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Small dead space heat and moisture exchangers do not impede gas exchange during noninvasive ventilation: a comparison with a heated humidifier

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Abstract *Objective:* Adverse respiratory and gasometrical effects have been described in patients with acute respiratory failure (ARF) undergoing noninvasive ventilation (NIV) with standard heat and moisture exchangers (HME). We decided to evaluate respiratory parameters and arterial blood gases (ABG) of patients during NIV with small dead space HME compared with heated humidifier (HH). *Design:* Prospective randomized crossover study. *Setting:* A 16-bed medical intensive care unit (ICU). *Patients:* Fifty patients receiving NIV for ARF. *Measurements:* The effects of HME and HH on respiratory rate, minute ventilation, $EtCO_2$, oxygen saturation, airway occlusion pressure at 0.1 s, ABG, and comfort perception were compared during two randomly determined NIV periods of 30 min. The relative impact of HME and HH on these parameters was successively compared with or without addition of a flex tube (40 and 10 patients, respectively). *Main results:* No difference was observed between HME and HH regarding any of the studied parameters, whether or not a flex tube was added. *Conclusion:* If one decides to humidify patients' airways during NIV, one may do so with small dead space HME or HH without altering respiratory parameters.

Keywords Humidification · Heat and moisture exchanger · Heated humidifier · Noninvasive ventilation · Acute respiratory failure

Introduction

During spontaneous breathing, inspired air conditioning is ensured by the upper airway [1]. During invasive mechanical ventilation, heat and moisture must be added to the inspired gases to compensate upper airway bypass. During noninvasive ventilation (NIV), nose and oropharynx are not bypassed, but they may not be able to achieve adequate levels of humidification, especially when minute ventilation is increased [2]. Humidification can then be achieved either with a heated humidifier (HH) or with a heat and moisture exchanger (HME). In a recent survey on NIV practices in postoperative patients, HH were used by 52% of physicians and HME by 26% [3].

Although numerous clinical evaluations indicate that HME performances are close to those of HH during invasive mechanical ventilation [1], HME have the potential to increase minute ventilation, $PaCO_2$, and work of breathing (WOB) during pressure support ventilation (PSV) in comparison with HHs [4–6]. This is due to the substantial dead space that HMEs add to the ventilatory circuit because of their large internal volume [7]. This increase in WOB may be more deleterious in patients undergoing NIV, with the risk of early NIV failure. Two physiological studies [8, 9] on patients undergoing NIV for acute hypercapnic respiratory failure showed an increase in WOB with HMEs. The HME used in these studies was Hygrobac-DAR, which has a substantial dead space of 84 mL. Despite these drawbacks, it seems that HMEs continue to be predominantly used during NIV [10]. We hypothesized that use of an HME with a smaller dead space would reduce the potential adverse effect of HME on patients' clinical parameters. We therefore conducted a clinical study to assess respiratory parameters and arterial blood gases (ABG) of patients under NIV with a HH compared with a HME with a small internal dead space of 38 mL.

Materials and methods

During an 8-month period, we prospectively studied patients requiring NIV in the 16-bed medical ICU of Bordeaux University Hospital. The study was approved by the local institutional and independent review board (Comité Consultatif pour la Protection des Personnes dans la Recherché Biomédicale Bordeaux A; No 2003/2006), and all patients or their next of kin gave written informed consent before enrollment. This research is registered in ClinicalTrials.gov (NCT00221819).

Patient selection

Eligible cases were patients with acute respiratory failure (ARF) requiring NIV with PSV, i.e., acute on chronic respiratory insufficiency (ACRF) [including chronic obstructive pulmonary disease (COPD) and restrictive patients], hypoxemic acute respiratory failure (HARF) (in patients without previous CRF), and patients difficult to wean from mechanical ventilation (defined by patients who remained hypercapnic at the end of the weaning trial). Exclusion criteria were usual contraindications of NIV, i.e., criteria for immediate intubation described previously [11, 12] and contraindications to the use of HMEs: hypothermia (defined by corporeal temperature below 32°C), broncho-pleural fistula, and poisoning with breath-eliminated drugs such as hydrocarbons.

