HAYDARPAŞA NUMUNE MEDICAL JOURNAL

DOI: 10.14744/hnhj.2020.60948
Haydarpasa Numune Med J 2022;62(4):417–423

ORIGINAL ARTICLE

Comparison of the Effects of Fentanyl and Dexmedetomidine Administered in Different Doses on Hemodynamic Responses During Intubation

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Abstract

Introduction: The present study is intended to compare the effects of dexmedetomidine administered in two different doses and of fentanyl before induction to prevent hemodynamic response caused by laryngoscopy and endotracheal intubation in ASA I-II group patients.

Methods: On obtaining the approval from the hospital ethics board and patient approvals, 60 general surgical patients between the age of 20 and 65 years who were in ASA I-II risk group were included in the study. In addition to routine monitoring, Bispectral index (BIS) monitoring was performed. Group F was injected 2 µg/kg fentanyl, Group D1 was injected 0.5 µg/kg dexmedetomidine, and Group D2 1 µg /kg dexmedetomidine as iv bolus for 1 min. After the injection, SBP, DBP, HR, and BIS values were recorded at definite intervals of 1, 3, 5, and 10 min after intubation.

Results: We have found that administration of 0.5 and 1 µg/kg IV dexmedetomidine and 2 µg/kg fentanyl before anesthesia administration suppressed the increase in heart rate and blood pressure in response to laryngoscopy and intubation. There was no significant predominance of high and low doses of dexmedetomidine over each other and fentanyl. In addition, there was no significant difference between thiopental consumption, while sedation scores and BIS values were significantly different.

Discussion and Conclusion: Dexmedetomidine is as effective as fentanyl in suppressing hemodynamic responses to laryngoscopy and intubation and can be used as an alternative to fentanyl.

Keywords: Dexmedetomidine; fentanyl; hemodynamic response; intubation.

It is one of the objectives of general anesthesia to ensure that vital organ and system functions remain within the physiological limits in patients who underwent surgical intervention. Physiopathological changes due to endotracheal intubation (ETI) are important in anesthesia induction. During laryngoscopy and insertion of the endotracheal tube, as a result of increased reflex excitation of laryngeal and tracheal tissues in sympathoadrenergic activity, there is an increase in arterial pressure and heart rate with catecholamine discharge[1,2]. This response further increases the risk, especially in patients with intracranial and cardiovascular problems such as hypertension,

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Submitted Date (Başvuru Tarihi): 12.10.2020 **Revised Date (Revize Tarihi):** 12.10.2020 **Accepted Date (Kabul Tarihi):** 11.11.2020

coronary artery disease, cerebrovascular disease, and it can cause complications[3,4]. Various methods are used to minimize the negative hemodynamic response caused by laryngoscopy and endotracheal intubation. These methods include blockade of sensory receptors and afferent nerves with local anesthetic agents, blocking the central effects of painful stimuli with opioids and suppression of efferent pathways and effector receptors with local anesthetics, beta-blockers, calcium channel blockers, and sympathetic ganglion blockers[5]. Opioids are the most common drugs used to reduce hemodynamic changes due to intubation. However, opioids can cause severe hypotension in some patients[6,7]. Therefore, in recent years, some drugs that have been known to have fewer side effects have been introduced. Today, the most commonly used of these drugs are beta-blockers and α2 agonists. α2 agonists reduce heart rate and arterial blood pressure by inhibiting noradrenaline release from sympathetic nerve endings through presynaptic inhibitory receptors in the sympathetic nervous system as well as provide sedation, anxiolysis, and analgesia[8,9]. They suppress the hemodynamic response caused by laryngoscopy and endotracheal intubation to create more stable conditions during anesthesia[9]. Dexmedetomidine, a specific α2 agonist with the highest selectivity, is increasingly common in intensive care and anesthesia applications[9-11]. Although there are many studies studying the effectiveness of dexmedetomidine in reducing the need for anesthetics and opioid in preventing hemodynamic responses resulting from laryngoscopy and endotracheal intubation, there is no complete consensus on the dose and duration of its administration[5]. In this study, we intended to compare the effects of two different doses of dexmedetomidine administered before induction and fentanyl in preventing hemodynamic response caused by laryngoscopy and endotracheal intubation in ASA I-II normotensive patients.

