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Research Article

EFFICACY OF ATRACURIUM VERSUS CISATRACURIUM IN PATIENTS UNDERGOING RETROGRADE CHOLANGIOPANCREATOGRAPHY PROCEDURE UNDER GENERAL ANAESTHESIA – A COMPARATIVE STUDY

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ABSTRACT

Objectives: The objectives of the study were to compare the efficacy of injection atracurium 0.5 mg/kg intravenous (IV) versus injection cisatracurium 0.2 mg/kg IV for intubation in patients undergoing endoscopic retrograde cholangiopancreatography procedure (ERCP).

Methods: Hundred adult patients of both sexes in the age group of 18–60 years belonging to the American Society of Anesthesiologists I/II category posted for ERCP procedures under general anesthesia were randomly allocated into two groups of 50 each. Group A received injection atracurium besylate 0.5 mg/kg intravenously and Group B received injection cisatracurium besylate 0.2 mg/kg intravenously. Parameters observed were time to the maximum blockade, intubating condition, time required for intubation, duration of action, hemodynamic parameters during intubation, and after 1, 2, 3, 5, and 15 min and any adverse effects.

Results: Demographic profile was comparable between the groups. Intubating condition as per Cooper *et al*. score was excellent in 36 patients in cisatracurium group as compared to 19 patients in atracurium group. The overall intubating condition was found to be better in Group B (p=0.00001). Time to the maximum blockade was significantly high with atracurium as compared to cisatracurium. The mean of intubation time was less with cisatracurium (135±11.1) than that of atracurium (144±9.48) in seconds, which was statistically significant. Duration of neuromuscular blockade was found to be prolonged in Group B as compared to Group A (p=0.000). Hemodynamic parameters during intubation and after 1, 2, 3, 5, and 15 min were comparable between the groups. No adverse effect was seen in both groups.

Conclusion: Cisatracurium 0.2 mg/kg provides excellent intubating conditions with rapid onset of action, longer duration of action, and no significant hemodynamic changes as compared with atracurium 0.5 mg/kg for ERCP procedures without any adverse effects.

Keywords: Efficacy, Atracurium, Cisatracurium, Endoscopic retrograde cholangiopancreatography

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INTRODUCTION

Endoscopic retrograde cholangiopancreatography (ERCP) is a technique that combines fluoroscopy and endoscopy to diagnosis and treat certain ailments regarding biliary or pancreatic ductal systems. There are two ways to perform ERCP, i.e., monitored anesthesia care (MAC) and general anesthesia (GA) [1]. Till date, there are no formed guidelines for the standard method of care with regard to the type of anesthesia and airway management during ERCP. Zachary *et al*., in his study, found GA to be better than MAC regarding airway protection and other adverse events, procedural failures with higher endoscopist, patient satisfaction, and early discharge [2]. ERCP, in general, takes 1–2 h duration.

To administer GA, a muscle relaxant is always preferred to facilitate smooth endotracheal intubation. Most of the patients posted for ERCP has dearranged liver function test. Since atracurium and cisatracurium do not undergo hepatic metabolism, thus they are the ideal muscle relaxants for ERCP. Cisatracurium is one of the ten isomers of atracurium. The potency of the neuromuscular blocking effect of cisatracurium is approximately three-fold that of atracurium besylate. Cisatracurium has ED_{95} of 50 μg/kg and atracurium has ED_{95} of 0.2 mg/kg. The main advantage of cisatracurium is the lack of histamine release; thus, it has better cardiovascular stability in comparison to atracurium and other histamine releasing neuromuscular blocking agents (NMBA).

Hence, in this study, we are comparing the efficacy of injection atracurium 0.5 mg/kg intravenous (IV) versus injection cisatracurium 0.2 mg/kg IV for intubation in patients undergoing ERCP procedure.

METHODS

Hundred adult patients of both sexes in the age group of 18–60 years belonging to the American Society of Anesthesiologists (ASA) I/II category posted for ERCP procedures under GA formed the study group. It was a prospective randomized, double-blind study. The study was performed after obtaining the Institutional Ethical Committee approval. Preprocedural assessment was done, the procedure explained and informed written consent obtained. Patients were randomly allocated by closed envelop method into two groups of 50 each. Group A received injection atracurium besylate 0.5 mg/kg intravenously and Group B received injection cisatracurium besylate 0.2 mg/kg intravenously. Exclusion criteria were ASA Grades – III and IV, Mallampati Grades – III and IV, anticipated difficult airway, patients who are on aminoglycosides and $MgSO_4$, known history of allergy to any of the study drugs and pregnant women.

