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An observational study to evaluate pressor response to laryngoscopy and tracheal intubation after pre-operative nebulisation of lignocaine

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***Abstract*---**Background & Aims: - Direct laryngoscopy and intubation are essential steps in general anaesthesia which elicit significant adreno sympathetic responses. Suppression of these responses is a concern in general anaesthesia. The aim of our study is to evaluate haemodynamic effects of pre-operative nebulisation with lignocaine due to pressor response. Materials and Methods :- Fifty patients within the age group of 18-65 years undergoing elective surgery under general anaesthesia were randomly allocated into two groups: Group L (n=25) nebulised with 5 ml lignocaine (2%) and Group C (n=25) nebulised with 5 ml normal saline, 15 minutes before surgery. Baseline values of heart rate (HR), systolic blood pressure(SBP), diastolic blood pressure(DBP), mean arterial pressure(MAP) and saturation(SpO2) were noted. HR, SBP, DBP, MAP and SpO2 were

noted immediately after intubation, at 2 minutes, 5 minutes and 10 minutes after intubation. Results:- There was significant fall in HR (88.76 ± 8.54) and MAP (93.32 ± 14.42) in group L as compared to group C. Conclusion:- This study suggests that pre-operative nebulisation with lignocaine significantly suppresses pressor response to laryngoscopy and intubation.

***Keywords*---**laryngoscopy, intubation, lignocaine, nebulization.

Introduction

The pressor response is defined as stimulation of pharyngeal and laryngeal nociceptors resulting in haemodynamic changes due to release of endogenous catecholemines.[1] The magnitude of pressor response is variable and proportional to the amount of force applied during visualization of the glottis[2] and the degree of trachea and laryngeal manipulation during advancement of endotracheal tube into trachea.[3]

This inappropriate response may affect the outcome of cases that are operated under general anaesthesia with endotracheal tube intubation, especially in patients with cardiovascular disease like uncontrolled hypertension and ischemic heart disease.[4] The management of this response is important as it prevents adverse events like tachycardia, systemic hypertension, pulmonary hypertension and arrhythmias.[5] Many intravenous drugs used to attenuate pressor response like xylocaine, opioids, β-blockers, calcium channel blockers etc. and also some drugs used via nebulisation to attenuate pressor response like Lignocaine, Magnesium Sulphate etc.

During the use of nebulisation, the liquid is broken up into droplets by the compressed air. The pneumatic nebulisation method produces large particles (10-25μm diameter) which mostly deposit in mouth and throat and smaller particles (5-10μm diameter) deposit in a transition from mouth to airway.[6,7] Nebulisation of drugs is more beneficial than other routes like gargle and intranasal because equal and effective distribution of drugs in the respiratory tract achieved with overcoming the other disadvantages like bitter taste, user availability, large volume required for gargle and drug rapid runoff into pharynx after intranasal route.

Lignocaine is an amino amide local anaesthetic. It has rapid onset and short duration of action. 70% of Lignocaine metabolised in the liver. Its Chemical structure has diethyl aminoacetyl-2-6-xylidine. Lignocaine can be given alone at a dose of 3 mg/kg and with adrenaline 6-7 mg/kg. Lignocaine has various routes of administration like topical, infiltration, intrathecal, peripheral nerve blocks, epidural, nebulisation.

Very few studies have been done on comparison between pre-operative nebulisation with different drugs in pressor response to tracheal intubation. So we decided to study the effects of pre-operative nebulisation of lignocaine on pressor response. The aim of our study was to evaluate the haemodynamic effects

of pre-operative nebulisation with lignocaine to pressor response to laryngoscopy and tracheal intubation with an objective to know about side effects if any.

Material and Methodology

After approval from the Institutional Ethics Committee, This observational study was conducted with written informed consent from all the patients who fulfilled the inclusion criteria and would be willing to participate in the study. Patients of either gender, aged between 18 and 65 years, willing to sign the written informed consent, belonging to ASA I and II, no known history of allergy and hypersensitivity to study drug and undergoing an elective surgical procedure in the supine position in general anaesthesia were included in the study whereas patients not willing to provide their voluntary written informed consent for participation in the study, with a known allergy, sensitivity or any other form of reaction to study drug, anticipated difficult airway (Mallampatti grade >2), belonging to ASA III or more, pregnant women, with >2 attempts of intubation were excluded in the study.