Study protocol

Two series of patients were consecutively studied. In the first series, we sought to compare the two humidification devices in our usual practice, i.e., keeping a flex tube between the Y-piece and the facemask. In our experience, the flex tube allows greater flexibility for the patient to move his head without risking disconnection of the mask from the ventilatory circuit. We used a device that combines a HME (38 mL dead space) with a flex tube (52 mL dead space) that has a total dead space of 90 mL in the HME group (Edith flex, Datex Ohmeda, Trappes, France). In the HH group (MR 850, Fisher & Paykel Healthcare, Auckland, New Zealand), a flex tube (Catheter mount smoothbore 180 mm, Intersurgical, Fontenay sous Bois, France) with a dead space of 33 mL was positioned between the Y-piece and the mask (Fig. 1). In the second series, we removed the flex tube in both groups to take into consideration its impact on the instrumental dead space. To do this, we compared another HME model, the Edith 1500 (Datex Ohmeda, Trappes, France) (38 mL dead space) which is devoid of flex tube to the same HH but without the flex tube (0 mL dead space) (Fig. 1).

Two 30-min NIV periods with PSV were compared, one with a HME and the other with a HH, separated by a 20–30-min period of spontaneous breathing with oral or nasal oxygen supply, to maintain SpO_2 >92%.

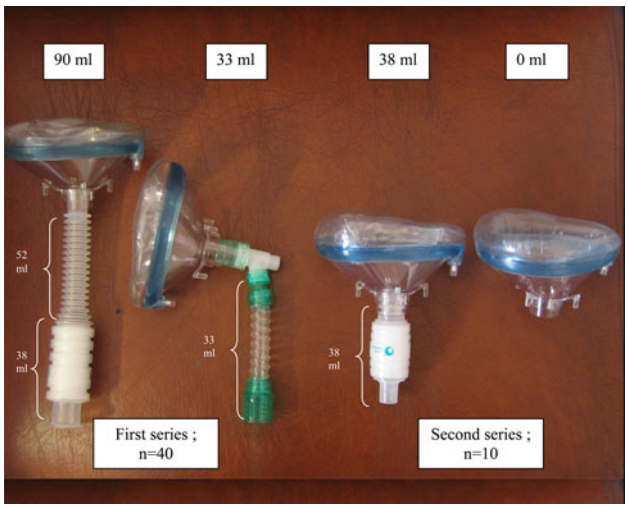

Fig. 1 Description of devices placed between Y-piece and facemask in both series of patients with reference to their dead space. In the first series of 40 patients, an Edith flex adding a 90 mL dead space, i.e., coupling a 52 mL dead space flex tube and a 38 mL dead space HME, was compared with a flex tube adding a 33 mL dead space in the HH group (*left side*). In the second series of ten patients, an Edith 1500 HME adding a 38 mL dead space was compared with no additional dead space in the HH group (*right side*)

Randomization was performed with sealed envelopes to determine the order of the NIV periods. The level of pressure support was initially set to obtain expired tidal volume between 7 and 10 mL/kg and respiratory rate (RR) smaller than 25 breaths/min. In COPD patients, positive end-expiratory pressure (PEEP) was progressively increased by 2 cmH_2O steps until unsuccessful inspiratory triggering efforts were removed. In patients without previous CRF, PEEP was increased until FiO_2 requirement was 70% or less. Other parameters such as inspiratory or expiratory triggers were set following usual recommendations. In case of air leaks, masks were secured more efficiently, or, if recurrent, a lower level of pressure was used. The ventilatory settings remained constant throughout both study periods. According to manufacturer's information, the Edith Flex HME and the Edith 1500 provide a resistance, respectively, of 1.4 and 2.5 $cmH_2O\ l^{-1}\ s^{-1}$ at 60 L/min. The HH Fisher & Paykel MR 850 has a resistance of 2.7 $cmH_2O\ l^{-1}\ s^{-1}$ at 60 L/min. The Edith Flex HME and the Edith 1500 provide 30 mgH_2O/L absolute humidity according to manufacturer's data, as previously confirmed during invasive ventilation for Edith Flex HME [13]. For study purpose, the same Evita IV ventilator (Dräger, Lübeck, Germany) was used to deliver PSV through the same facemask (Kingsystems Corporation, Noblesville, USA) with 180 mL internal volume (when applied on a flat surface).