Materials and Methods

On obtaining the approval from the hospital ethics board and patient approvals, 60 general surgical patients of ASA I-II risk groups aged between 20 and 65 were included in the study. Patients were informed about the method of anesthesia. None of the patients were pre-medicated. Patients with thyroid dysfunction, patients with heart, liver, and kidney disease, those with long-term use of opioid, sedative, or β-blocker, those morbidly obese, pregnant, and breastfeeding patients, those with a history of allergy and bradycardia and those expected to have intubation difficulties were excluded from the study. Heart rate (HR), systolic arterial pressure (SAP), diastolic arterial pressure (DAP), and peripheral oxygen saturation (SpO_2) were monitorized and basal values were recorded after the patients were taken to the operating room. The depth of anesthesia was monitored by a Bispectral Index Monitor (BIS, Aspect A-2000, Aspect Medical Systems; Natick, MA) and using disposable electrodes. In patients who were randomly divided into three groups using closed envelope selection method, vascular access was established on the dorsum of the hand, and 0.9% NaCl infusion was started before the study drug was administered. The Group F was given 2 μg/kg of fentanyl, the Group D1 0.5 μg/kg of dexmedetomidine, and the Group D2 1 μg/kg of dexmedetomidine IV. These administered doses were injected in 5 mL of saline as a slow bolus in 1 min. SAP, DAP, HR, SpO_2, BIS values, side effects, and sedation scores were recorded at min 2, 5, 8, and 10 for 10 min after injection. Sedation scoring was performed using Ramsay sedation scale (1=Anxious, agitated, 2=Awake and cooperative, 3=Responds to commands only, 4=Brisk response to light glabellar tap and auditory stimulus, 5=Sluggish response to the above-mentioned stimuli, and 6=No response to the above-mentioned stimuli). After 10 min of administering the study drug, anesthesia induction began. Patients in all three groups were injected with 1.5–2 mg/kg of thiopental in 10 sec for induction purposes. A dose of 25–50 mg was added with an interval of 15 seconds until the BIS value dropped below 60. 0.1 mg/kg of vecuronium was administered for muscle relaxation. After the lungs were ventilated with 100% O_2 for 3 min, endotracheal intubation was performed. After induction (1 min before intubation), SBP, DBP, HR, and BIS values were recorded at minutes 1, 3, 5, and 10 after intubation. Anesthesia maintenance was achieved with desflurane, 30% O_2, and 70% N_2O with a BIS of 40–60. During the study, 50 μg of fentanyl was applied when SAB rose above 20% of basal values. Hypotension was defined as a decrease in SAB value below 70 mmHg. It was treated with a dose of 5 mg ephedrine bolus. When HR rose above 20% of basal values, 50 μg of fentanyl was applied. When HR dropped below 45 beats/min, 0.5 mg of atropine was administered. Respiratory depression was considered $SpO_2 <$ 90. Total doses of thiopental, fentanyl, ephedrine, and atropine used during the study were recorded. All patients were exhaled with 100% O_2 by terminating desflurane with the closure of the skin sutures at the end of the operation. They were antagonized by residual neuromuscular block of 35 μg/kg of neostigmine and 0.015 mg/kg of atropine, and then, they were extubated.

Statistical Analysis

Version 15.0 of the Statistical Package for the Social Sciences for Windows Relase (SPSS, Chicago, IL) package program was used to analyze the data. One-way analysis of variance was used to compare the three groups in terms of age and weight, while frequency tables were used to compare them in terms of gender, ASA, hypotension, bradycardia, and respiratory depression. One-way analysis of variance was used to perform intergroup comparison of the hemodynamic parameters and t-test for dependent samples in intra-group comparison. Significance level was considered 0.05.

Results

There was no statistically significant difference between the groups in terms of demographic characteristics (p>0.05). Systolic arterial pressure (SAP) and diastolic arterial pressure (DAP) values did not differ between the groups according to the measurements performed in minutes 2, 5, 8, and 10 before anesthesia induction. There was no statistically significant difference between Group D1 and Group D2 in terms of HR (heart rate) values, while HRs of both groups was significantly lower than the fentanyl group (p<0.05). HR values before induction by group are shown in Table 1.