The patients enrolled in this study were randomly divided into two groups, 25 in each group depending on the pre-emptive nebulised drug used: lignocaine group(group L) patients received lignocaine (2%) 5ml (100mg) and control group(group C) patients received normal saline 5ml. The equipment and drugs required for the study are a compressed nebuliser machine, nebuliser mask, lignocaine vial (2%), normal saline, and syringe with needle (5 cc). The investigator anaesthesiologist and patients were blinded to the nebulising solution. Patients were nebulised via compressor nebulizer for 15 minutes. Intravenous access was obtained on the dorsum of hand with 20 G IV cannula. Patients were then transferred to the operation theatre immediately.

After shifting the patient to the operating room, inj. RL 500 ml was started. Patients were monitored for heart rate, non-invasive blood pressure, SpO2 and electrocardiogram by multipara monitor. After all pre-operative preparation, the patient was pre-oxygenated with 100% O_2 for 3-5minutes. All patients were premedicated with Inj.Ondensetron 0.1 mg/ kg IV , inj. Glycopyrrolate 0.004mg/ kg IV, inj. Midazolam 0.02mg/ kg IV, inj. Tramadol 2 mg/ kg IV. Induction was done with inj.Propofol 2mg/kg IV, endotracheal intubation was facilitated with Inj. Succinylcholine 2mg/kg IV. Laryngoscopy was attempted only after fasciculation disappeared.

Trachea was intubated by an expert anaesthesiologist with a soft seal cuffed sterile poly vinyl chloride endotracheal tube of 8.5 (I.D.) in male and 7.5 (I.D.) in female patients. Endotracheal tube cuff was inflated till the audible leak disappeared. Duration of Intubation (T_{ti}) was noted. Heart rate, systolic blood pressure, diastolic blood pressure and SpO2 were measured at the following intervals; Baseline (before induction), after induction, after endotracheal intubation at 2 minutes, 5 minutes and 10 minutes.

We took into consideration like attempts of laryngoscopy and duration of laryngoscopy during assessment of pressor response to tracheal intubation. Hypertension was considered when the BP value was 20% above baseline value or

SBP>140 mmHg. Hypotension was considered when BP value was lower than 20% of baseline or SBP<90 mmHg. Tachycardia was considered when HR value was higher than 20% of baseline or HR>100 bpm. Bradycardia was considered when HR value was lower than 20% of baseline or HR<50 bpm.

Anaesthesia was maintained with O_2 + N_2O (50% - 50%) mixture, Isoflurane and inj. Atracurium 0.5mg/kg IV bolus and then 0.1mg/kg IV maintenance doses. At the end of surgery, inhalational agents were stopped and 100% oxygen was administered. Neuromuscular blockade was reversed by inj. Neostigmine 0.05mg/kg IV and inj.Glycopyrrolate 0.008mg/kg IV. Suction was done using appropriate gauge catheters under direct vision via gentle laryngoscopy so as to avoid trauma to the oropharynx. Trachea was extubated when patient was fully awake and conscious after deflating the cuff. Patients were given oxygen via facemask and shifted to post-operative ward for observation.

Statistical Analysis

Data was collected, tabulated using MS-EXCEL 2010 version. Numerical variables were presented as mean & standard deviation (SD) while categorical variables were presented as frequency and percentage. As regard to numerical variables, unpaired student t-test was used, whenever appropriate, for between-groups comparisons while for categorical variables, chi–square test was used. The statistical analysis was performed in the form of Paired T-test. The results were considered significant statistically only when P value was less than 0.05.

Results

Table 1 shows the mean age, weight and gender in both groups. They were comparable between the two groups and there was no significant difference in the effects of nebulisation in these parameters ($p > 0.05$).