Clinical and physiological measurements

Measurements were recorded in the last 5 min of each 30-min NIV period with HME and HH. Clinical data included RR (averaged on five measurements spread over 5 min), respiratory comfort assessed by using a visual analog scale on which patients located their feelings between 0 (no dyspnea and very comfortable) to 10 (major dyspnea and not comfortable), and duration of the NIV periods. Physiological data were displayed on the monitor by using a spirometry and capnometry sensor (D LITE^{TM}, Datex Ohmeda, Trappes, France) positioned between the flex tube and the facemask, providing in each group an additional dead space of 9.5 mL. Inspiratory, expiratory tidal volumes, and expired CO_2 were averaged on ten consecutive cycles. Minute ventilation was calculated as the product of averaged RR with averaged expired tidal volume. Airway occlusion pressure at 0.1 s ($P_{0.1}$) was measured with integrated function of the Evita IV ventilator and averaged on five consecutive measurements. Levels of pressure support, PEEP, and arterial oxygen pulse pressure (SpO_2) were recorded at the end of each NIV period. ABG were measured just before the beginning of the NIV period and in the last 5 min of NIV periods using the Rapidlab 855 analyzer (Bayer, Sudbury, UK).

Statistical analysis

Statistical analysis was performed by using the StatView 5 package (SAS Institute, Cary, NC, USA). Data are expressed as mean ± standard deviation (SD). Measurements before NIV and after each NIV period were compared by analysis of variance for repeated measurements. Other quantitative and qualitative variables were compared using *t* test (paired *t* test when appropriate) and chi-square statistics, respectively. All tests were two-tailed. When distribution was not normal or when number of patients was small, nonparametric tests were used (Friedman analysis and Mann–Whitney *U* test). Dunn and Bonferroni multiple-comparison tests were used to detect differences between paired measures when appropriate (baseline versus HH, baseline versus HME, HH versus HME). A P value <0.05 was considered statistically significant.

Results

Study population

Fifty patients were included (40 in the series with a flex tube and 10 in the series without). Patient baseline characteristics are presented in Table 1. Acute on chronic respiratory failure was the main indication for NIV (28/50). There was no difference between the two groups of patients (with or without flex tube) in terms of age, severity score, or ABG (Table 1). Median time between admission and the first NIV period for ARF was 2 h [1–6] in all patients except in those of the difficult-to-wean subgroup, for whom NIV was started just after extubation. All 50 patients completed the study. No patient had premature cessation of NIV, and all remained stable during the procedure. Once the patients were stabilized under NIV, the setting of the ventilator was compared between the two conditions, and no difference was observed in either pressure support or PEEP level (Table 2).

Comparison of Edith Flex HME (90 mL) and HH with the flex tube (33 mL)

Mean duration of study periods was 31.5 ± 4 min for HH and 31.3 ± 2.4 min for HME. Table 3 shows that there was no difference in respiratory parameters, $P_{0.1}$, or dyspnea score between HH and HME. ABG values significantly improved under NIV compared with baseline spontaneous breathing values (Table 3), whatever the humidifying device. In the subgroup of patients with acute hypercapnic respiratory failure who suffered the deepest respiratory acidosis (mean pH 7.28 ± 0.06), NIV

Table 1 Patient characteristics

	Flex tube ($n = 40$)	No flex tube ($n = 10$)[b]
Age (years)	65 ± 16.0	69.0 ± 17.0
Gender (male/female)	17/13	8/2
SAPS II	40 ± 15.6	44 ± 12.6
Indication for NIV		
Acute on chronic respiratory insufficiency[a] (ACRF)	18	10
Hypoxemic acute respiratory failure (HARF)	15	
Difficult-to-wean patients (DTW)	7	
Median time between ICU admission and inclusion (h)	23.5 [12.5–51]	28.5 [16–48.2]

NIV Noninvasive ventilation, *SAPS* Simplified Acute Physiology Score

[a] Patients with chronic respiratory insufficiency included COPD or restrictive patients

[b] Patients who performed NIV without flex tube were exclusively patients with ACRF