Preanesthetic evaluation and counseling for the procedure ERCP were done the day before and reviewed on the day of the procedure. The night before ERCP tablet Alprazolam 0.5 mg was given to all the patients. On the day of the procedure, IV cannulation was done with 18G cannula. All the ASA standard monitors such as electrocardiogram, non-invasive blood, pulse oximetry, capnograph, and temperature were connected. All baseline parameters noted such as heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and arterial oxygen saturation (SPO_2) were noted. Patients were premedicated with injection glycopyrrolate 0.2 mg IV, injection ondansetron 0.1 mg/kg IV, injection ranitidine 50 mg IV, and injection fentanyl 1 μg/kg IV.

Preoxygenation was done with 100% oxygen for 3 min. Train of four (TOF) – WATCH SX 100 nerve stimulator attached. TOF WATCH SX turned on. Once the current and twitch height were standardized, the instrument switched to TOF mode where supra maximal TOF stimuli are applied to the ulnar nerve every 15 s. Calibration and baseline responses obtained before administering neuromuscular blocking drug. All patients received priming dose ($1/10^{th}$ of the bolus dose) of the study drug according to the allocated group. Group A received priming dose of atracurium (i.e., 0.05 mg/kg) IV, and Group B received priming dose of cisatracurium (i.e., 0.02 mg/kg) IV just before induction to shorten the onset time.

Induction of general anesthesia for all patients was done with injection etomidate 0.3 mg/kg IV with loss of verbal response considered to be the endpoint of induction. This was followed by an intubating dose of study drug .Group A received remaining bolus of intubating dose of atracurium (0.45 mg/kg) IV and Group B received remaining bolus of intubating dose of cisatracurium (0.18 mg/kg) IV. TOF WATCH SX showed TOF ratio as percentage and results recorded at 30 s interval. Following parameters were observed perioperatively:

1. Time to maximum blockade:
   Time interval between administration of the dose of relaxant and disappearance of all four twitches in TOF monitor. Intubation was done when TOF ratio was 0%.
2. Intubating condition and time required for intubation:
   Assessment of intubation was done by scoring system given by Cooper *et al.* [3].

Cooper *et al.*, scores

Criteria	0	1	2	3
Jaw relaxation	Impossible	Minimal	Moderate	Good
Vocal cord status	Closed	Closing	Moving	Open
Diaphragmatic status	Severe coughing or bucking	Mild coughing	Slight diaphragmatic movement	None

   Intubating conditions were assessed clinically and scored as excellent (8–9), good (6–7), fair (3–5), and poor (0–2).
3. Duration of action
   Time is taken after drug administration and TOF 0 to regain muscle activity to 25%, i.e., TOF count 2 when a repeat of maintenance dose given.
4. Hemodynamic parameters during intubation and after 1, 2, 3, 5, and 15 min
5. Any adverse effects.

Intubating conditions and time required for intubation were graded by a senior anesthesiologist blinded to group allocation. Intubation was confirmed by capnography and connected to a ventilator for intermittent positive pressure ventilation until completion of ERCP procedure N_2O 60% and O_2 40%, and isoflurane 0.8–1%. Onset time and intubating conditions for atracurium and cisatracurium assessed in allocated groups, respectively. The number of attempts of intubation was assessed and compared between both groups. Hemodynamic parameters such as HR, SBP, DBP, and MAP were recorded before induction, immediately after induction, during laryngoscopy and intubation, and immediately after1, 2, 3, 5, 10, and 15 min after tracheal intubation. After completion of the procedure, the patient was reversed with inj. Neostigmine (0.05 mg/kg) and inj. Glycopyrrolate (0.01 mg/kg). Any adverse events during intubation were recorded in both the group.

Statistical analysis

Statistical analysis was performed by SPSS version 23. All parametric data were measured by student's t-test and expressed as mean ± standard deviation. The non-parametric data measured by Chi-square test and expressed as absolute numbers. Sample size calculation was done keeping power of study 80% and alpha error of 20% from a study by El-Kasaby *et al.* [4].