Table-1
Demographic data

Parameter	Group L	Group C	P Value
Age in years (mean ±2SD)	43±13	42±13	0.062
Gender Male/Female	13/12	14/11	0.065
Weight in kilogram (mean ±SD)	51±8.3	52±9.2	0.064

Table-2
Heart Rate at different time intervals

	GROUP - C (Mean ± SD)	GROUP - L (Mean ± SD)	P - Value
Baseline Parameter	85.10 ± 12.17	90.26 ± 12.26	0.069
Immediately after intubation	90.87 ± 11.08	88.76 ± 8.54	0.044*
At 2 min after intubation	91.04 ± 9.61	87.32 ± 9.67	0.042*
At 5 min after intubation	88.63 ± 9.54	86.67 ± 13.49	0.046*
At 10 min after intubation	85.38 ± 9.16	85.48 ± 10.93	0.039*

Table-3
Systolic Blood Pressure at different time intervals

	GROUP - C (Mean ± SD)	GROUP - L (Mean ± SD)	P - Value
Baseline Parameter	123.88 ± 12.26	128.50 ± 20.87	0.128
Immediately after intubation	131.66 ± 15.09	121.56 ± 17.81	0.022*
At 2 min after intubation	131.24 ± 14.50	122.03 ± 19.12	0.040*
At 5 min after intubation	129.24 ± 14.25	118.85 ± 20.17	0.032*
At 10 min after intubation	125.71 ± 14.03	117.49 ± 16.62	0.037*

Table-4
Diastolic Blood Pressure at different time intervals

	GROUP - C (Mean ± SD)	GROUP - L (Mean ± SD)	P - Value
Baseline Parameter	79.78 ± 8.10	82.20 ± 14.09	0.164
Immediately after intubation	85.72 ± 9.02	79.21 ± 12.73	0.030*
At 2 min after intubation	84.37 ± 9.50	79.02 ± 9.88	0.030*
At 5 min after intubation	81.71 ± 8.77	75.95 ± 11.79	0.037*
At 10 min after intubation	80.24 ± 8.16	75.66 ± 8.98	0.035*

Table-5
Mean Arterial Pressure at different time intervals

	GROUP - C (Mean ± SD)	GROUP - L (Mean ± SD)	P - Value
Baseline Parameter	94.48 ± 9.59	97.63 ± 16.35	0.152
Immediately after intubation	101.03 ± 11.04	93.32 ± 14.42	0.027*
At 2 min after intubation	99.99 ± 11.17	93.36 ± 12.96	0.033*
At 5 min after intubation	97.55 ± 10.6	90.25 ± 14.58	0.035*
At 10 min after intubation	95.40 ± 10.12	89.60 ± 11.53	0.035*

* significant p values

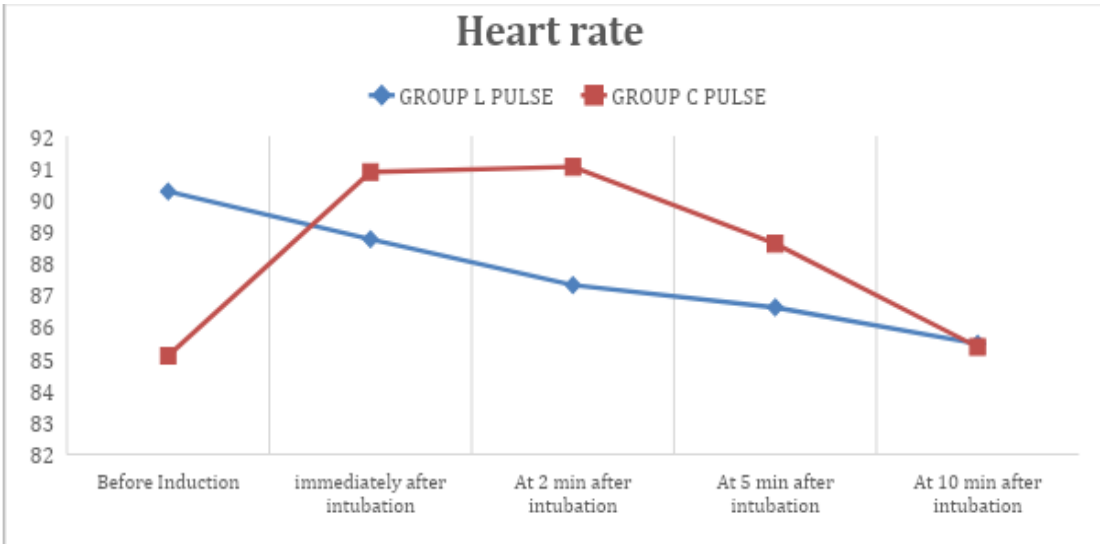

Figure-1: Heart rate, showing changes in mean heart rate at before induction, immediately after intubation, at 2, 5 & 10 minutes after intubation

