Received: 23 November 2021 | Accepted: 28 June 2022

DOI: 10.1002/ppul.26050

ORIGINAL ARTICLE

WILEY

Breath-dependent pressure fluctuations in various constant- and variable-flow neonatal CPAP devices

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Abstract

Objective: In continuous positive airway pressure (CPAP) devices, pressure can be generated by two different mechanisms: either via an expiratory valve or by one or more jets. Valved CPAP devices are referred to as constant-flow devices, and jet devices are called variable-flow devices. Constant-flow CPAP devices are said to reduce the imposed work of breathing due to lower breath-dependent pressure fluctuations. The present study investigates the performance of various constant- and variable-flow CPAP devices in relation to breath-dependent pressure fluctuations.

Design: Experimental study comparing the pressure fluctuations incurred by seven neonatal CPAP devices attached to an active neonatal lung model.

Methodology: Spontaneous breathing was simulated using a tidal volume of 6 ml at pressure levels of 5, 7, and 9 mbar. The main outcomes were respiratory pressure fluctuations, tidal volume, and end-expiratory pressure.

Results: All CPAP devices tested showed respiratory pressure fluctuations, varying from 0.631 to 3.466 mbar. The generated tidal volume correlated significantly with the pressure fluctuations ($r = -0.947$; $p = 0.001$) and varied between 5.550 and 6.316 ml. CPAP devices with jets showed no advantage over CPAP devices with expiratory valves. End-expiratory pressure in the nose deviated from the set pressure between −1.305 and 0.644 mbar and varied depending on whether the pressure was measured in the device or in the tube extending to the nose.

Conclusion: During standard spontaneous breathing, breath-dependent pressure fluctuations in constant- and variable-flow devices are comparable. Pressure measurements taken in the tubing system can lead to a considerable deviation of the applied pressure.

KEYWORDS

constant flow, nasal CPAP, pressure fluctuations, preterm infants, variable flow

1 | INTRODUCTION

Following the publication of Gregory et al. in 1971, continuous positive airway pressure (CPAP) has become an integral part of neonatology.[1] Initially applied using a helmet, the introduction of the first binasal CPAP was first described in 1973.[2] The positive end-expiratory pressure (PEEP) in this device was controlled primarily by the expiratory valve. Such CPAP devices operating with the expiratory valve are now called constant-flow CPAP devices.[3] In 1988, an alternative binasal CPAP device was described by Moa et al.[4] This was able to dispense without the expiratory valve, and instead used jets positioned near the nasal airways. By swirling the flow coming out of these jets, the kinetic energy of the flowing respiratory gas was converted into pressure. To change the PEEP, the flow must be varied, which is why the devices are called variable-flow CPAP devices.[5] This concept was based on the Benveniste valve initially developed in 1968 for mechanical ventilation during anesthesia and later published in 1976 as a mononasal CPAP for infants.[6,7] Since the study of Moa et al., jet flow CPAP devices have been considered to compensate for pressure fluctuations better than CPAP devices with expiratory valves.[3,4] The pressure fluctuations are the central factor that defines the extrinsic work of breathing imposed by the CPAP device.[8] Therefore, patients using variable-flow CPAP devices are thought to have less work of breathing than patients using constant-flow CPAP devices,[3,8] and consequently, variable-flow devices are regarded as a better choice.

The purpose of this study was to test the performance of various constant- and variable-flow CPAP devices based on their respiratory pressure fluctuations.

2 | METHOD

Seven CPAP devices currently in the market were investigated while attached to a neonatal active lung simulator (GINA®, Schaller Medizintechnik), which mimicked the spontaneous breathing in a preterm infant weighing approximately 1000 g. The settings of the lung simulator are summarized in Table 1.

A nosepiece, consisting of two perforations 4.0 mm in diameter and 3.0 mm apart, replicated the nasal cavity divided by a septum, with which CPAP devices were connected via prongs to the lung simulator. The test setup can be visualized in Figure 1.

The following CPAP devices were tested:

1. BabyFlow® with size M prongs (Drägerwerk AG Co KGaA).
2. EasyFlow nCPAP with size M prongs (Fritz Stephan GmbH).
3. FlexiTrunk™ with BC4030 Prongs (Fisher and Paykel Healthcare Ltd.).
4. Inspire nCPAP™ with size S prongs (Inspiration Healthcare Limited).
5. Inspire rPAP™ with size S prongs (Inspiration Healthcare Limited).
6. Medijet® with size M prongs (medin Medical Innovations GmbH).
7. Miniflow® with size M prongs (medin Medical Innovations GmbH).

