Comparison of Actual Performance in the Flow and Fraction of Inspired O₂ among Different High-Flow Nasal Cannula Devices: A Bench Study

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Academic Editor: Paola Pierucci

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Background. High-flow nasal cannula (HFNC) oxygen therapy has been recommended for use in coronavirus disease 2019 (COVID-19) patients with acute respiratory failure and many other clinical conditions. HFNC devices produced by different manufacturers may have varied performance. Whether there is a difference in these devices and the extent of the differences in performance remain unknown. Methods. Four HFNC devices (AIRVO 2, TNI softFlow 50, HUMID-BH, and OH-70C) and a ventilator with an HFNC module (bellavista 1000) were evaluated. The flow was set at 20, 25, 30, 35, 40, 45, 50, 60, 70, and 80 L/min, and the FiO₂ was set at 21%, 26%, 30%, 35%, 40%, 45%, 50%, 60%, 70%, 80%, and 90%. Then, one side of the cannulas was clipped to simulate the compression, bending, or blocking of the nasal cannulas. The flow and FiO₂ of the delivered gas were recorded and compared among settings and devices. Results. The actual-flow and actual-FiO₂ delivered by different settings and devices varied. AIRVO 2 had superior performance in flow and FiO₂ accuracy. bellavista 1000 and OH-70C had good performance in the accuracy of actual-flows and actual-FiO₂ respectively. bellavista 1000 and HUMID-BH had a larger flow range from 10 to 80 L/min, but only bellavista 1000 could provide a stable flow with an excessive resistance up to 60 L/min. TNI softFlow 50 had the best flow compensation and could provide sufficient flow with excessive resistance at 20–50 L/min. Conclusions. The variation in flow, FiO₂ settings, and devices could influence the actual-flow and actual-FiO₂ delivered. AIRVO 2 and OH-70C showed better FiO₂ accuracy. TNI softFlow 50, bellavista 1000, and HUMID-BH could lower the risk of insufficient flow support due to accidental compression or blocking of the cannulas. In addition, ventilators with HFNC modules provided comparable flow and FiO₂ and could be an alternative to standalone HFNC devices.

1. Introduction

High-flow nasal cannula (HFNC) oxygen therapy can deliver heated and humidified high-flow oxygenated gas via nasal cannulas with flow ranges from 10 to 80 L/min in adults depending on the manufacturer. Such flow can cover the physiological inspiratory flow needed by patients to achieve a stable fraction of inspired O₂ (FiO₂) of 21–100%. Previous studies have shown that HFNC therapy is easy to apply and prevents nasal epistaxis [1, 2]. In addition, HFNC therapy has multiple physiological advantages, including generating positive end-expiratory pressure (PEEP) [3], washing out dead space [4], decreasing inspiratory effort [3, 5], and improving lung volume and compliance [5]. Evidence suggests that HFNC therapy has some benefits in providing better oxygenation than conventional oxygen therapy (COT) [6, 7]. HFNC therapy could reduce intubation-related adverse events when used as a preoxygenation device [8]. In addition, HFNC therapy decreased the intubation rate but did not impact mortality in patients with acute hypoxemic respiratory failure [9]. Another study showed that HFNC therapy can reduce 90-day mortality compared with noninvasive ventilation (NIV) [10]. Among cardiothoracic surgery patients, compared with NIV, HFNC therapy did not result in a worse rate of reintubation [11]. HFNC therapy also reduced the reintubation rate compared
with COT after extubation in lower-risk respiratory failure patients [12]. A recent observational study showed that, in acute hypercapnic exacerbation of chronic obstructive pulmonary disease (AECOPD) patients, HFNC therapy was effective in improving the dyspnea score, gas exchange, and mucus production [13]. HFNC therapy is noninferior to NIV as initial ventilatory support for CO$_2$ clearance in mild-to-moderate AECOPD patients [14]. Recently, HFNC therapy has been recommended for use in coronavirus disease 2019 (COVID-19) patients with acute respiratory failure (ARF) [15].