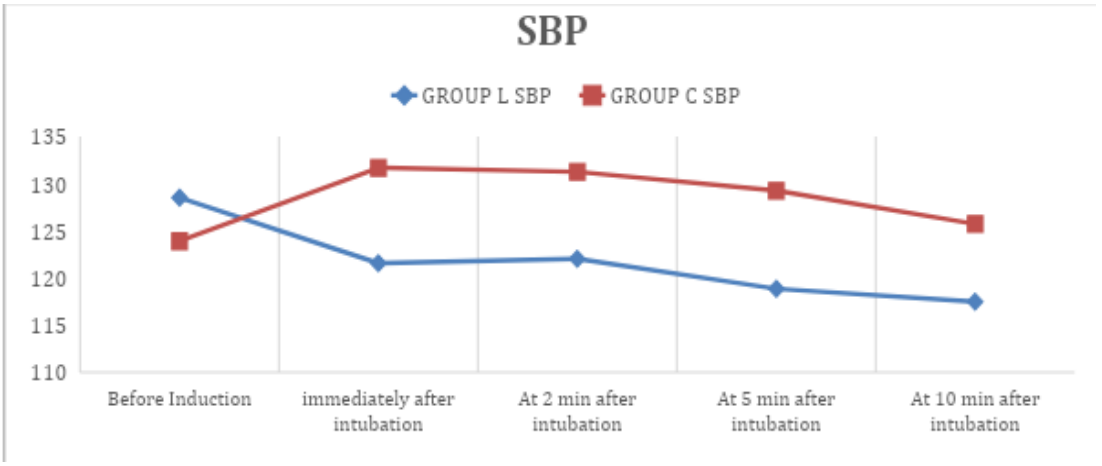

Figure-2 :- Systolic blood pressure, showing changes in mean systolic blood pressure at before induction, immediately after intubation, at 2, 5 & 10 minutes after intubation

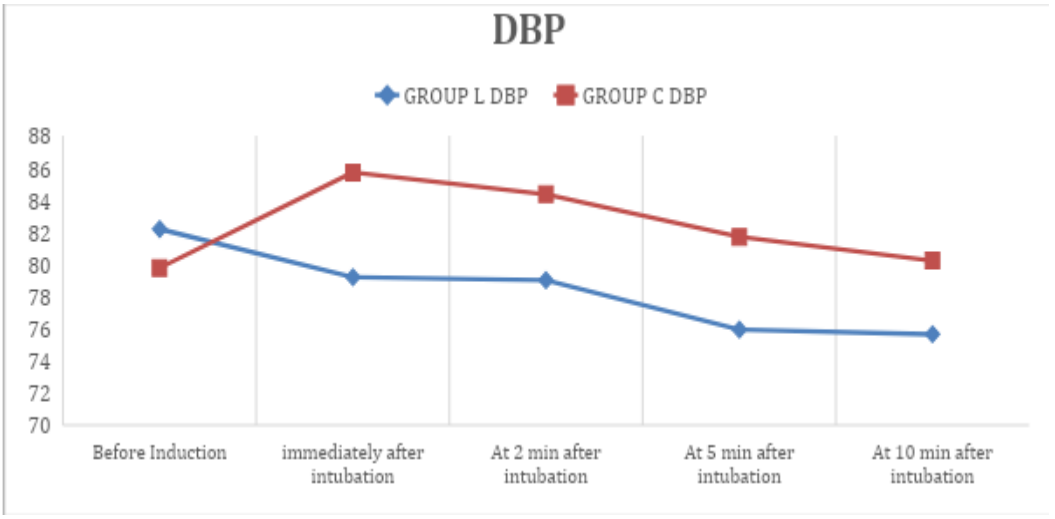

Figure-3 :- Diastolic blood pressure, showing changes in mean diastolic blood pressure at before induction, immediately after intubation, at 2, 5 & 10 minutes after intubation