TABLE 1 Setting of the active lung model

Resistance[a]	Ra1
Endotracheal tube[b]	5.0 mm
Compliance	0.5 ml/mbar
Respiratory rate	67/min
Inspiratory time	0.3 s
Pleural negative pressure[c]	−20 mbar
Pressure curve[d]	Cosine function

[a]The resistance is adjusted mechanically on the device by a rotary knob. This allows parallel metal tubes with different thicknesses to be selected through which the respiratory gas then flows. These simulate the resistance of the deep airways. Since the flow resistance changes depending on the flow rate, no numerical value is assigned to this setting. According to the manufacturer, this setting corresponds to the flow resistance of a small premature baby.

[b]For the simulation of the upper airway, the endotracheal tube 5.0 recommended by the manufacturer was selected.

[c]The pleural negative pressure must be set to simulate spontaneous breathing. Thus, a tidal volume of approximately 6 ml/kg was achieved.

[d]According to the manufacturer, a pressure curve following a cosine function corresponds to normal spontaneous breathing. A random variation of 5% was also preset for pleural pressure and inspiratory time.

Inspire nCPAP™ and Medijet® generate pressure via jets and are, therefore, classified as variable-flow CPAP devices.[3,4] The Medijet uses only one jet, and pressure is built up in a larger antechamber in front of the prongs. The design of the Medijet is very similar to that of the original Benveniste valve.[9] In this study, Inspire nCPAP™ and Medijet® were used with a fabian +nCPAP evolution ventilator (Acutronic Medical Systems AG) functioning in nasal continuous positive airway pressure mode. For both devices, the set pressure was generated by a flow controlled by the ventilator.

BabyFlow®, EasyFlow nCPAP, FlexiTrunk™, and Miniflow® are CPAP devices in which the pressure in the tubing system is generated by the interaction between the driving flow and the expiratory valve at the end of the expiratory tubing. They, therefore, all belong to the group of constant-flow CPAP devices.[4] The FlexiTrunk™ was used with a bubble CPAP system (Fisher and Paykel) that includes a surge chamber with a dip tube at the end of the expiratory arm. The set pressure in the CPAP device is determined by immersing the dip tube in water. The surge chamber is not capable of measuring, controlling, or regulating pressure. The fabian +nCPAP evolution ventilator in the O_2 therapy mode was used only to drive flow. FlexiTrunk™, BabyFlow®, EasyFlow nCPAP, and Miniflow® require not only the driving flow but also the expiratory valve of the mechanical ventilator. This allows balancing of Inspiratory and expiratory pressure fluctuations within milliseconds. For the study, the fabian +nCPAP evolution ventilator was used in invasive CPAP mode with the flow sensor disabled.

The primary application of the Inspire rPAP™ is in resuscitation and initial care immediately after birth. The device, when equipped with prongs, is also suitable for short CPAP bridges, for example,