Table 2 Respiratory parameters during NIV

Type of device (n)	With a flex tube		P value	Without a flex tube		P value
	HH (40)	HME (40)		HH (10)	HME (10)	
Pressure support (cmH_2O)						
In ACRF patients	16.2 ± 4.9	15.8 ± 4.6	0.95	16.5 ± 3.4	16.8 ± 3.8	0.28
In HARF patients	15.1 ± 2.8	14.7 ± 3.3	0.77			
In DTW patients	15.9 ± 2.4	15.9 ± 2.4	1			
PEEP (cmH_2O)						
In ACRF patients	3.7 ± 0.97	3.7 ± 0.96	0.99	3.7 ± 1.34	3.8 ± 1.7	0.73
In HARF patients	5.6 ± 1.5	5.6 ± 1.4	1			
In DTW patients	3.9 ± 1.9	4.0 ± 2.0	0.89			
FiO_2						
In ACRF patients	0.30 ± 0.1	0.30 ± 0.1	0.65	0.47 ± 0.11	0.56 ± 0.19	0.34
In HARF patients	0.54 ± 0.1	0.54 ± 0.1	1			
In DTW patients	0.35 ± 0.1	0.35 ± 0.1	1			
SpO_2						
In ACRF patients	94 ± 4.6	94.54 ± 4.3	0.60	95.0 ± 6.1	96.0 ± 4.2	0.33
In HARF patients	97 ± 3.0	97 ± 1.6	0.57			
In DTW patients	98 ± 1.8	97 ± 1.5	1			
RR (breaths/min)						
In ACRF patients	22 ± 7.8	22 ± 6.8	0.56	19 ± 4.6	19 ± 6.1	0.80
In HARF patients	24 ± 6.5	24 ± 7.0	1			
In DTW patients	27 ± 6.2	23 ± 8.8	0.33			
VTe (mL)						
In ACRF patients	728 ± 562	756 ± 502	0.83	610 ± 158	655 ± 229	0.31
In HARF patients	751 ± 322	732 ± 292	0.86			
In DTW patients	632 ± 175	724 ± 258	0.45			
VE (mL)						
In ACRF patients	14,870 ± 7,832	15,277 ± 8,732	0.61	11,562 ± 2,538	11,698 ± 2,850	0.88
In HARF patients	20,600 ± 8,300	20,717 ± 7,664	0.94			
In DTW patients	17,138 ± 5,228	17,822 ± 5,858	0.46			
$EtCO_2$						
In ACRF patients	34.6 ± 8.90	33.8 ± 9.22	0.41	35.6 ± 9.45	33.0 ± 8.58	0.35
In HARF patients	27.7 ± 5.39	26.7 ± 6.35	0.22			
In DTW patients	30.3 ± 11.28	30.2 ± 11.28	0.96			
$P_{0.1}$ (cmH_2O)						
In ACRF patients	2.7 ± 1.6	2.3 ± 1.0	0.59	2.0 ± 1.6	1.9 ± 1.2	0.85
In HARF patients	3.3 ± 1.7	3.6 ± 1.6	0.64			
In DTW patients	2.3 ± 1.4	2.8 ± 1.2	0.45			

ACRF acute on chronic respiratory insufficiency, *HARF* hypoxemic acute respiratory failure, *DTW* difficult to wean, *PEEP* positive end-expiratory pressure, *RR* respiratory rate, *VTe* expiratory tidal volume, *VTi* inspiratory tidal volume, *VE* minute ventilation, *$EtCO_2$* end-tidal CO_2

Table 3 Gas exchanges and respiratory comfort score in NIV patients with flex tube