The BIS values in the minutes 2, 5, 8, and 10 (before induction) were significantly lower in the Group D2 compared to the Groups D1 and F; sedation scores were also significantly higher in the Group D2 than the other two groups in parallel with BIS values (p<0.05). BIS values before induction by group are shown in Table 2, and sedation scores are shown in Table 3.

In the post-induction period 1 min before intubation, BIS values were significantly lower in the Group D2 compared to Group F (p<0.05). In the minutes 1 and 3 after intubation, BIS values were significantly lower in the Groups D1 and D2 compared to the group F (p<0.05). There was no difference between the groups in terms of the BIS values in the minutes 5 and 10 after intubation. The values are shown in Table 4.

In the post-induction period, the HR, SAP, and DAP values measured 1 min before intubation and in the minutes 1, 3, 5, and 10 after the intubation did not differ significantly between the groups. The HR, SAP, and DAP values throughout the study are shown in the figure 1, 2, and 3 by group.

Table 1. HR values before induction

	Group D1	Group D2	Group F	f	p
Basal	85±17.0	85.10±10.3	85.20±16	0.001	0.999
Preop 2	69.6±13.9	61.35±11	84.05±14.5	15.063	0.000*
Preop 5	71.5±13.9	68.95±10.9	81.20±13.4	5.077	0.009*
Pre-op 8	71.8±13.2	67.95±8.6	80.20±13	5.642	0.006*
Pre-op 10	71.7±13	66.70±7.7	82.85±13.3	10.055	0.000*

*p<0.05.

Table 2. BIS values before induction

	Group D1	Group D2	Group F	F	p
Basal	97.65	97.40	97.40	0.7	0.503
Pre-op 2	95.30	88.35	94.90	6.66	0.003*
Pre-op 5	91.30	82.00	93.60	12.7	0.000*
Pre-op 8	89.70	80.05	94.25	15.4	0.000*
Pre-op 10	89.90	76.55	94.60	21.5	0.000*

Table 3. Pre-induction sedation values

	Group D1	Group D2	Group F	f	p
Basal	2.00	1.80±0.4	1.95±0.2	2.976	0.059
Pre-op 2	2.15±0.4	2.45±0.7	2.30±0.5	1,634	0.204
Pre-op 5	2.50±0.6	3.40±1.1	2.50±0.7	7,544	0.001*
Pre-op 8	2.95±0.9	3.95±1.1	2.55±0.7	11.658	0.000*
Pre-op 10	3.00±1.0	4.15±1.0	2.60±0.7	15.589	0.000*

*p<0.05.

Table 4. BIS values after induction

	Group D1	Group D2	Group F	f	p
Pre-intubation minute 1	39.80±13.1	31.60±9.1	45.60±17.1	5,408	0.007*
Post-intubation minute 1	54.70±16.1	53.05±18.7	67.25±7.8	5.386	0.007*
Post-intubation minute 3	46.95±12.7	49.90±13.5	59.40±12.4	5,100	0.009*
Post-intubation minute 5	37.55±10.2	40.80±11.6	44.85±11	2.244	0.15
Post-intubation minute 10	34.95±7.6	39.55±8.1	35.15±7.6	2.24	0.29

*p<0.05.

The result of intra-group comparison of hemodynamic parameters;

Measurements made in the 1st minute after intubation showed an increase in HR in the Groups D1 and F. The increase in the Group D1 was not significant, whereas the increase in HR in the Group F was statistically significant (p<0.05). In the D2 group, the HR values were statistically insignificantly lower than the basal values in all post-intubation measurements.

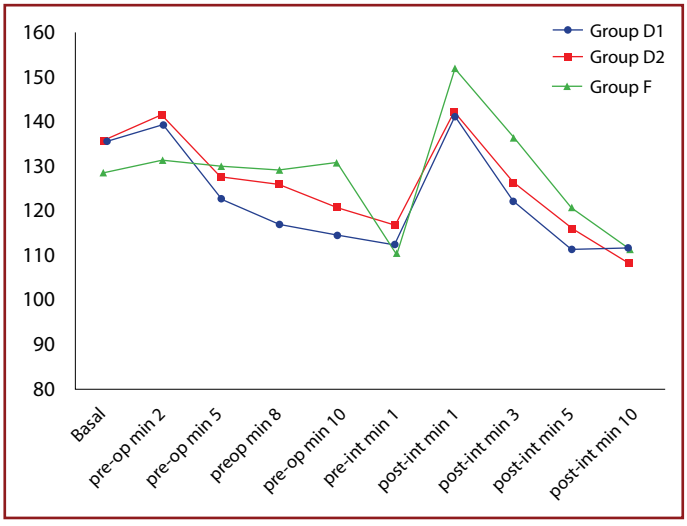

Figure 1. SAP values.