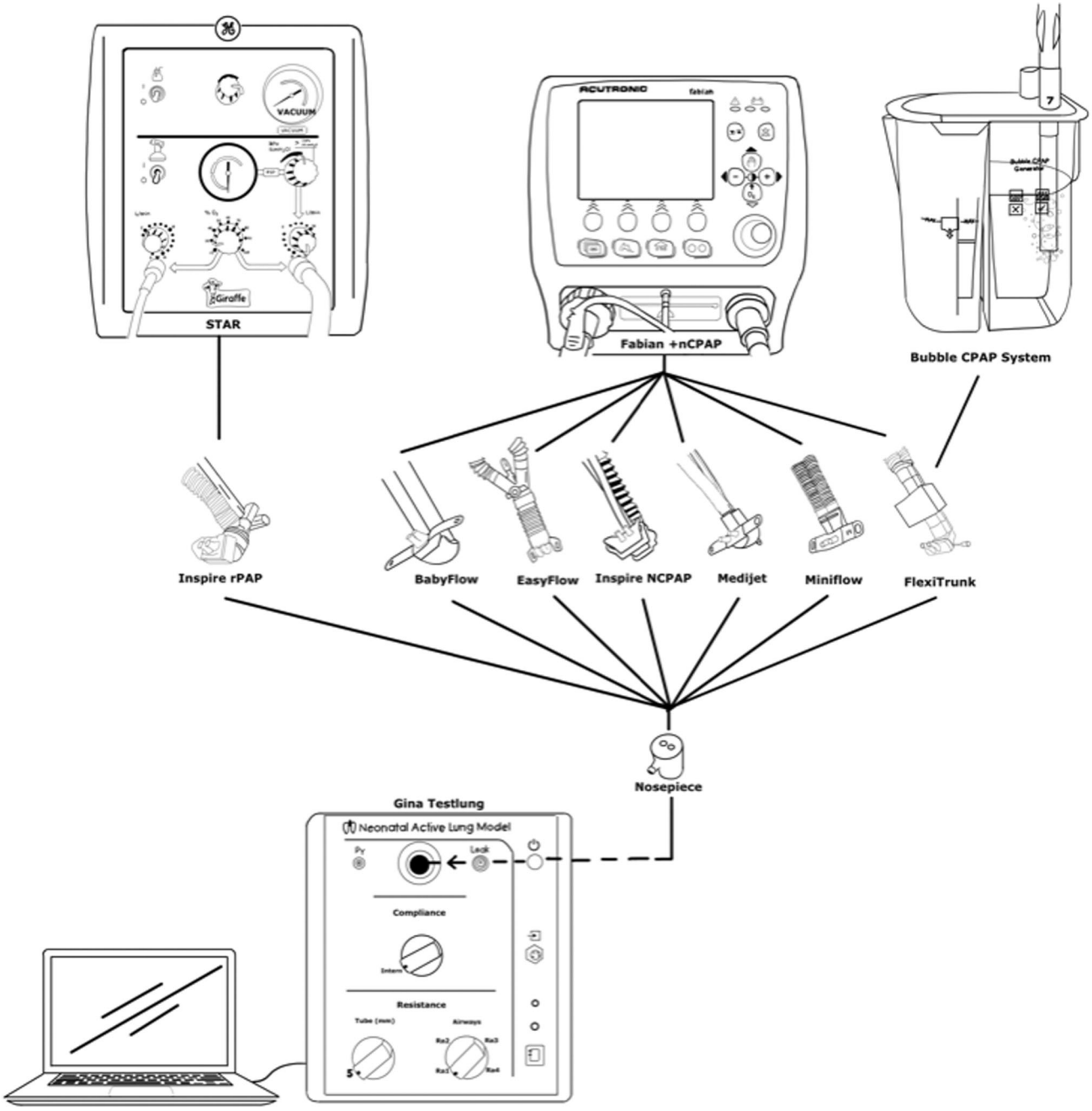

FIGURE 1 Experimental setup with flow driver, ventilator, surge chamber, continuous positive airway pressure devices, and a nasal piece with the pressure measurement point "nose" and the GINA test lung.

when transporting patients to the ward. It does not use jets or a true expiratory valve, yet the pressure inside the device remains markedly stable during ventilation.[10] The Inspire rPAP™ requires two separate streams and was therefore coupled with a Giraffe Stand-Alone Infant Resuscitation System (GE Healthcare), which also provides the ability to monitor the pressure in one of the ventilator tubes. In the CPAP device, these two countercurrents meet and then exit through a common outlet.

In this study, measurements were made with the CPAP devices, at preset PEEP values of 5, 7, and 9 mbar. In the case of the Inspire nCPAP™ and the Medijet®, the PEEP values were set by the fabian +nCPAP evolution ventilator. Since the CPAP pressure can only be influenced by the flow rate of the jets, these devices have only one corresponding flow for each pressure setting. This was automatically regulated by the fabian +nCPAP evolution ventilator. Accordingly, only one measurement per PEEP value was recorded with these devices. All other devices are capable of generating identical PEEP values at different flow settings by adjusting the expiratory valve. Therefore, baseline measurements of the 5 and 15 L/min flows were taken with these devices at each PEEP value. These flows correspond

to the minimum and maximum allowable single flow of the Inspire rPAP™ device. The flows are also within the allowable flow range of the FlexiTrunk (4–15 L/min) and do not exceed the parameters used in medical practice. For the measurements with the Inspire rPAP™ device, the two different flows of 5 and 15 L/min were each applied to the so-called peak inspiratory pressure/positive pressure ventilation (PIP/PPV) flow. The target PEEP was then set by adjusting the CPAP flow. For the FlexiTrunk™, PEEP was adjusted by immersing the dip tube into the bubble CPAP generator. The depth of immersion was held constant for both applied flows, as no pressure measurement was possible in this device.

The CPAP device, prong size, and flow generator or ventilator used are summarized in Table 2.

The primary outcome parameters of the study are the amplitude of the breath-dependent pressure fluctuations, the actual end-expiratory pressure, and the generated tidal volume. In addition, as a secondary outcome, we tested whether the actual pressure reaching the nose differed from the pressure measured in the respective CPAP devices.

For each setting, measurements were recorded over a period of approximately 2.5 min and documented every 50 ms. These data were used to determine the tidal volume, the difference between the lowest pressure during inspiration and the highest pressure during expiration (pressure variation), and PEEP for all recorded breathing cycles.

Because the lung simulator has only one external input for pressure measurement outside the device, the pressure could not be measured simultaneously in the nose and in the CPAP device. To determine the corresponding pressures, separate measurements were taken for each of these two measurement points.

To measure the device pressure of Inspire nCPAP™, Medijet, EasyFlow nCPAP, Miniflow®, and Babyflow®, a T-piece was inserted into the pressure measurement lines of the fabian +nCPAP evolution ventilator. To measure the device pressure of the Inspire rPAP™, an additional T-piece was positioned at the beginning of the PIP/PPV line. When using the FlexiTrunk™ with the bubble CPAP system, no pressure measurement line is provided; however, the device has an appropriate connection so that it can be used with a ventilator instead of the bubble CPAP system. Measurement was taken through this port.