Most of the previous studies in this field focused on exploring how parameter settings affect physiological effects, such as actual inhaled FiO$_2$ [16, 17], humidification [18–21], the PEEP effect [17, 22, 23], and dead space flushing [23–27], on cylinder or 3D-printed models and even human volunteers [28]. According to previous studies, flow plays a determinant role in the physiological effects of HFNC therapy. HFNC devices produced by different manufacturers may have varied performance, especially in terms of flow delivery. Few studies have compared different HFNC devices by the actual-flow and actual-FiO$_2$ at the cannulas. The degree of the difference among the manufacturers remains unknown, and therefore, it is meaningful to compare different devices. Furthermore, the results might provide clinicians with a deeper understanding of the difference among settings and devices to help select the most suitable equipment for the specific clinical condition.

2. Materials and Methods

2.1. Equipment and Instruments. Four HFNC devices (AIRVO 2, Fisher & Paykel Healthcare, Auckland, New Zealand; TNI softFlow 50, TNI Medical AG, Würzburg, Germany; HUMID-BH, RESPIRACARE, Shenyang, China; OH-70C, Microme, Hunan, China) and a ventilator with HFNC module (bellavista 1000, Intmedical, Buchs, Switzerland) were included and tested using their own breathing circuits, humidification chambers, nasal cannulas, and other accessories. Details are shown in Table 1.

The Medical Intensive Care Unit (MICU) of the West China Hospital provided the high-flow equipment.

A typical HFNC system comprises a flow generator, active heated humidifier, single-limb heated circuit, and nasal cannula [29]. The international standard for HFNC equipment, particularly the requirements for basic safety and essential performance of ventilatory high-flow therapy equipment (ISO/DIS 80601-2-90), is still under development by the International Organization for Standardization. The flow-generating mechanism and structure of these devices in this study are summarized in Table 2.

A VT PLUS HF gas flow analyzer (Fluke Biomedical) was used to measure the actual-flow rate of the gas delivered by HFNC devices. A MaxO$_2$ oxygen analyzer (Maxtec) was used to measure FiO$_2$. Beijing Aerospace Changfeng Co., Ltd. provided the instruments mentioned above.

2.2. Preparations. A specially designed adapter in Figure 1 helps to measure the parameters directly from the interface. Two 6 × 4 PU tubes provide ports for nasal cannulas and standardize the different diameters of different interfaces. The 22 mm cap allows attachment to different measuring instruments. This structure does not change the direction of the flow. Thus, the measuring instruments can record the most real performance of these HFNC devices.

For FiO$_2$ measurement, cannulas were attached to a conventional ventilation limb, and a sampling tube allowed a small flow of delivered gas to pass through the oxygen analyzer. As Figure 1 shows, tests were performed separately because sampling for FiO$_2$ measurement can produce a side flow that may affect the flow measurement.

Tests were performed in a ward of the Medical Intensive Care Unit, West China Hospital. The environmental temperature was controlled during the test procedure. Any equipment that might influence the testing was removed from the room. All HFNC devices and measuring instruments were adequately preheated and calibrated before testing.

2.3. Protocol. All the testing processes were repeated three times for FiO$_2$ testing and twice for flow testing at different times to reduce disturbance from possible environmental changes and avoid contingency.

HFNC devices were set at 31°C, and the MR850 heated humidifier was set in noninvasive mode. As excess water vapor would affect the accuracy of the VT PLUS gas flow analyzer and MaxO$_2$ oxygen analyzer, no water was added to the humidification chamber during FiO$_2$ and flow measurements.

The flow was set at 20, 25, 30, 35, 40, 45, 50, 60, 70, and 80 L/min depending on their maximum flow, which was named set-flow. At each level of set-flow, the FiO$_2$ was set at 21%, 26%, 30%, 35%, 40%, 45%, 50%, 60%, 70%, 80%, and 90%, which was named set-FiO$_2$.

The FiO$_2$ and flow rate of the delivered gas from the cannulas were named actual-FiO$_2$ and actual-flow, respectively. For each setting combination, after stabilization for 1 min, the actual-FiO$_2$ and actual-flow were recorded 3 times at an interval of 10 seconds. Then, one side of the cannulas was clipped to increase the resistance of the nasal cannulas. After another 1 min of stabilization, the clipped-flow was recorded in the same way to estimate the ability to provide sufficient flow under extreme situations.