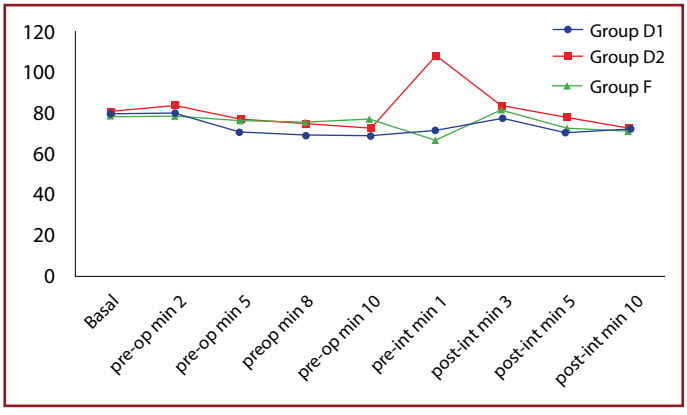

Figure 2. DAP Values.

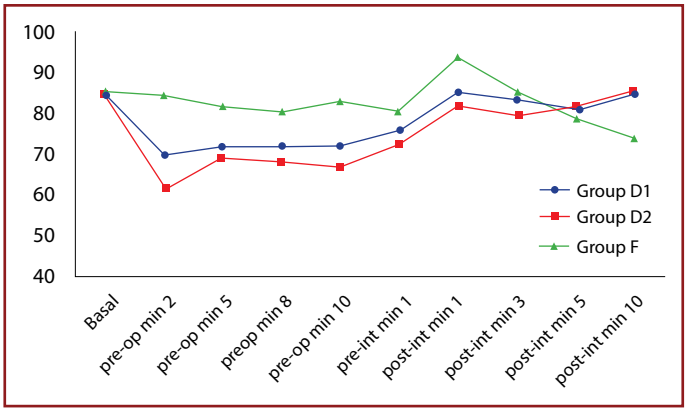

Figure 3. HR values.

In all three groups, SAP values were higher than basal values in the 1st minute after intubation. However, this height was statistically significant only in the fentanyl group (p<0.05). SAP measurements performed in the minutes 3, 5, and 10 after intubation decreased statistically significantly compared to the basal values in the dexmedetomidine groups, while the SAP values in the fentanyl group showed a significant decrease only after the post-intubation minute 10 (p<0.05).

In all three groups, a statistically significant elevation was detected in DAP values in the 1st min after intubation. Significant decrease in basal values was observed in the group D1 at the minutes 5 and 10 and at the min 10 in the Group D2 (p<0.05). There was a decrease in the fentanyl group at the minutes 5 and 10, but it was not statistically significant.

The amount of thiopental used in anesthesia induction and the total amount of fentanyl, atropine, and ephedrine used during the study are shown in Table 5. No difference was found between the groups.

During the study, no side effects were observed in Group D1. Bradycardia was observed in 2 patients and hypotension in 3 patients in the Group D2, while hypotension was observed in 1 patient and bradycardia in 1 patient in the Group F. None of the patients developed respiratory depression. The incidence of bradycardia, hypotension, and respiratory depression is shown in Table 6.

Table 5. Total thiopental, fentanyl, atropine, and ephedrine requirements by group (Mean±SD)

	Group D1	Group D2	Group F	f	p
Tiopental (mg)	408±75.3	386±74.1	415±52.2.8	0.98	0.38
Fentanyl (µg)	12.5±27.5	7.5±18.3	10±26.2	0.21	0.81
Atropine (mg)	0	0.1±0.2	0.025±0.11	2.97	0.06
Ephedrine (mg)	0	0.5±1.53	0.25±1.11	1.03	0.36

*p<0.05.