In the FlexiTrunk™, bubble formation in the surge chamber resulted in a high-frequency pressure oscillation that superimposed the pressure fluctuations caused by respiration. A direct determination of the pressure curve is therefore not possible. To represent the respiration-dependent fluctuations, all parameters for the FlexiTrunk™ were determined not only with the real measured values but also with a smoothed pressure curve. For this purpose, a smoothed pressure curve with a moving average was calculated. This pressure curve corresponded more closely to the true pressure by which the curve fluctuated because of the air bubbles. The results obtained with the smoothed pressure curves are marked with an asterisk in Table 3. In Figure 2, the original measured values are shown in light gray and the fluctuations of the calculated pressure curve are shown in black. In the results given in the text, only the values of the smoothed pressure curve are considered.

Tidal volume was always measured directly in the lung simulator, regardless of whether the pressure measurement was taken in the nose or the device. For this reason, tidal volume was averaged over the measurements from both measurement points.

2.1 | Statistics

Descriptive statistics were performed to describe the characteristics of each device. All results are given as mean with standard deviation (SD). Differences in measurements between the two measurement points (in CPAP device and in the nose) were statistically analyzed using Wilcoxon's paired-samples test. In addition, the correlation between the amplitude of the respiratory cycle-dependent pressure fluctuations and the achieved tidal volume was calculated using Spearman's correlation and Pearson's correlation. A p value < 0.05 was considered statistically significant.

No animals or humans were involved in these experiments, and no ethical review was required.

3 | RESULTS

Averaged over all measured values, a tidal volume of 6.044 ml (±0.233) was achieved with the BabyFlow®. In the nose, breath-dependent pressure variations of 2.129 mbar (±0.226) on average

TABLE 2 Tabular summary of a test setup with CPAP device, prong size, and flow generator or ventilator with which flow was tested

CPAP device	Prong size	Ventilator/flow generator	Ventilation mode/setting	Expiratory valve	Set flow
BabyFlow®	Medium	fabian +nCPAP evolution	CPAP	fabian +nCPAP evolution	5 and 15 L/min
EasyFlow nCPAP	Medium	fabian +nCPAP evolution	CPAP	fabian +nCPAP evolution	5 and 15 L/min
FlexiTrunk™	BC4030	fabian +nCPAP evolution	O_2 therapy	Bubble CPAP system	5 and 15 L/min
Inspire nCPAP™	Small	fabian +nCPAP evolution	NCPAP (tube set: MediJet)	Two jets, no valve	Auto
Inspire rPAP™	Small	STAR	-	No jet, no valve	5 and 15 L/min
Medijet®	Medium	fabian +nCPAP evolution	NCPAP (tube set: InfantFlow)	One jet, no valve	Auto
Miniflow®	Medium	fabian +nCPAP evolution	CPAP	fabian +nCPAP evolution	5 and 15 L/min

Abbreviation: CPAP, continuous positive airway pressure; NCPAP, nasal continuous positive airway pressure.