	Baseline	HH ($n = 40$)	HME ($n = 40$)
pHa			
In all patients	7.36 ± 0.09	7.40 ± 0.07[£]	7.39 ± 0.07*
In ACRF patients ($n = 18$)	7.28 ± 0.05	7.36 ± 0.06[§]	7.36 ± 0.05[§]
In HARF patients ($n = 15$)	7.43 ± 0.06	7.42 ± 0.07	7.40 ± 0.07
In DTW patients ($n = 7$)	7.41 ± 0.08	7.44 ± 0.06	7.42 ± 0.07
$PaCO_2$ (mmHg)			
In all patients	57.8 ± 21	51.2 ± 16[£]	52.5 ± 15[£]
In ACRF patients ($n = 18$)	73.9 ± 16	58.1 ± 16[§]	59.2 ± 15[§]
In HARF patients ($n = 15$)	42.5 ± 11	44.7 ± 14	46.1 ± 14
In DTW patients ($n = 7$)	49.4 ± 17	47.4 ± 15	48.9 ± 13
PaO_2 (mmHg)			
In all patients	71.5 ± 21	118.5 ± 69[§]	130.9 ± 64[§]
In ACRF patients ($n = 18$)	69.2 ± 24	85.7 ± 23	99 ± 39[£]
In HARF patients ($n = 15$)	72.4 ± 17	158.7 ± 95[§]	174.1 ± 75[§]
In DTW patients ($n = 7$)	75.6 ± 20	122.5 ± 46[£]	126.6 ± 39[£]
HCO_3^- (mmol/L)			
In all patients	30.7 ± 7	30.3 ± 7	30.2 ± 6
In ACRF patients ($n = 18$)	33.6 ± 8	32.2 ± 7	32.2 ± 7
In HARF patients ($n = 15$)	26.9 ± 5	28 ± 6	27.8 ± 5
In DTW patients ($n = 7$)	31.3 ± 7	30.5 ± 7	30.2 ± 5
Respiratory comfort score	ND	3.7 ± 0.4	3.6 ± 0.3

pHa arterial pH, *$PaCO_2$* arterial partial pressure of carbon dioxide, *ND* not done
* $P < 0.05$, HH and HME group versus baseline; [£] $P < 0.01$, HH and HME group versus baseline; [§] $P < 0.001$, HH and HME group versus baseline

Table 4 Gas exchanges in NIV patients without flex tube

	Baseline	HH ($n = 10$)	HME ($n = 10$)
pHa	7.30 ± 0.05	7.35 ± 0.07*	7.35 ± 0.08*
$PaCO_2$ (mmHg)	60.1 ± 13	52.8 ± 13*	52.5 ± 15*
PaO_2 (mmHg)	81.1 ± 23	110.0 ± 43	138.0 ± 85
HCO_3^- (mmol/L)	28.5 ± 7	28.6 ± 7	28.2 ± 7

* $P < 0.01$, HH and HME group versus baseline

with HMEs improved ABG to the same extent as HH (Table 3).

Comparison of Edith 1500 HME (38 mL) and HH without the flex tube (0 mL)

Table 2 shows that there was no difference in respiratory parameters or in $P_{0.1}$ between HH and HME. ABG values significantly improved under NIV compared with baseline spontaneous breathing values, whatever the humidifying device (Table 4).

Discussion

The main finding of this study is that ventilatory parameters and ABG are not modified by the use of a small dead space HME compared with HH in patients undergoing NIV for ARF. This result was also found in the subgroup of hypercapnic patients, potentially more affected by the adverse effects previously observed with HMEs. Finally, results were similar with or without insertion of a flex tube between the HME or the HH and the Y-piece.

Although the question of adding or not a humidification device during NIV remains unanswered, and despite the fact that up to 26% of clinicians use HMEs in this setting [3], it has been suggested that HMEs should not be used during NIV [8, 9]. Indeed, due to their internal volume, some HMEs add significant dead space to the circuit [7], and studies have shown that these HMEs have the potential to increase minute ventilation, $PaCO_2$, and WOB during invasive PSV in comparison with HH [4, 6]. Obviously, similar effects are to be expected during NIV. By contrast with two randomized crossover studies [8, 9] using a large internal volume (84 mL) HME that showed a modest increase in $PaCO_2$ and concomitant decrease in pH, our study illustrates that use of smaller HME does not impact respiratory parameters and ABG. One explanation for these discrepancies could be the differences in instrumental dead space between HH and HME groups, which were only 57 and 38 mL in patients with or without flex tube, respectively, compared with 84 mL in previous studies [8, 9]. These results should also be related to the presence of a flex tube. Indeed, in the first part of the study, instrumental dead space was 90 mL in the HME group, very similar to the 84 mL in both previous studies [8, 9], but was greater in the HH group

(33 mL due to the flex tube) than in both previous studies (0 mL). However, the absence of a significant effect of HMEs on blood gases remained in the second part of the study when the flex tube was removed in both conditions (HME and HH). In this setting, instrumental dead space in the HME group was only 38 mL, considerably less than in both previous studies [8, 9]. Lellouche et al. [8] also studied the effect of an HME with a smaller dead space (45 mL) and found the same unfavorable effects on patients' effort indices as compared with those observed with the large HME. Noticeably, however, measurements were only performed in zero end-expiratory pressure (ZEEP), thus limiting the clinical relevance of this finding.