RESULTS

Demographic profiles in terms of age, sex, and weight were comparable between Groups A and B (Tables 1 and 2).

Intubating condition as per Cooper *et al.* score was excellent in 36 patients in cisatracurium group as compared to 19 patients in the atracurium group. Table 3 shows that the overall intubating condition was found to be better in Group B (p=0.00001). All patients were able to be intubated (Fig. 1).

Time to maximum blockade in seconds

Time to the maximum blockade, as described as the time interval between administration of the dose of relaxant and disappearance of all four twitches in TOF monitor, was significantly high with atracurium as compared to cisatracurium, as shown in Table 4.

The mean of intubation time was less with cisatracurium (135±11.1) than that of atracurium (144±9.48) in seconds which was statistically significant. Duration of the blockade is the time taken after drug administration and TOF 0 to regain muscle activity to 25%, i.e., TOF count 2 when maintenance dose is given. It was found from Table 5 that the duration of neuromuscular bloakade was found to be prolonged in Group B as compared to Group A (p=0.000).

Baseline hemodynamic parameters were comparable between Group A and Group B, as shown in Fig. 2.

HR, SBP, and DBP during intubation and immediately after 1, 2, 3, 5, 10, and 15 min after tracheal intubation were comparable in both the groups, as shown in Figs. 3-5, respectively. None of the patients had any adverse effects or drug reactions.

Table 1: Demographic ProfILE

	Group Mean	Group AA Standard deviation	Group B Mean	Group B Standard deviation	p value
Age	42.92	9.73	41.98	10.1	0.637
Weight	59.18	9.87	60.62	7.41	0.411

Table 2: Distribution of female and male among the groups

	Female (%)	Male (%)	p value
Group A	33 (66.00)	17 (34.00)	0.679
Group B	30 (60.00)	20 (40.00)	
Total	63 (63.00)	37 (37.00)	

Table 3: Overall intubating conditions

	Intubating conditions (Cooper *et al.* score)					
	Excellent	Good	Fair	Poor	Mean±SD	p value
Group A n=50	19	21	10	0	0.82±0.7475	0.00001
Group B n=50	36	12	2	0	0.24±0.4314	