TABLE 3 Measurement results of all individual measurements

			PEEP 5						PEEP 7						PEEP 9					
Device	Flow	Measuring point	*P*-end-exp (mbar)	±SD	ΔP-fluct (mbar)	±SD	V_t (ml)	±SD	*P*-end-exp (mbar)	±SD	ΔP-fluct (mbar)	±SD	V_t (ml)	±SD	*P*-end-exp (mbar)	±SD	ΔP-fluct (mbar)	±SD	V_t (ml)	±SD
BabyFlow	15 L/min	Nose	4.53	0.08	1.68	0.07	5.88	0.20	6.40	0.03	2.17	0.06	5.95	0.21	8.34	0.03	2.27	0.07	6.14	0.22
		Device	4.43	0.03	1.44	0.05			6.35	0.03	1.83	0.06			8.31	0.04	1.87	0.06		
	5 L/min	Nose	4.61	0.03	2.03	0.06	6.05	0.21	6.62	0.05	2.23	0.10	6.06	0.20	8.65	0.04	2.33	0.11	6.16	0.22
		Device	4.64	0.03	1.85	0.10			6.67	0.03	2.05	0.09			8.64	0.03	2.09	0.09		
EasyFlow nCPAP	15 L/min	Nose	5.47	0.04	1.82	0.06	5.96	0.19	7.38	0.03	2.24	0.08	6.04	0.21	9.29	0.04	2.32	0.08	6.21	0.21
		Device	4.57	0.06	1.33	0.08			6.51	0.07	1.77	0.08			8.34	0.10	1.82	0.10		
	5 L/min	Nose	4.94	0.05	1.96	0.08	6.20	0.23	6.88	0.04	1.83	0.07	6.27	0.21	8.90	0.03	1.82	0.09	6.36	0.21
		Device	4.87	0.05	1.68	0.08			6.83	0.06	1.54	0.08			8.81	0.04	1.54	0.08		
FlexiTrunk (*)	15 L/min	Nose	6.36	0.30	0.89	0.31	6.27	0.23	8.16	0.27	0.91	0.34	6.39	0.24	9.61	0.24	0.86	0.28	6.31	0.25
		Device	6.24	0.30	0.80	0.32			7.89	0.29	0.79	0.31			9.66	0.29	0.78	0.29		
	5 L/min	Nose	4.85	0.14	0.50	0.17	6.21	0.22	6.86	0.12	0.47	0.12	6.38	0.22	8.62	0.08	0.41	0.09	6.33	0.21
		Device	4.89	0.11	0.35	0.13			6.82	0.13	0.35	0.12			8.72	0.10	0.29	0.10		
FlexiTrunk	15 L/min	Nose	6.45	1.06	3.39	0.68	6.27	0.23	8.14	1.20	3.56	0.66	6.39	0.24	9.82	1.05	3.50	0.65	6.31	0.25
		Device	6.30	1.14	3.54	0.76			8.04	1.16	3.55	0.66			9.81	1.09	3.62	0.73		
	5 L/min	Nose	4.93	0.61	1.94	0.43	6.21	0.22	6.95	0.62	1.87	0.45	6.38	0.22	8.73	0.45	1.45	0.36	6.33	0.21
		Device	4.97	0.61	1.66	0.43			6.91	0.68	1.75	0.46			8.82	0.50	1.40	0.39		
Inspire nCPAP	According to PEEP	Nose	5.48	0.07	1.31	0.09	6.11	0.22	7.62	0.08	1.59	0.11	6.11	0.21	9.82	0.11	1.82	0.13	6.14	0.22
		Device	5.10	0.09	0.58	0.08			7.04	0.13	0.72	0.12			9.01	0.15	0.86	0.15		
Inspire rPAP	15 L/min	Nose	2.31	0.02	0.66	0.04	6.15	0.23	4.34	0.04	0.69	0.05	6.18	0.21	6.85	0.06	0.69	0.07	6.29	0.22
		Device	3.45	0.03	0.44	0.04			5.33	0.06	0.45	0.04			7.91	0.07	0.43	0.06		
	5 L/min	Nose	4.81	0.07	0.47	0.10	6.31	0.23	6.54	0.20	0.57	0.15	6.49	0.23	9.36	0.09	0.71	0.10	6.47	0.23
		Device	5.20	0.06	0.27	0.14			6.62	0.14	0.39	0.16			9.50	0.08	0.43	0.07		
Medijet	According to PEEP	Nose	5.26	0.12	3.02	0.18	5.60	0.20	7.47	0.13	3.49	0.19	5.56	0.19	9.54	0.18	3.91	0.23	5.48	0.22
		Device	5.36	0.11	2.86	0.16			7.60	0.13	3.33	0.17			9.69	0.20	3.73	0.24		
Miniflow	15 L/min	Nose	6.75	0.03	2.22	0.06	5.85	0.21	8.68	0.05	2.45	0.08	5.97	0.23	10.72	0.25	2.51	0.10	6.09	0.23
		Device	4.40	0.03	1.11	0.04			6.40	0.04	1.29	0.05			8.33	0.04	1.33	0.04		

(Continues)

TABLE 3 (Continued)

Device	Flow	Measuring point	PEEP 5					PEEP 7					PEEP 9				
			P-end-exp (mbar)	±SD	ΔP-fluct (mbar)	±SD	V_t (ml)	*P*-end-exp (mbar)	±SD	ΔP-fluct (mbar)	±SD	V_t (ml)	*P*-end-exp (mbar)	±SD	ΔP-fluct (mbar)	±SD	V_t (ml)	±SD
	5 L/min	Nose	4.44	0.04	2.29	0.08	5.90	6.32	0.04	2.65	0.10	5.86	8.14	0.03	2.92	0.11	5.94	0.22
		Device	4.59	0.02	1.50	0.06		6.65	0.04	1.72	0.08		8.69	0.03	1.93	0.09		

Abbreviations: ΔP-fluct, amplitude of inspiratory and expiratory pressure fluctuations; PEEP, positive end-expiratory pressure; *P*-endexp, end-expiratory pressure; SD, standard deviation; V_t, tidal volume.
(*) Results for a smoothed pressure curve calculated by moving average.

were observed. PEEP in the nose deviated on average by a total of −0.486 mbar (±0.130) from the set target value.

With EasyFlow nCPAP, the mean tidal volume was 6.175 ml (±0.251), nasal pressure fluctuations averaged 1.999 mbar (±0.221), and nasal PEEP deviated from the target by an average of 0.142 mbar (±0.245).

For the FlexiTrunk™, the average tidal volume was 6.313 ml (±0.238), pressure variations averaged 0.672 mbar (±0.320) in the nose, and PEEP deviated from the set point by an average of 0.411 mbar (±0.709) in the nose.