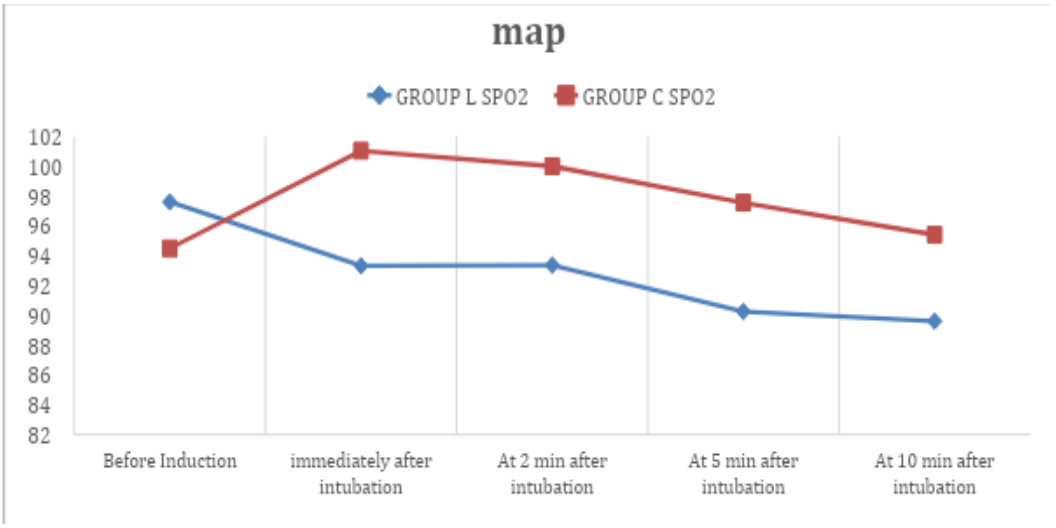

Figure-4:- Mean arterial pressure, showing changes in mean arterial pressure at before induction, immediately after intubation, at 2, 5 & 10 minutes after intubation

Figure 1 shows changes in mean HR over time between two groups. There was increase in mean HR in group C (90.87±11.08) from baseline immediately post intubation and not attained baseline even at 10 minutes after intubation whereas there was a significant fall in mean HR below baseline immediately after intubation in group L (88.76±8.54) ($p<0.05$) and remained sustain below baseline even at 10 minutes (85.48±10.93) ($p<0.05$) after intubation.

Figure 2 shows changes in mean SBP over time between two groups. There was an increase in mean SBP from baseline post intubation in group C (131.66±15.09)

and not attained baseline even at 10 minutes after intubation whereas there was significant fall in mean SBP post intubation in group L (121.56±17.81)($p<0.05$) and remained sustain below baseline even at 10 minutes (117.49±16.62)($p<0.05$) after intubation.

Figure 3 shows changes in mean DBP over time between two groups. There was an increase in mean DBP from baseline immediately after post intubation in group C (85.72±9.02) and not attained baseline even at 10 minutes after intubation whereas there was significant fall in mean DBP below baseline immediately after intubation in group L (79.21±12.73) ($p<0.05$) and remained sustain below baseline even at 10 minutes (75.66±8.98) ($p<0.05$) after intubation. Figure 4 shows changes in mean MAP between the two groups. There was an increase in mean MAP from baseline post intubation in group C (101.03±11.04) and not attained baseline even at 10 minutes after intubation whereas there was significant fall in mean MAP from baseline in group L (93.32±14.42) ($p<0.05$) and remained sustain below baseline even at 10 minutes (89.60±11.53) ($p<0.05$) after intubation. None of the patients had cough or gag reflex post extubation in group L who were pre operatively nebulised with lignocaine. All laryngoscopies and tracheal intubations were attempted by expert anaesthesiologist, so there was not a single case reported for traumatic injury during laryngoscopy and tracheal intubation.

Discussion

Laryngoscopy and tracheal intubation elicit a significant sympatho adrenal response. These changes may be detrimental in such patients having a risk of developing arterial hypertension or myocardial ischemia. The precise mechanism of this sympatho adrenal response is unclear but probably due to intense stimulation of the upper respiratory tract. Suppressing a hypertensive response to intubation is very important for properly administered general anaesthesia. Stoelting found that short-duration laryngoscopy, ideally <15s is an effective method to minimize increase in MAP during endotracheal intubation[8]. Drugs such as inhalational agents, narcotics, β-blockers, alpha blockers, calcium channel blockers and vasodilators have been used to suppress these responses. Intubation in the deeper plane also decreases this response but they can be ineffective or have adverse effects including bradycardia and hypotension.