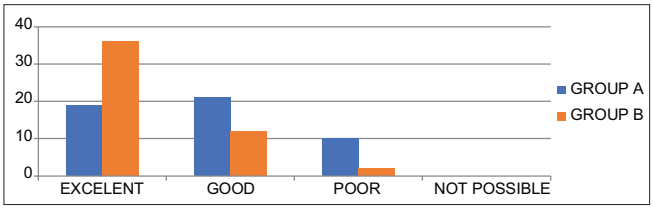

Fig. 1: Comparison of intubating conditions

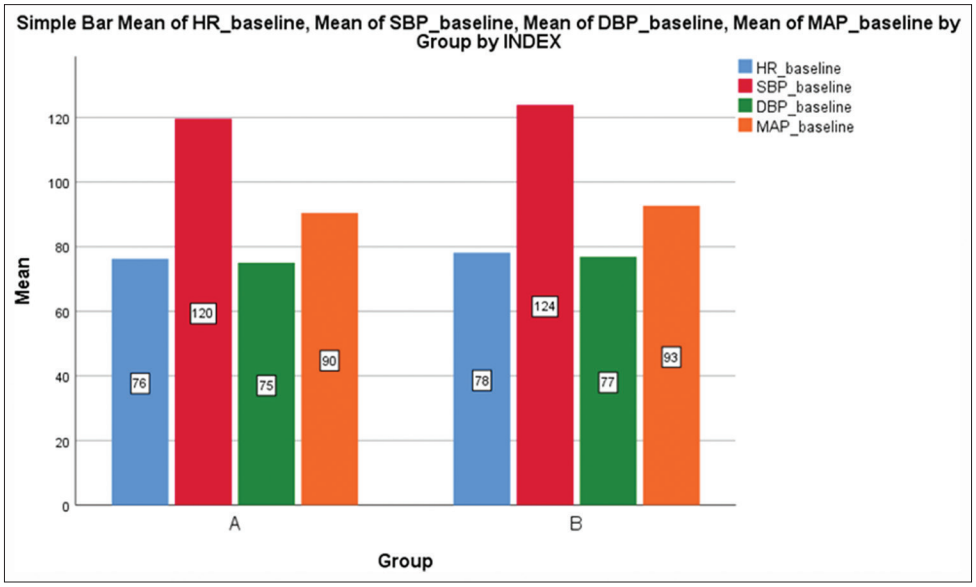

Fig. 2: Comparison of baseline hemodynamic parameters

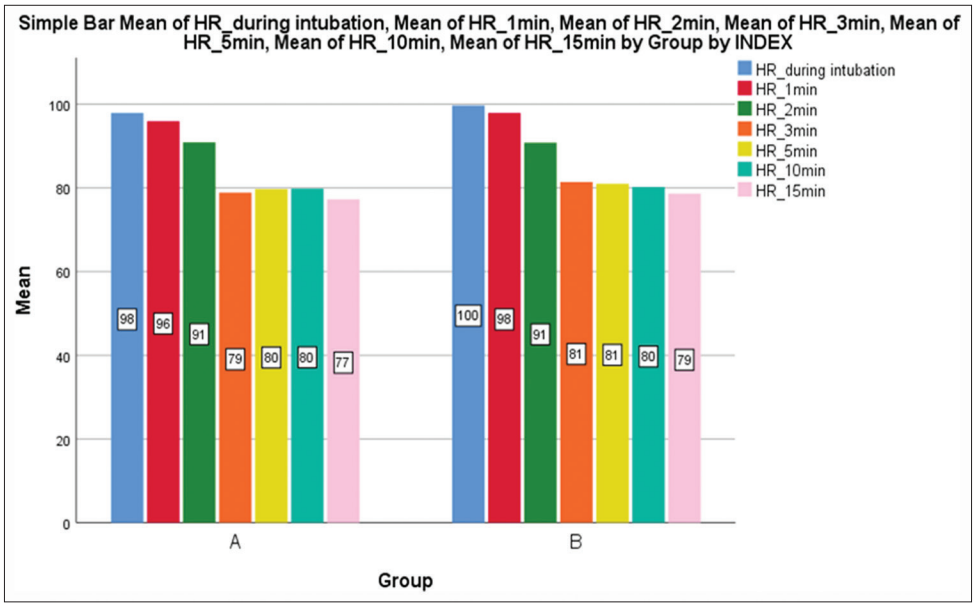

Fig. 3: Comparison of heart rate between the groups during intubation, after 1, 2, 3, 5, 10, and 15 min

Table 4: Comparison of time to maximum blockade

	Group Mean	Group A A Standard deviation	Group B Mean	Group B Standard deviation	p value
Time to maximal blockade	142.2	14.5	97.2	14.92	0.000

Table 5: Comparison of intubation time

	Group A Mean	Group A Standard deviation	Group B Mean	Group B Standard deviation	p value
Intubation time in seconds	144	9.48	135.4	11.1	0.000
Duration of blockade in minutes	43.34	3.47	52.06	3.88	0.000

DISCUSSION

Endotracheal intubation is an integral part of GA during the surgical procedures. From age-old practice, ERCP procedures, including other endoscopic procedures, were conducted under deep sedation. Recent studies, including Zachery *et al.*, have been found that the success rate of ERCP procedures is higher with GA than deep sedation. Adverse effects are also found to be less with GA.

Short-acting or intermediate-acting muscle relaxants are preferred. Of the agent's available vecuronium is avoided in these gallstone or obstructive biliary pathology diseases, as the liver function is unknown in them, and moreover these drugs get metabolized in the liver. The other intermediate-acting agents available such as atracurium and