2.4. Statistical Analysis. Normally distributed variables are expressed as the mean ± SD, and nonnormally distributed variables are expressed as the median (interquartile range). The Kruskal–Wallis H test was used to compare the effect of different set-FiO$_2$ on actual-flows and set-flows on actual-FiO$_2$ in a single device. We also used the Kruskal–Wallis H test to compare the actual parameters in different devices under the same settings. The Wilcoxon signed rank test was
Table 1: Details of HFNC devices.

<table>
<thead>
<tr>
<th>Devices</th>
<th>Heated humidifier</th>
<th>Temperature setting</th>
<th>Humidification chamber</th>
<th>Breathing circuit</th>
<th>Nasal cannulas</th>
<th>Flow setting (range, minimum increment)</th>
<th>FiO₂ setting</th>
</tr>
</thead>
<tbody>
<tr>
<td>TNI SoftFlow 50</td>
<td>Built-in</td>
<td>30, 31, 32, 33, 34, 35, 36, 37°C</td>
<td>INTERSURGICAL AF2310</td>
<td>TNI SoftFlow applicator clinic (large)</td>
<td>TNI SoftFlow applicator clinic (large)</td>
<td>10–50 L/min, 0.5 L/min</td>
<td>Oxygen flowmeter (21–100%, 1%)</td>
</tr>
<tr>
<td>AIRVO 2</td>
<td>Built-in</td>
<td>31, 34, 37°C</td>
<td>Fisher &amp; Paykel MR290</td>
<td>900PT501 tube</td>
<td>F&amp;P optiflow OPT844 (medium)</td>
<td>10–25 L/min, 1 L/min; 25–60 L/min, 5 L/min</td>
<td>Oxygen flowmeter (21–100%, 1%)</td>
</tr>
<tr>
<td>HUMID-BH</td>
<td>Built-in</td>
<td>31, 34, 37°C</td>
<td>RESPIRACARE NAC-1 M</td>
<td>AIRT-B1-III</td>
<td>RESPIRACARE autofill humidification chamber HC-B1</td>
<td>10–40 L/min, 1 L/min; 40–80 L/min, 5 L/min</td>
<td>Oxygen flowmeter (21–100%, 1%)</td>
</tr>
<tr>
<td>OH-70C</td>
<td>Built-in</td>
<td>31, 32, 33, 34, 35, 36, 37°C</td>
<td>Flexicare Veoflo High-Flow Nasal Cannula (small)</td>
<td>Micomme H-180</td>
<td>INTERSURGICAL AF2310</td>
<td>10–25 L/min, 1 L/min; 25–70 L/min, 5 L/min</td>
<td>Software setting (21–100%, 1%)</td>
</tr>
<tr>
<td>Bellavista 1000</td>
<td>Built-in</td>
<td>31, 32, 33, 34, 35, 36, 37°C</td>
<td>INTERSURGICAL AF2310</td>
<td>INTERSURGICAL HFOT single-limb circuit</td>
<td>Nasal cannula</td>
<td>2–80 L/min, 1 L/min</td>
<td>Software setting (21–100%, 1%)</td>
</tr>
</tbody>
</table>

Note: aAir supply may be responsible for flow accuracy. bOxygen supply would affect the FiO₂ accuracy. Flowmeters cannot provide enough oxygen flow when higher FiO₂ at high-flow levels is needed. cChanges in settings would alter the input air and oxygen flow or pressure, which will challenge the air-oxygen mixer and cause an inaccurate output. dThe FiO₂ monitor influences the FiO₂ accuracy.

Table 2: The structure and mechanism differences among devices.