For the Inspire nCPAP™, the average tidal volume was 6.122 ml (±0.214), pressure variations averaged 1.578 mbar (±0.240) in the nose, and PEEP deviated from the set point by an average of −0.644 mbar (±0.162) in the nose.

For the Inspire rPAP™, the average tidal volume was 6.316 ml (±0.259), pressure variations averaged 0.631 mbar (±0.125) in the nose, and PEEP deviated from the set point by an average of −1.305 mbar (±1.242) in the nose.

For Medijet®, the average tidal volume was 5.550 ml (±0.209), pressure variations averaged 3.466 mbar (±0.416) in the nose, and PEEP deviated from the set point by an average of −0.419 mbar (±0.188) in the nose.

For Miniflow®, the average tidal volume was 5.934 ml (±0.230), pressure variations averaged 2.557 mbar (±0.262) in the nose, and PEEP deviated from the set point by an average of 0.316 mbar (±1.216) in the nose.

All measured values are listed in detail in Table 3. The measured mean values are shown as a graphical comparison in Figure 2.

Spearman's correlation between tidal volume and pressure variation in the nose was −0.964 ($p = 0.003$), and the Pearson correlation: −0.947 ($p = 0.001$). A graphical representation is shown in Figure 3.

All devices showed differences between in-device and in-nose measurements. Even small differences were statistically significant due to the high number of measurements and the precision of the uniform replicates. To be able to assess the respective relevance, these differences are shown graphically in Figure 2. All measured values and their statistical analysis are listed in Supporting Information: Supplement 1.

4 | DISCUSSION

The study was able to show that inspiratory and expiratory fluctuations occur in all the CPAP devices tested. The magnitude of the pressure fluctuations as well as the generated tidal volume differed between the devices. There was a significant correlation between increasing tidal volume and decreasing pressure fluctuations. These observations were consistent with the results of previous studies,[11] which also showed higher respiratory volumes in conjunction with lower pressure fluctuations. However, differences in comparison with previous literature were also observed, particularly in testings using the FlexiTrunk. In bubble CPAP testings