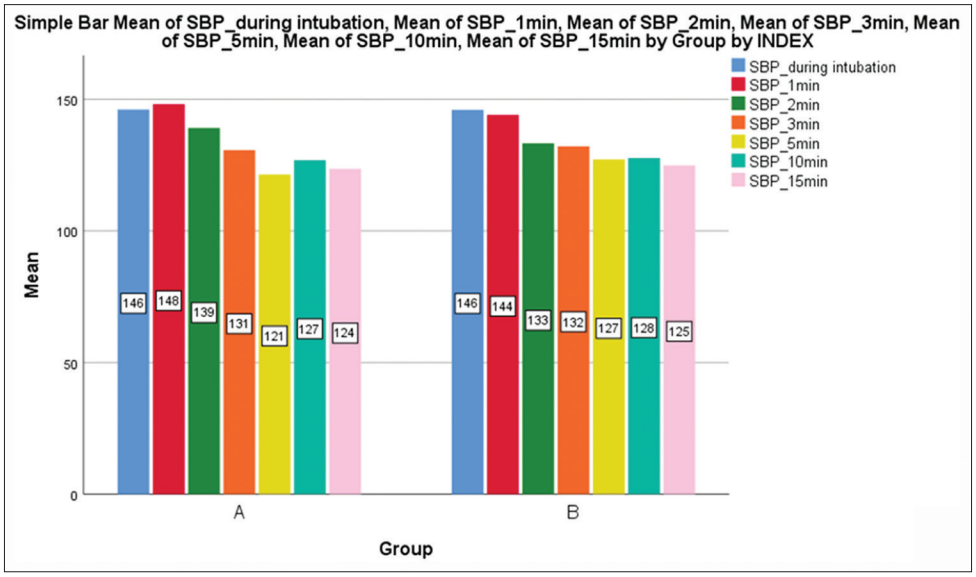

Fig. 4: Comparison of systolic blood pressure between the groups during intubation, after 1, 2, 3, 5, 10, and 15 min

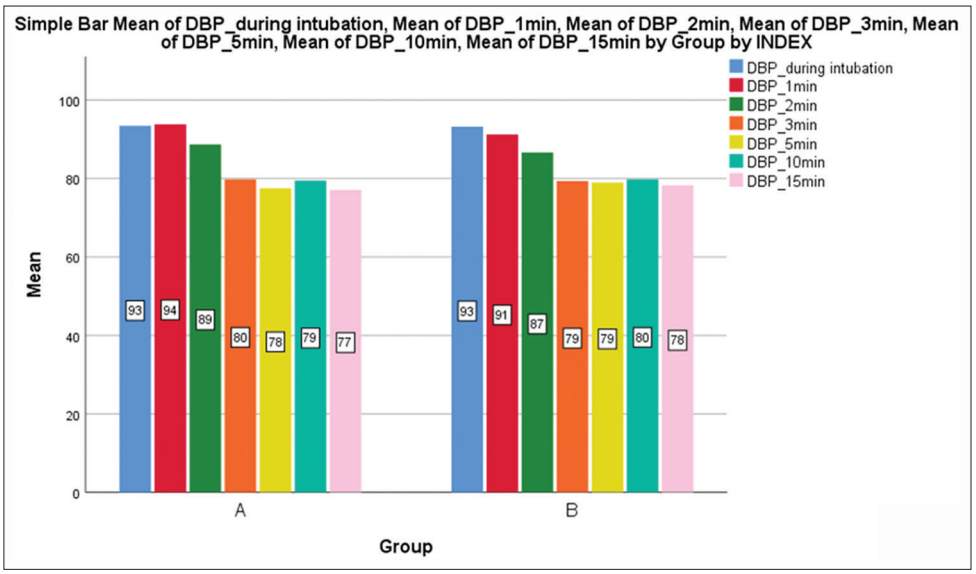

Fig. 5: Comparison of diastolic blood pressure between the groups during intubation, after 1, 2, 3, 5, 10, and 15 min

cisatracurium undergoes Hoffman elimination and ester hydrolysis in compared to vecuronium so are the preferred NMBD for these procedures [5,6].

These ERCP procedures take 1–2 h duration; thus, short-acting agents are mostly preferred. Since these patients posted for ERCP were prone to hemodynamic instability, we preferred these agents and compared atracurium with cisatracurium for onset time, duration of action and hemodynamic parameters during intubation.

Cisatracurium, which is one of the isomers of atracurium, has neuromuscular blocking capacity of approximately three folds that of atracurium besylate. It has ED_{95} of 50 μg/kg and atracurium has ED_{95} of 0.2 mg/kg. The main advantage of cisatracurium is the lack of histamine release, which provides better cardiovascular stability in comparison to atracurium and other histamine-releasing NMBA. Hence, these two drugs are compared in this study.