<table>
<thead>
<tr>
<th>Devices</th>
<th>Air supply</th>
<th>Oxygen supply</th>
<th>Air-oxygen mixer</th>
<th>FiO₂ monitor</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIRVO 2</td>
<td>Integrated turbines</td>
<td>Low-pressure oxygen supply from separated oxygen flowmeters</td>
<td>Manually adjusts oxygen flow to titrate the aimed FiO₂ based on monitored or calculated FiO₂ in real time</td>
<td>Ultrasonic oxygen analyzer</td>
</tr>
<tr>
<td>TNI SoftFlow 50</td>
<td>Wall supply</td>
<td>Wall supply</td>
<td>Proportional valves</td>
<td>Not mentioned in public information</td>
</tr>
<tr>
<td>HUMID-BH</td>
<td>Wall supply</td>
<td>Oxygen flowmeter (21–100%, 1%)</td>
<td>FiO₂ monitor</td>
<td></td>
</tr>
<tr>
<td>OH-70C</td>
<td>Wall supply</td>
<td>Oxygen flowmeter (21–100%, 1%)</td>
<td>FiO₂ monitor</td>
<td></td>
</tr>
<tr>
<td>Bellavista 1000</td>
<td>Wall supply</td>
<td>Oxygen flowmeter (21–100%, 1%)</td>
<td>FiO₂ monitor</td>
<td></td>
</tr>
</tbody>
</table>

Note: aAir supply may be responsible for flow accuracy. bOxygen supply would affect the FiO₂ accuracy. Flowmeters cannot provide enough oxygen flow when higher FiO₂ at high-flow levels is needed. cChanges in settings would alter the input air and oxygen flow or pressure, which will challenge the air-oxygen mixer and cause an inaccurate output. dThe FiO₂ monitor influences the FiO₂ accuracy.

Figure 1: Continued.
used to compare differences between settings and actual parameters. The analysis mentioned above can help us to learn the output accuracy of each tested device. The Wilcoxon rank test was used to compare actual-flows with clipped-flows at the same settings to show the effect of increased resistance (clipping one side of the cannulas) on actual-flows in each device.

All statistical tests were 2-sided, and $P < 0.05$ was considered statistically significant. All statistical analyses were performed using IBM SPSS statistical software version 23 for Windows.

3. Results and Discussion

3.1. Flow

3.1.1. Difference between Actual-Flows and Set-Flows in a Single Device and Different Devices. As Figure 2(a) shows, there were significant differences between the actual-flows and the corresponding set-flows in all five devices at most set-flow levels ($P < 0.001$). AIRVO 2 had the minimum difference between actual-flows and set-flows among the five devices (Figure 2) (Table 3).

3.1.2. Influence of Set-FiO2 on Actual-Flows in a Single Device. The influence of different settings on actual-flows in different devices is demonstrated in Supplemental Table 1 and Figure 2. An increase in set-FiO2 caused a significant increase in actual-flow at all set-flow levels in TNI softFlow 50, OH-70C, HUMID-BH, and bellavista 1000 ($P < 0.001$) but not AIRVO 2. For AIRVO 2, when set-flows were fixed at 20 and 25 L/min ($P = 0.99$ and 0.5), there was no statistically significant change in actual-flow, while set-FiO2 increased (Figure 2(b); Table 3). Another interesting finding was that changes in set-FiO2 influenced the actual-flow more significantly at higher set-flows in AIRVO 2 and TNI softFlow 50 (Figures 2(b) and 2(c)).

3.1.3. Difference between Actual-Flows and Clipped-Flows in a Single Device and Different Devices. There were significant differences in actual-flow before and after one side of the cannulas was clipped at any set-flow levels in all devices ($P < 0.001$) but not TNI softFlow 50. The flow change rate was defined as the change in flow after one side of the cannula was clipped and calculated as the actual-flow minus the clipped-flow and then divided by the actual-flow. Notably, TNI softFlow 50 had the best ability to provide the desired flow (flow change rate $\leq 0.28\%$) and could almost fully compensate for the flow at various levels of set-flow (20–50 L/min) (Table 4).

When the resistance increased by clipping one side of the cannulas, all five devices could provide a stable flow (flow change rate smaller than 10%) at low set-flow levels but presented different compensatory abilities at higher set-flow levels (Figure 3). When the set-flow was higher than 40 L/min, the flow change rate increased significantly.

3.2. FiO2

3.2.1. Difference between Actual-FiO2 and Set-FiO2 in a Single Device and Different Devices. The influence of different settings on actual-FiO2 in different devices is demonstrated in Supplemental Table 2. There was a significant difference between the actual-FiO2 and set-FiO2 in all five devices at all set-flow levels ($P < 0.05$ for all), except for AIRVO 2 at 30% ($P = 0.717$) (Figure 4). In addition, the actual-FiO2 values of different devices presented significant differences at all set-FiO2 levels ($P < 0.001$). Figure 4(a) and Table 5 show that the actual-FiO2 of AIRVO 2 were the closest to the set-FiO2, while the actual-FiO2 of the other four devices were lower or higher.