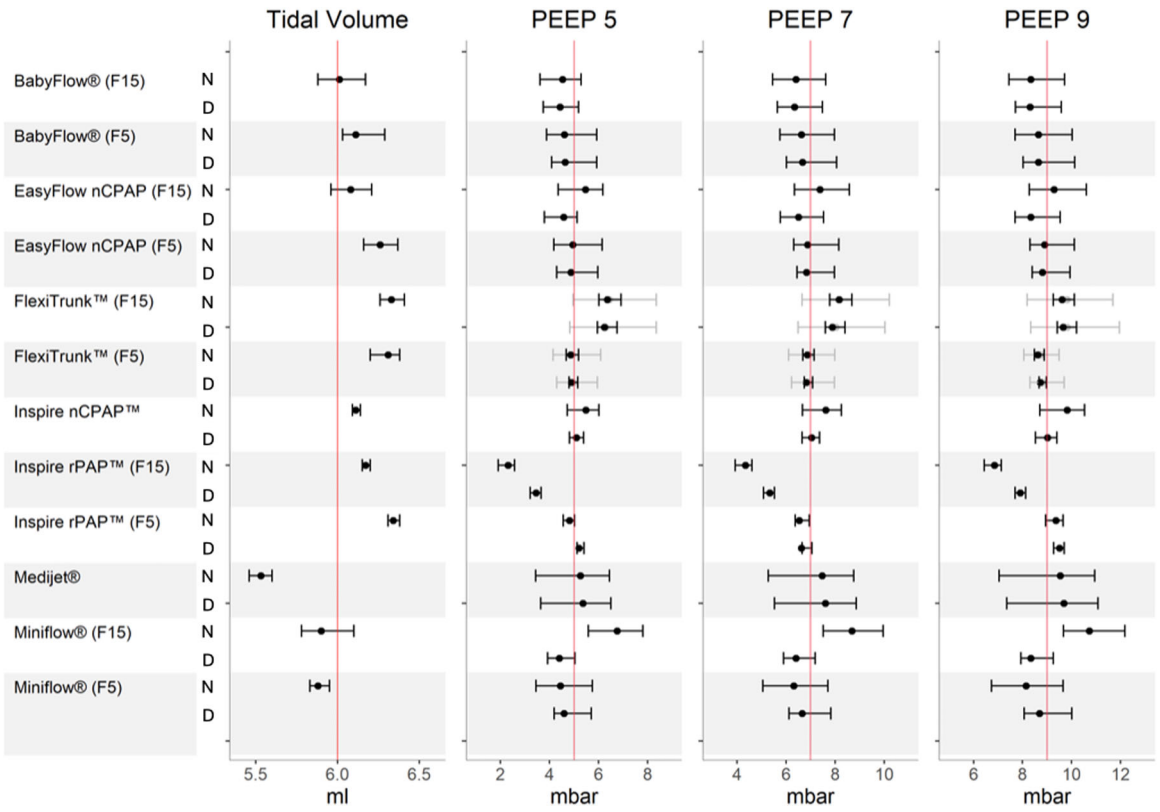

FIGURE 2 Graphical representation of the measured values at the pressure measurement point nose (N) or device (D). Tidal volume was averaged over all positive end-expiratory pressure (PEEP) values. The Forest plot shows the mean values and the scatter over all measurements. Forest plots of pressure measurements show the mean and inspiratory and expiratory pressure fluctuations. The scatter of the values has been omitted for the clarity of the plot. In the case of the FlexiTrunk™, the mean value and pressure fluctuations of the original pressure curve are shown in gray and those of the smoothed mean pressure curve in black. [Color figure can be viewed at wileyonlinelibrary.com]

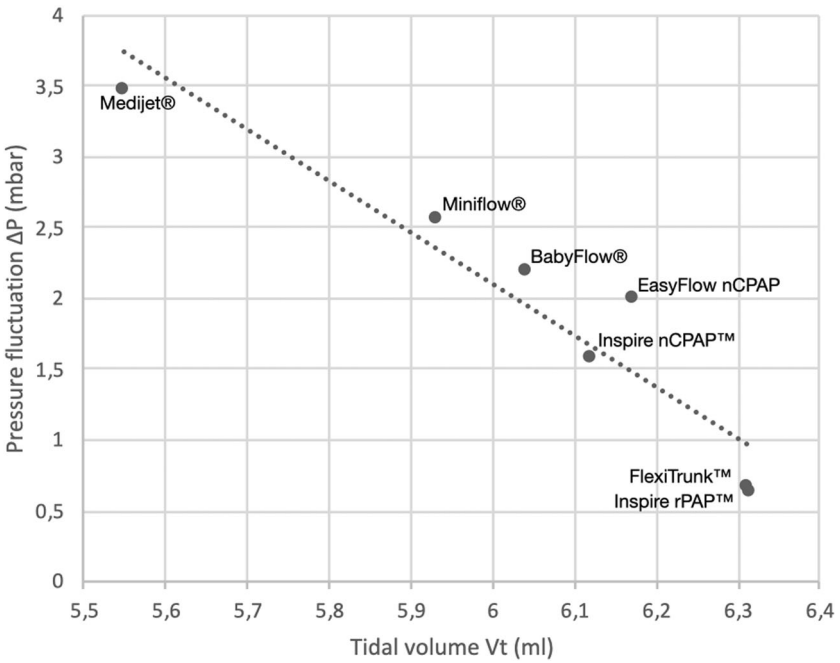

FIGURE 3 Graphical representation of the relationship between tidal volume and inspiratory and expiratory pressure fluctuations of the CPAP devices. For this graph, only the measurements in the nose were considered.

reported by Cook et al. and Drevhamar et al., higher amplitudes for pressure fluctuations and, correspondingly, lower tidal volumes were documented than were reported in the present study. Here, the FlexiTrunk™ showed very large tidal volumes with minimal pressure fluctuations. In terms of technical design, the FlexiTrunk™ is a classic constant-flow CPAP with constant respiratory gas flow and a rigidly adjustable expiratory valve. Similar results were demonstrated by the Inspire rPAP™ though this device utilizes neither jets nor an expiratory valve. In contrast, the Medijet®, which generates its pressure via jet, had the lowest tidal volume and the greatest pressure fluctuations. Breath-dependent pressure fluctuations were also comparable for the other devices tested. Overall, the results argue against the widely held belief that CPAP devices with jets generally have lower pressure fluctuations than CPAP devices operated with an expiratory valve.[3,12]

Fundamentally, the clinical impact of pressure fluctuations must be questioned. Despite numerous reports on the effects of pressure fluctuations on the work of breathing,[5,8,10] there is no clinical study that has examined the long-term outcome based on the CPAP device. From a physical perspective, it should be noted that if the pressure curve remains unchanged, any reduction in tidal volume will also result in a reduction in work of breathing. Therefore, to compensate for the lower tidal volume, one would have to assume that preterm infants exert more respiratory effort during larger pressure variations in the CPAP device. However, this is at odds with the findings of Bordessoule et al.,[13] who recorded the lowest respiratory effort on a Medijet®, the device with the largest pressure fluctuations in our study.