Table 6. Incidence of bradycardia, hypotension, and respiratory depression by group (n, %)

	Group D1 (n=20)	Group D2 (n=20)	F (n=20)
Hypotension	0	2 (10%)	1 (5%)
Bradycardia	0	3 (15%)	1 (5%)
Respiratory depression	0	0	0

Discussion

In this study, where two different doses of dexmedetomidine before anesthesia induction are compared with fentanyl, it was observed that administration of dexmedetomidine of 0.5 and 1 µg/kg resulted in significant reduction in the pre-induction HR values compared to administration of 2 µ/kg of fentanyl. The BIS values in the high dose dexmedetomidine group were significantly reduced compared to the groups of low dose dexmedetomidine and fentanyl, while the sedation scores were significantly higher values in parallel with their BIS values. Post-intubation measurements showed that different doses of dexmedetomidine and fentanyl caused similar changes in SAP, DAP, and HR.

In the conscious fiber optic intubations performed by Grant et al. [12] using dexmedetomidine, the researchers stated that there were changes higher than 15% in heart rate and blood pressure compared to the basal values. In many studies involving gynecological laparoscopy operations, premedication of dexmedetomidine administered intramuscularly or intravenously at a dose of 1–2.5 µg/kg suppressed the hemodynamic response to laryngoscopy and tracheal intubation[13-16]. Similarly, administration of 0.6 µg/kg of IV dexmedetomidine within the last minute before anesthesia induction was shown to reduce hemodynamic response to laryngoscopy and endotracheal intubation and the need for pre-operative fentanyl or isoflurane compared to placebo[17,18]. It is noted that the effect of dexmedetomidine reducing the need for anesthetic agents may be due to its sedative and hemodynamic effects[14,19]. In parallel with the results of these studies, the present study has also revealed that administration of dexmedetomidine in 0.5 and 1 µg/kg as a pre-operative bolus was as effective as fentanyl in suppressing the hemodynamic responses to laryngoscopy and intubation.

In their study, Bloor et al. [20] reported that the 0.25, 0.5, 1, and 2 µg/kg doses of dexmedetomidine administered within 2 min following the infusion do not differ from placebo in terms of HR but causes significant reduction compared to the basal values.

In the measurements performed within 10 min before anesthesia induction in groups where we administered 0.5 and 1 µg/kg of dexmedetomidine, a statistically significant decrease in HR was detected compared to the fentanyl group.

In their study, where Aho et al. [21] examined the effects of 0.3 and 0.6 µg/kg dexmedetomidine and 2 µ/kg fentanyl on perioperative hemodynamics, they reported that the increase in HR after intubation with 0.6 µg/kg dexmedetomidine was lower compared to fentanyl. In our study, there was no difference between the groups in terms of the post-intubation measurements. In the intra-group comparison, the increase in HR in the fentanyl group at the 1st min after intubation was found statistically significant based on the basal values. In the high dose dexmedetomidine group, all post-intubation measurements were reduced compared to the basal values, but this result was not statistically significant.

In the same study, Aho et al. [21] found that the increase in SAP compared to the basal values was significantly lower in the high dose dexmedetomidine group and the fentanyl group compared to the low dose dexmedetomidine and saline groups. The researchers did not detect a statistically significant difference between the high dose dexmedetomidine and fentanyl groups. Changes in DAP values were found to be similar.

In our study, there was no significant difference between the groups in terms of SAP values, while in all groups there was an increase in SAP values compared to the basal values in the 1st minute after intubation. However, this increase was found statistically significant only in the fentanyl group. Significant decrease in SAP values compared to the basal values was detected in the dexmedetomidine groups in the post-intubation minutes 3, 5, and 10. There was no statistically significant difference between the groups in terms of DAP values.

In recent years, publications on the use of dexmedetomidine for sedation purposes have been increasing. Various studies have shown that dexmedetomidine provides adequate sedation in interventions with regional or local anesthesia, where infusion of dexmedetomidine in different doses is administered[22-24]. The sedation status of patients in the pre-induction period after drug administration was monitored using iBIS monitoring and RAMSAY sedation scoring. BIS values were significantly lower in the high dose dexmedetomidine group compared to the groups of low dose dexmedetomidine and fentanyl. In their study, where Aho et al. [21] administered 0.6 µg/kg of dexmedetomidine and 2 µ/kg of fentanyl before induction, they evaluated sedation effect with scoring system and did not report any difference between the groups. In our study, we believe that the difference between the groups is due to the use of BIS monitoring technique, which is an objective measurement of the sedation effect.