3.2.2. Influence of Set-Flow on Actual-FiO2 in a Single Device. Actual-FiO2 of AIRVO 2, TNI softFlow 50, and HUMID-BH showed a trend that, with the increase in set-FiO2 and set-flow, the difference between the actual-FiO2 and set-FiO2 became greater (Figures 4(b), 4(c), and 4(e)). Another interesting point was that the actual-FiO2 of these devices were less affected by set-flows at several specific set-FiO2 levels (Table 5).
Figure 2: The flow deviation at different set-flow levels in five devices (a). Flow deviation at different set-FiO₂ levels when set at different set-flow levels in AIRVO 2 (b), TNI softFlow 50 (c), OH-70C (d), HUMID-BH (e), and Bellavista 1000 (f). The flow deviation equals the actual-flow minus the corresponding set-flow.
3.3. Discussion.

- This study provides new insights into the changes and quantitative analysis of the actual output of each device under different settings. Among the five devices evaluated, the variation in flow settings, FiO2 settings, and devices can influence the actual flow and actual-FiO2 delivered. The following points were obtained:

1. There were significant differences between the actual and set values of flow and FiO2. Chikata et al. tested Optiflow (Fisher & Paykel Healthcare) and found a similar trend: as the set-FiO2 increased, the differences between the actual-FiO2 and the set-FiO2 increased [16]. When set-FiO2 was fixed, changes in set-flow would also affect the actual-FiO2. The air-oxygen mixer might be the reason behind the influence of different FiO2 values on the actual-flow and vice versa and the deviation of the measured flow and FiO2 with the set-flow and FiO2. Changes in settings would alter the input flow or the air and oxygen pressure, which will challenge the air-oxygen mixer and cause an inaccurate output. The variation in oxygen flow below a certain threshold (decided by the accuracy of the built-in flow sensor and algorithm) might not trigger the adjustment of the air flow, resulting in the deviation of the final flow output.

2. TNI softFlow 50, bellavista 1000, and HUMID-BH showed a better ability to provide the desired flow when the resistance abnormally increased. Although the adjustment process was a complex systematic work, the performance of the turbine was the main determining factor.

3. AIRVO 2 had the best performance in the accuracy of actual-flow and actual-FiO2. In addition to the air-oxygen mixer factor discussed above, the difference in the FiO2 titration target can also partly explain the different performances of FiO2 accuracy in manual adjustment devices (AIRVO 2, TNI softFlow 50, and HUMID-BH). In AIRVO 2, the real-time FiO2 and flow were measured by an ultrasonic oxygen analyzer, which formed a feedback regulation and achieved the best accuracy. If the real-time FiO2 is calculated by the flow of oxygen and air, the concentration of oxygen supply, which is considered to be 100% but usually is not, may cause a deviation in FiO2 output. The sensitivity and vulnerability of the oxygen analyzers might also account for the difference between the actual-FiO2 and the set-FiO2. Dai et al. [30] found that there was no significant difference in actual-FiO2 and actual-flow between AIRVO 2 and HUMID-BH under various test conditions. However, in Dai's study, FiO2 in both devices was titrated according to the oxygen analyzer (OxiQuant B, Envitec Corporation) at the end of the heated circuit.

4. Bellavista 1000, a ventilator with a built-in high-flow module, performed well in flow accuracy and was secondary to AIRVO 2. From the structure point, ventilators have the same or even a more advanced high-flow generator and air/oxygen mixing equipment as standalone HFNC devices. Ventilators with HFNC modules could provide comparable flow and FiO2 and be an alternative to standalone HFNC devices.