In our study, our primary aim was to evaluate pressor response after pre-operative nebulisation of lignocaine. Lignocaine is an amino amide local anaesthetic which decreases airway reflexes, bronchial hyper reactivity and suppress haemodynamic response of intubation because of its analgesic and anti-inflammatory actions by decreasing the excitation of airway sensory C fibres plus the release of sensory neuropeptides.[9]

Lignocaine has been used in various modalities such as IV, topical, instillation, nebulisation or inhalation. Each route has its own merits and demerits. Lignocaine hydrochloride given by nebulisation has a good safety profie.[10] In our study, we used aerosolized nebulised lignocaine to suppress pressor response to laryngoscopy and intubation. In adults, lignocaine levels in blood after nebulisation at normal doses were found to be safe and well tolerate.[11] Nebulised

Lignocaine can be easily administered, acts immediately with short duration, has minimal side effects and cost effective. The nebulisation procedure was well tolerated by the patients and all patients enrolled in the study completed the nebulisation procedure. 1 patient in the group L experienced sore throat during the period of nebulisation and one patient from group L has been found with hoarseness of voice at the end of nebulisation.

In our study, we used 2% lignocaine for nebulisation of the patients. Woodruff et al. conducted a study on awake fibre optic intubation observed that 2% and 4% nebulised lignocaine had similar haemodynamic responses to topicalization and airway manipulation. At 4% concentration, there may be delay in return of airway reflexes if surgery is completed in less than an hour .Hence, this study is designed to evaluate the efficacy of nebulisation of lesser concentration of lignocaine (2%) in attenuating the pressor response to laryngoscopy and intubation.[12]

The dose of 5 ml was chosen in order to ensure comparability between two groups. It is suggested that 50% of the mists were lost around the patient mouth during expiration and breath holding.[13] We used continuous nebulisation so the estimated loss of nebulised lignocaine is > 50%. In our study, patients were nebulised using a standard gas driven nebulizer with 5 ml of 2% lignocaine 15 minutes before attempting laryngoscopy. Bromage and Robson studied blood levels of lignocaine after various mode of administration and endorsed that systemic absorption of lignocaine obtunds laryngeal reflexes.[14] Abou-madi M, Keszler H, Yacoub JM has studied that nebulised lignocaine acts both by topical anaesthesia of the airway and by increasing the depth of anaesthesia by systemic absorption and its effects can be potentiated by the use of antisialagogues. It is very effective surface anaesthetic causing rapid absorption from mucosal surface. The peak blood concentration is achieved within 4-15 minutes after instillation.[15]
We conducted this study on 50 ASA I and II patients undergoing elective surgery under general anaesthesia requiring laryngoscopy and intubation. We administered lignocaine (2%) by nebulisation. The mean age, weight and sex of the patients between the two groups were comparable. The present data demonstrate that there is no increase but significant fall in haemodynamic variables from the baseline in group L as compared to group C. There was increase in mean HR, SBP, DBP and MAP from baseline in group C and not a single haemodynamic parameter attained base line even at 10 minutes after intubation whereas in group L there was significant fall in mean HR, SBP, DBP and MAP immediately after intubation and remained below baseline up to 10 minutes after intubation. We did not get any significant fall in oxygen saturation (SpO2) throughout the study period in both the groups. Reid and Bruce in their study recognized that irritation of any kind particularly that of mechanical agents into respiratory tract, initiates pulmono-cardiac reflexes (vasovagal).[16] 1 out of 25 patients in group C developed arrhythmias which were atrial ectopic as compared to group L where none of the patients had arrhythmias. Abou-Madi et al. opined in their study that arrhythmia suppression effect of the aerosol was partly due to systemic absorption of lignocaine.[15]

Limitations of study

Not being able to measure plasma lignocaine concentrations, effect of lignocaine on other organ systems like reduction of intracranial hypertension etc. We have not done this study on emergency patients and patients with associated cardiac diseases. So further studies can be planned with higher sample size.

Conclusion

This study concludes that pre-operative nebulisation with 5 ml 2% lignocaine for 15 minutes before transferring the patient into operation theatre significantly suppresses pressor response during laryngoscopy and intubation.

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Nil.

Conflicts of interest
There is no conflict of interest.

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