BIS values after intubation were significantly lower than the fentanyl group in the groups administered dexmedetomidine in the 1st and 3rd min. When evaluating this result, we found that the depth of anesthesia was greater, although

the hemodynamic parameters were not reflected in the groups where dexmedetomidine was administered.

In the study by Lawrence and De lange, in comparison to the placebo group, 24% bradycardia was reported during dexmedetomidine infusion with a decrease in hemodynamic response to tracheal intubation due to single dose intravenous infusion of 2 μg/kg of dexmedetomidine within 5 min[25]. Because most of the side effects due to dexmedetomidine often occur during the administration of the drug. In our study, bradycardia was not observed in any patients in the group D1 during the pre-induction period after dexmedetomidine administration, while there were 3 patients (15%) in the group D2 and 1 patient (5%) in the group F developing bradycardia.

In studies conducted with doses of 0.6 μg/kg of dexmedetomidine, no bradycardia was reported as a result of glycopirolate administration for premedication purposes[17,18,21]. In our research, we did not perform anticholinergic premedication to observe side effects due to dexmedetomidine. In the presence of bradycardia, we administered as a single dose of 0.5 mg of atropine IV bolus.

In the study by Jaakola et al.,[17] they compared dexmedetomidine with placebo and showed significant reduction in fentanyl requirement in the dexmedetomidine group compared to placebo and reported that 0.6 μg/kg of dexmedetomidine significantly reduced thiopental requirement compared to placebo. According to the literature data, need for thiopental decreases by 17% after low dose IV or IM administration of dexmedetomidine, while it decreases by 30% at high doses[14,17]. In our study, there was no significant difference between the groups in terms of fentanyl and thiopental requirements. The least need for thiopental was observed in the Group D2 and the highest need was in the group F. However, there was no significant difference between the three groups. This result can be attributed to the comparison of fentanyl, which is an opioid, with two different doses of dexmedetomidine instead of the placebo group.

In the study, where Belleville et al. [26] investigated the effects of dexmedetomidine doses of 0.25, 0.5, 1, and 2 μg/kg administered within 2 min after infusion on sedation, ventilation, and metabolic rate, it is reported that dexmedetomidine causes episodes of irregular breathing and short obstructive apnea and a decrease in SpO_2 during episodes depending on its doses. They reported that the reduction in SpO_2 occurs significantly more frequently at doses of 1 and 2 μg/kg compared to the placebo group. In addition, despite the decrease in the value of SpO_2 during apnea episodes, they reported that SpO_2 is over 95% in the room air and that SpO_2 has decreased below 94% in four patients of the high dose groups. We did not detect SpO_2 in room air below 90% in any of the groups with the doses of dexmedetomidine we administered.

Vasoconstriction effects of α2 agonists are reported to cause temporary hypertension at high plasma concentrations (2 μg/kg) by stimulating α2 adrenoreceptors located in vascular smooth muscles[9,10,14,22]. In our study, none of the patients developed hypertension. We believe that this result is due to the low dose of the drugs we administered.

Conclusion

We have found that administration of 0.5 and 1 μg/kg IV dexmedetomidine and 2 μg/kg fentanyl before anesthesia induction suppressed the increase in heart rate and blood pressure in response to laryngoscopy and intubation in general surgery patients. The high and low doses of dexmedetomidine used in our study did not have a significant predominance over each other and over fentanyl. In addition, there was no significant difference between the different doses of dexmedetomidine and fentanyl on the thiopental consumption used in induction, while sedation scores and BIS values were found to be significantly different. Based on the results herein, dexmedetomidine is as effective as fentanyl in suppressing hemodynamic responses to laryngoscopy and intubation and can be used as an alternate if necessary.

Ethıcs Committee Approval: Ankara Oncology Training And Research Hospital Chief physician Drug Research Ethics Committee 94/2008.

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept: E.T.Y.; Design: N.K.; Data Collection or Processing: E.T.Y.; Analysis or Interpretation: E.T.Y.; Literature Search: E.T.Y.; Writing: E.T.Y.

Conflict of Interest: None declared.

Financial Disclosure: The authors declared that this study received no financial support.

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