Bench evaluation in clinical conditions provides an informative way to assess the actual performance of HFNC devices. The difference in measured flow and FiO2 with set values might mislead clinicians to overestimate or underestimate the patient’s condition. The clinical consequences of these differences cannot be ruled out and need to be considered. More bench and clinical studies are needed to determine and quantify the degree and consequences of these differences. Increasing the number of devices tested, improving the airway models in bench studies, or conducting clinical tests in healthy volunteers or representative patients are important. However, though clinical studies can make the testing of a wide range of flow and FiO2 levels on

Table 3: Characteristics of the actual-flow in five devices.

<table>
<thead>
<tr>
<th>Devices</th>
<th>Flow deviation (L/min)</th>
<th>Effect of set-FiO2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≤40 L/min</td>
<td>45–60 L/min</td>
</tr>
<tr>
<td>AIRVO 2</td>
<td>−0.2 (−0.8, 0.3)</td>
<td>−0.9 (−3.6, 0.1)</td>
</tr>
<tr>
<td>Bellavista 1000</td>
<td>−0.7 ± 0.848</td>
<td>−1.4 (−2.2, −0.3)</td>
</tr>
<tr>
<td>TNI softFlow 50</td>
<td>1.3 (0.8, 2.3)</td>
<td>1.2 (0.8, 2)</td>
</tr>
<tr>
<td>HUMID-BH</td>
<td>−1.6 (−2.4, −0.9)</td>
<td>−2.7 (−6.7, −1.6)</td>
</tr>
<tr>
<td>OH-70C</td>
<td>4.4 (3.9, 5.2)</td>
<td>5.7 (5.1, 7.1)</td>
</tr>
</tbody>
</table>

The data are presented as the median (IQR) and mean ± SD. The flow deviation equals the actual-flow minus the corresponding set-flow.

Table 4: Characteristics of the flow change rate in five devices.

<table>
<thead>
<tr>
<th>Devices</th>
<th>Flow change rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≤35 L/min</td>
</tr>
<tr>
<td>TNI softFlow 50</td>
<td>0 (−0.3, 0)</td>
</tr>
<tr>
<td>Bellavista 1000</td>
<td>3.9 (3.6, 4.1)</td>
</tr>
<tr>
<td>HUMID-BH</td>
<td>6.9 (4.2, 10.2)</td>
</tr>
<tr>
<td>OH-70C</td>
<td>5.8 (4.1, 8.6)</td>
</tr>
<tr>
<td>AIRVO 2</td>
<td>8.3 (7.1, 9.9)</td>
</tr>
</tbody>
</table>

The data are presented as the median (IQR). The flow change rate refers to the change in flow after one side of the cannula is clipped.
Figure 3: Changes in flow after clipping in different devices. (a) Flow change rate in five devices. (b) Clipped-flow deviation in five devices. The flow change rate was calculated as the actual-flow minus the clipped-flow and then divided by the actual-flow. Clipped-flow deviation equals clipped-flow minus the corresponding set-flow.

Figure 4: Continued.
Figure 4: The FiO2 deviation at different set-FiO2 levels in five devices (a). The FiO2 deviation at different set-flow levels when set at different set-FiO2 levels in AIRVO 2 (b), TNI softFlow 50 (c), OH-70C (d), HUMID-BH (e), and bellavista 1000 (f). The FiO2 deviation equals the actual-FiO2 minus the corresponding set-FiO2.

Table 5: Characteristics of actual-FiO2 in five devices.

<table>
<thead>
<tr>
<th>Devices</th>
<th>≤40% FiO2 deviation (%)</th>
<th>45%–50% FiO2 deviation (%)</th>
<th>&gt;50% FiO2 deviation (%)</th>
<th>Effect of set-flow</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIRVO 2</td>
<td>–0.4 (–0.8, –0.1)</td>
<td>–0.6 (–0.9, –0.1)</td>
<td>–1.4 (–2, –0.8)</td>
<td>Best accuracy at 40 L/min&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>TNI softFlow</td>
<td>–1 (–1.2, –0.7)</td>
<td>–1.5 (–1.7, –1.3)</td>
<td>–2.8 (–4, –2.4)</td>
<td>No effect at 26%, 30%, and 50%; cannot reach higher FiO2 at high-flow levels&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>OH-70C</td>
<td>0.3 (–0.7, 1.5)</td>
<td>–1.7 (–2, –1.4)</td>
<td>–2.4 (–2.7, –2.2)</td>
<td>Best accuracy at 35&lt;sup&gt;d&lt;/sup&gt;; effect increased at 60–70 L/min</td>
</tr>
<tr>
<td>Bellavista 1000</td>
<td>0.9 (0, 1.6)</td>
<td>2.5 (1.9, 3)</td>
<td>2.6 (2.1, 3.5)</td>
<td>Minor effect at 26%&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
<tr>
<td>HUMID-BH</td>
<td>–0.9 (–1.6, –0.5)</td>
<td>–3 (–4.1, –2.5)</td>
<td>–5.9 (–6.8, –5)</td>
<td>Varied effect with no obvious pattern</td>
</tr>
</tbody>
</table>