To reduce the onset time, priming technique has been used. A small sub paralyzing dose of the nondepolarizer (≈20% of the ED_{95} or ≈10% of the intubating dose) is administered 2–4 min before the intubating dose of the compound for priming [7]. This priming accelerates the onset of blockade for most of non-depolarizing NMBDs only by 30–60 s, thereby indicating that intubation can be performed within 90 s of the second dose.

In this study, nondepolarizing, intermediate acting, benzylisoquinolinium compounds atracurium, and cisatracurium were chosen and their neuromuscular function was assessed using TOF. The main advantage of cisatracurium is that there has been no data regarding histamine release at doses up to 8 times the ED95, whereas atracurium causes histamine release in humans at doses >2.5 × ED_{95} [8,9]. The onset time or time to maximum blockade for 2 × ED_{95}, 4 × ED_{95}, 8 × ED_{95} is 5.2 min, 2.7 min, and 1.9 min, respectively, and as the dose increases, clinical duration also increases from 45 min, 60 min, and 91 min, respectively. The intubating dose of cisatracurium is 0.15–0.2 mg/kg, provides excellent intubating conditions. The dose 0.2 mg/kg of cisatracurium used in this study.

Laryngeal adductors are more resistant to the action of cisatracurium than adductor pollicis, but onset and recovery are faster at larynx [10]. Adductor pollicis most commonly used to monitor neuromuscular blockade. Ulnar nerve was used to monitor in this study.

Atracurium is a bis quaternary ammonium benzylisoquinoline compound of the intermediate duration of action. Atracurium has histamine-releasing properties. The intubating dose is 2 ED_{95}, i.e., 0.5 mg/kg, onset of action is 3.2 min, and clinical duration of action is 46 min[8]. 2 ED_{95}, i.e., 0.5 mg/kg is used this study.

In this study, atracurium 2 ED_{95}, i.e., 0.5 mg/kg and cisatracurium 4 ED_{95}, i.e., 0.2 mg/kg dose are compared for onset time, intubating conditions, and hemodynamic parameters.

Duggappa *et al*. have studied that the onset time of atracurium on priming with 0.05 mg/kg, i.e., $1/10^{th}$ of the intubating dose 0.5 mg/kg was 147 s [11].

Deepika *et al*. have studied that the onset time of cisatracurium on priming with 0.02 mg/kg, i.e., $1/10^{th}$ of the intubating dose 0.2 mg/kg, 0 was found to be 103 s [12].

Bluestein *et al*. have studied that the duration of action of 0.1 mg/kg, 0.2 mg/kg of cisatracurium, and 0.5 mg/kg of atracurium were found to be 44 min, 55 min, and 43 min, respectively [13].

Teymourian *et al*. have compared modified dose and high dose of cisatracurium for rapid sequence induction (RSI) and found that 0.2 versus 0.4 mg/kg of cisatracurium had the same effect in providing appropriate laryngoscopy condition for RSI after 90 s [14]. It is safer to use 0.2 mg/kg instead of 0.4 mg/kg cisatracurium to achieve acceptable conditions for RSI.

In our prospective randomized, double-blind study, 100 patients satisfying selection criteria underwent general anesthesia with cisatracurium 0.2 mg/kg and atracurium 0.5 mg/kg. The onset of action, which was the disappearance of all four twitches and TOF ratio 0%, the duration of action, and hemodynamic variables were assessed.

The mean onset of action or the time to maximum blockade was significantly faster in Group B (cisatracurium 0.2 mg/kg) than Group A (atracurium 0.5 mg/kg), the onset of action was 97 s for Group B, 142 s for Group A which is similar to Deepika *et al*. and Duggappa *et al*. None of the group showed any adverse reaction.

CONCLUSION

Cisatracurium 0.2 mg/kg provides excellent intubating conditions with rapid onset of action, longer duration of action, and no significant hemodynamic changes as compared with atracurium 0.5 mg/kg for ERCP procedures without any adverse effects.

AUTHORS CONTRIBUTION

First, second, and third author contribution includes study design, experiments, and drafted an original manuscript. Third and fourth author carried out the data analyses and reviewed the drafted manuscript. All authors approved the final version of the manuscript.

CONFLICTS OF INTEREST

The author declares that they have no conflicts of interest.

AUTHORS FUNDING

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