum* toxin has emerged as a less invasive alternative. *C botulinum* toxin is a potent neurotoxin that blocks the release of acetylcholine from presynaptic cholinergic nerves in the neuromuscular junction (15,16). Consequently, there is a weakening and resultant relaxation of the sphincters. The effect is transient but can last weeks to months. Multiple studies in patients with anal achalasia have demonstrated significant clinical improvement in constipation symptoms after injection of the toxin into the hypertonic anal sphincter (17–19). Given the potential for improvement with clinical intervention, ensuring the accuracy of the RP is paramount.

Two patients in our cohort had previously received injections of botulinum toxin for constipation. The first was a 3-year-old who received botulinum toxin injections to the anal sphincter 6 months before ARM and IV propofol, and whose RP decreased after the propofol bolus. Interestingly, the other individual, a 3-year-old girl, was the lone patient whose RP did not show a response to propofol. This patient had received botulinum toxin injections more recently, at 3 months before enrolling. This finding suggests that the patient may already have been at maximal anal sphincter relaxation secondary to the effects of the botulinum toxin, or that the mechanism of sphincter relaxation by propofol is mediated by pathways that can be inhibited by botulinum toxin.

One important factor to consider is that an inhalational agent, sevoflurane, was used to induce anesthesia. There has long been concern that the RP is decreased while under the influence of GA. This study demonstrated that the RP (measured while under GA) will decrease even further after a propofol bolus, suggesting that propofol has additional properties that can affect RP; however, although the sevoflurane was turned off before the propofol bolus, there likely were residual effects of the inhaled anesthetic, which may work in synergy with propofol to cause further decrease in the RP. In some centers, propofol is used differently, for example, inducing GA with higher doses of propofol than the one used here. One could hypothesize that the relaxation dose of propofol may be dose dependent; however, this was not tested in the present study.

ARM is a key tool in evaluating outlet obstruction defecation disorders and can guide interventional therapy. Although an ARM is optimally performed on an awake patient to further evaluate defecation dynamics, in young children, anesthesia is often required to perform an adequate examination when accounting for patient comfort and compliance. When considering the various choices of anesthesia, propofol should be used with caution given the potential to significantly lower RP and obscure cases of borderline anal achalasia.

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