<sup>a</sup> The data are presented as the median (IQR). The FiO2 deviation equals actual-FiO2 minus the corresponding set-FiO2. When the set-flow rate was 40 L/min and set-FiO2 was 26%, 35%, 40%, 60%, and 70% (P < 0.488, 0.857, 0.322, 0.372, respectively), actual-FiO2 was not significantly different from the corresponding set-FiO2. When set-FiO2 was fixed at 26%, 30%, and 50%, actual-FiO2 under different set-flows had no significant difference in TNI softFlow 50 (P = 0.700, 0.155, 0.166). The control system of TNI softFlow 50 stopped the rising process, triggering the "oxygen flow is too high" alarm. The alarm cannot be eliminated until the oxygen flow is lowered. When set-FiO2 was 35%, most of actual-FiO2 at varied set-flows were not significantly different compared with set-FiO2 (P = 0.439, 0.833, 0.103, and 0.37 for set-flow = 20, 25, 30, and 60 L/min, respectively). When set-FiO2 was 26%, most of actual-FiO2 at varied set-flows were not significantly different compared with set-FiO2 (P = 0.37, 0.37, 0.857, and 0.713 for set-flow = 20, 25, 50, 60, and 70 L/min, respectively).
the same patient more applicable in the clinical setting, it would be ethically questionable to do so.

Finally, FiO₂ monitoring and feedback regulation are recommended for future HFNC devices. This technique ensures the output accuracy and improves the reliability and safety of the treatment based on our results in AIRVO 2.

There are several limitations in this study. First, there were unavoidable individual differences in the devices we evaluated. There were inevitable possible sample differences in the same model and manufacturer as well. Second, we did not use water for all devices, which was not representative of the clinical use of HFNC devices. The gas was heated but not humidified, and how the absence of humidification and water vapor affected the testing results remains unknown. Future studies are needed to investigate this influence. All the tests were performed at 31°C, and no water was added to achieve accurate flow measurements and minimal equipment aging. According to the ideal gas equation, the measured flow may be higher in actual scenes at high setting temperatures. Third, the environmental temperature and humidity in the ward might affect the results.

4. Conclusions

The variation in flow, FiO₂ settings, and devices can influence the actual-flow and actual-FiO₂ delivered. The clinical consequences of the deviation cannot be ruled out and need to be considered. AIRVO 2 and OH-70C showed better FiO₂ accuracy. TNI softFlow 50, bellavista 1000, and HUMID-BH could lower the risk of insufficient flow support due to accidental compression, bending, or blocking of the nasal cannulas. Ventilators with HFNC modules could provide comparable flow and FiO₂ and be an alternative to standalone HFNC devices.

Data Availability

The data used to support the findings of this study are included within the supplementary information files.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors’ Contributions

Yuyan Zhou and Zhong Ni contributed equally to this study.

Acknowledgments

The authors would like to thank Dr. Li Ling (Chinese Evidence-Based Medicine Center, West China Hospital, Sichuan University) for valuable advice regarding methodology. The instruments used for the measurement of all the devices, including a VT PLUS HF gas flow analyzer (Fluke Biomedical) and MaxO₂ oxygen analyzer (Maxtec), were provided by Beijing Aerospace Changfeng Co., Ltd.

Supplementary Materials

Supplemental Table 1: effects of set-flow, set-FiO₂, and devices on actual-flow. Supplemental Table 2: effects of set-flow, set-FiO₂, and devices on actual-FiO₂. (Supplementary Materials)

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