Leakage compensation could now be considered as an alternative quality criterion. This has also been considered a major advantage of jet CPAP devices since Moa et al.[4] Leakage compensation, like the compensation of breath-dependent pressure fluctuations, is based on the provision of an additional flow. This works directly through the jets in the Inspire nCPAP™ and the Medijet® for smaller leaks. In addition, the fabian +nCPAP evolution can increase the flow of breathing gas to compensate for larger leaks. FlexiTrunk™ with bubble CPAP system and the Inspire rPAP™ are always operated with excess flow due to their technical function, which can compensate for leaks. In the case of BabyFlow®, EasyFlow nCPAP, and Miniflow®, leakage compensation was carried out via the electronic control of the expiration valve in the fabian +nCPAP evolution. In principle, leakage compensation via flow adaptation would also work with these CPAP devices, which is also practiced by other ventilators in the market. Thus, all CPAP devices tested in this study basically had leakage compensation or were operated with it. For this reason, leakage compensation is not a unique feature of variable flow CPAP devices, which is why this study was conducted without leakage.

Another important observation in this study was the discrepancies between the set CPAP pressure value and the pressure measured in the nose in some devices. Differences of a few percentage points can be explained by measurement inaccuracies between individual measurement devices. However, this does not apply to the Miniflow® and Inspire rPAP™ devices when operating at 15 L/min. The differences between set and measured pressure values were far too great. The deviations can ultimately only be explained by flow resistances. Unlike all other devices, both the Inspire rPAP™ and the Miniflow® do not measure the pressure directly in the CPAP device. In the case of the Inspire rPAP™, the pressure is measured approximately 130 cm upstream of the actual CPAP device. With the Miniflow®, the pressure is measured approximately 10 cm behind the device. These distances seem to be of great importance if there is a very high flow rate reaching the area where the pressure is measured. Due to the flow resistance in the hose, there is a relevant pressure drop from or to the measuring point at high flow rates. However, because the Miniflow® is regulated by the ventilator, the actual pressure in the nose is higher than that recorded at the measurement point. With the Inspire rPAP™, there is no such electronic compensation; therefore, the pressure at the measurement point, and even more so, the pressure in the nose, is so far below the set pressure, at high flow in the PIP/PPV line. Hence, high flow should be avoided in these devices.

A limitation of this study is that the ventilators or flow sources used to operate the CPAP devices were not manufacturer-specific to the individual devices. However, in the case of the Inspire rPAP™, STAR is explicitly approved as a flow driver for this device, contains all of the required features required for operating the Inspire rPAP™, and is therefore expected to provide comparable pressure measurements to the manufacturer's driver when used with the device. Thus, it is not anticipated that the pressure loss problems observed during this study, when higher flows were administered, could be resolved by using an original driver. The same argument applies to the use of the Fabian +nCPAP evolution as the ventilator or flow driver in this study. This ventilator is equipped with preprogrammed modalities specific for Medijet® and Inspire nCPAP™, marking it as specifically compatible for these devices. The use of the Fabian +nCPAP evolution with the Babyflow®, EasyFlow nCPAP, and Miniflow® allowed for better comparison and analysis of pressure variations within each CPAP device. While it may be assumed that other ventilators or other flow generators could influence or control the CPAP devices differently, the physical characteristics of the CPAP devices are independent of the ventilator.

Another limitation of the study is that compliance was held constant at all PEEP levels. As a result, tidal volume also remained constant, regardless of the pressure level. Thus, the clinical effect of CPAP, namely, the improvement in compliance due to alveolar pre-expansion, could not be represented. This study focused on the physical characteristics of the CPAP devices and does not aim to assess clinical relevance. Thus, the rigidly held compliance has no bearing on the objective or results.

5 | CONCLUSION

Inspiratory and expiratory pressure fluctuations occur in all CPAP devices. The amplitude of the pressure fluctuations correlates with the tidal volume produced. The presence of a jet and subsequent

labeling as a variable CPAP device does not denote low-pressure fluctuations, nor does the possession of an expiratory valve signify high fluctuations. These values Depending on whether the pressure is measured in the inspiratory or expiratory tube and not directly in the nosepiece, the pressure reaching the patient's nose may deviate considerably from the regulated pressure.

AUTHOR CONTRIBUTIONS

All authors were actively involved in planning and conducting the study and in writing the paper.

ACKNOWLEDGMENTS

We would like to thank Natalee Annon-Eberharter for proofreading the paper as a native speaker and thus significantly improving it. This study was performed without financial support from companies or other donors. The individual CPAP devices were not provided by the respective companies specifically for this study. They are used for training purposes at workshops and were therefore available.

CONFLICT OF INTEREST

Martin Wald has been a consultant for the companies Fritz Stephan GmbH and medin Medical Innovations GmbH and has given paid lectures for Medtronic Österreich GmbH during the past 3 years. He has also organized workshops sponsored by the above companies. The remaining authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The raw data from the in vitro simulations are available upon request. Please contact the corresponding author.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Auer-Hackenberg L, Stroicz P, Hofstätter E, Brandner J, Haselmann C, Wald M. Breath-dependent pressure fluctuations in various constant- and variable-flow neonatal CPAP devices. *Pediatric Pulmonology*. 2022;57:2411-2419. doi:10.1002/ppul.26050