It is possible that, as suggested by Lellouche et al. [8], the effect of increasing dead space may not be linear. In addition, and in line with this suggestion, one must bear in mind that measuring devices accounted for an extra 27 mL dead space in Lellouche et al.'s study [8], thus perhaps further worsening the unfavorable effects of HME compared with HH. In our study, the capnometry sensor provided only a 9.5 mL additional dead space in each group. In any case, one must keep in mind that the increase in $PaCO_2$ seen with the HME in all these studies is very small and does not exceed 2–3 mmHg.

From a clinical point of view, we also investigated patient comfort during NIV by using a visual analog scale. Even if this scale has not been prospectively validated before, it does provide an important indirect assessment of NIV tolerance with each of the humidification devices, because intolerance is one of the major causes of NIV failure. We found that patients gave the same rating of their comfort whether they received NIV through the HME or the HH, suggesting—indirectly—that they did not perceive any difference in inspiratory effort, in agreement with the similar $P_{0.1}$ measured with both devices.

Our study has several limitations. The occurrence of air leaks during NIV may be a potential drawback to the use of HMEs. In our study, high level of pressure obtained following predetermined NIV goals could have favored air leaks. Although not systematically recorded, the best precautions were used to optimize facemask sealing so as to limit leaks. Indeed, expired air leaks could impair adequate capacity of HME to retain heat and humidity and hence to recycle them during the next expiration. Hygroscopic evaluation of the HME was not performed in this study, since our group had already made this evaluation in a previous study [13]. Results indicated adequate levels of absolute humidity, even in COPD patients [13]. Although our former study did not include NIV patients, Lellouche et al. [14] have recently found that HMEs could provide adequate humidity levels during NIV despite air leaks. We agree, however, that direct hygroscopic evaluation could have strengthened our previous findings.

One could also criticize the heterogeneity of the patients included in our study. However, the fact that absence of unfavorable effects of HME was seen throughout the variety of respiratory failures requiring NIV strengthens the internal validity of the results and their applicability in the clinical setting.

Moreover, as in the other studies, patients were studied during a 30-min period only and with an ICU ventilator and a facial mask, thus precluding any definite conclusion during longer NIV periods or NIV delivered by other ventilators or masks.

Finally, limitations of our study include the fact that, like Jaber et al. [9], we could only approximate inspiratory efforts with $P_{0.1}$ measurement, which is not completely validated during NIV but has already been used by others to assess WOB during pressure support [15–17]. Despite this limitation, we found no significant differences in $P_{0.1}$ between HH and HME. In addition, resistances were not measured in our study, precluding any firm conclusion regarding their precise contribution to discrepancies between previous studies and ours. However, as indicated above, an important feature of the HME we tested lies in its particularly low resistance of 1.4 $cmH_2O\ l^{-1}\ s^{-1}$ in comparison with the 3.5 $cmH_2O\ l^{-1}\ s^{-1}$ measured by Lellouche et al. [8] for the HH, which may explain the absence of difference we observed in $P_{0.1}$. Although there was no deleterious effect on respiratory parameters, gas exchanges, and $P_{0.1}$, we cannot completely exclude a slight effect of the HME used on the WOB, particularly during longer NIV periods. So, pending the final results of a large randomized trial comparing NIV with HME or HH [18], the influence of the humidification device (HME or HH) on the outcome of longer NIV periods remains unknown. However, preliminary results of this study [18] indicate that intubation rate was not different in the HH group (37.6%) compared with the HME group (30.6%), leading authors to suggest that the physiologic effects observed in short-term studies may play a role only in marginal cases [18], cases that may have not been evaluated in our study. It seems that these potential effects are outweighed by others during "true-life" NIV. This may explain why clinicians continue to use HMEs in approximately half of their patients undergoing NIV, as reported by Demoule et al. [10].

In conclusion, our study suggests that NIV can be satisfactorily performed with an HME, providing its dead space is sufficiently reduced. These results are not limited to a specific category of patients requiring NIV and may contribute, with others, to the development of future guidelines on humidification and NIV [19].

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Conflict of interest statement All authors declare no conflicts of interest.

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