PAPER • OPEN ACCESS

The comparison of two exhaled nitric oxide analyzers: NIOX VERO and SUNVOU-CA2122

Journal of Breath Research

PAPER

The comparison of two exhaled nitric oxide analyzers: NIOX VERO and SUNVOU-CA2122

Wei Lei[1,2] , Fei Li[1,2], Xiao-miao Tang[1,2], Shuang Bian[1], Jia-jia Wang[1] and Jian-an Huang[1]

[1] Department of Pulmonary and Critical Care Medicine, The First Affiliated Hospital of Soochow University, Suzhou, Jiangsu Province 215006, People's Republic of China
[2] These authors contributed equally to this work.

E-mail: huang_jian_an@163.com

Abstract

As a marker of eosinophilic airway inflammation, fractional exhaled nitric oxide (FeNO) was widely used in clinical practice. NIOX VERO (VERO) and SUNVOU-CA2122 (CA2122) are two commonly used eNO analyzers in China. However, what's the difference and agreement between the two devices and whether the two types of devices can be replaced by each other in the application of common respiratory diseases have not been reported. The purpose of this study was to compare the two types of devices and to evaluate the difference between them in clinical use and whether they could be replaced. FeNO levels in 244 respiratory patients (including asthma, chronic obstructive pulmonary disease, chronic cough) were measured by CA2122 analyzer and VERO analyzer, respectively. The FeNO values obtained by the two devices were compared and the differences were analyzed. The success rate, the number of attempts and the total time required for a successful measurement by CA2122 and VERO were compared. The FeNO values measured by CA2122 online and offline were also compared. FeNO values obtained by CA2122 were slightly higher than those of VERO [median(range): 29.0(9–271) parts per billion (ppb) vs 25.5 (5–263) ppb, $P = 0.000$]. There was a high correlation between FeNO values measured by the two types of devices ($r = 0.964$, $P = 0.000$). By comparison, there was a high degree of agreement between the FeNO values measured by two devices, in all patients with different respiratory diseases. FeNO values measured online and offline by CA2122 were highly correlated and there was a high degree of agreement between online and offline methods. The success rate of CA2122 was higher than VERO, and the number of attempts (2.1 vs 2.4) and the total time (110.5 ± 35.7 vs 117.5 ± 48.1 s) required for a successful measurement by CA2122 were lower than those of VERO. CA2122 and VERO can be replaced by each other, and FeNO values can be converted if necessary. CA2122 has some advantages in success rate, the mean attempts and time required for successful measurement of FeNO.

1. Background

Fractional exhaled nitric oxide (FeNO), as an indicator of airway inflammation, can well reflect the degree of airway eosinophil inflammation and judge the responsiveness of corticosteroid therapy. It can be used not only in the diagnosis and management of asthma, but also in the etiology diagnosis and differentiation of chronic cough. In addition, it has certain application value in the respiratory system diseases such as chronic obstructive pulmonary disease (COPD), pulmonary hypertension, interstitial lung disease, obstructive sleep apnea, primary ciliary dyskinesia, and even in the researches of respiratory effects of environmental exposures [1–11].

FeNO measurement has the advantages of quantitative, noninvasive, simple, practical, and safe. Currently, there are two main equipment manufacturers for the measurement of FeNO in China: NIOX VERO (Aerocrine, Sweden, manufacturers homepage: www.niox.com) and SUNVOU-CA2122 (SUNVOU, China, manufacturers homepage: www.sunvou.com), both equipment are handheld devices. The clinical application of NIOX VERO

(VERO) is earlier and has been recognized by many countries, while SUNVOU-CA2122 (CA2122) is relatively late in clinical application. At present in China, VERO can only measure FeNO online, while CA2122 can measure FeNO online as well as offline. Although there have been studies comparing the consistency of FeNO measured by CA2122 and VERO, the limitation lies in that all the subjects were asthmatic patients. Thus, it was still not clear how consistent the two instruments were in other respiratory diseases [12]. Online and offline consistency comparisons of other instruments had been reported in some previous studies [13, 14]. However, there were still no reports concerning the consistency between the offline FeNO and online FeNO measured by CA2122 until now.

The purpose of this study is to explore the consistency of CA2122 and VERO by randomized controlled study, including the following points: (a) whether the data of FeNO measured online by two kinds of equipment are consistent; (b) whether the data of FeNO measured online and offline is consistent; (c) whether the time consumed in the measurement process is the same; (d) whether the number of attempts needed for the measurement success and the success rate are the same.

2. Methods

2.1. Subjects
This study was conducted with patients who took FeNO measurement in our hospital from March 2018 to February 2019. Patients who had previously undergone the FeNO test were not enrolled in the study. According to the age of the subjects, the subjects are divided into six groups, namely <30 years old, 30–39 years old, 40–49 years old, 50–59 years old, 60–69 years old, and ⩾70 years old. Each age group includes ⩾30 subjects as the study objects according to their gender. Informed consent was signed by all patients prior to the study.

2.2. Study methods
FeNO values of each patient were measured by two kinds of equipment, and the sequence of measurement was assigned randomly. The interval between the two measurements should be at least 30 s.

2.3. FeNO measurement
CA2122 was calibrated by two standard gases with NO concentration of 60 ppb (parts per billion) and 250 ppb before the research. The calibration error met the technical requirements of the product (error <3 ppb or <10%). VERO had been calibrated before leaving the factory according to the manufacturer's instructions, as a result there was no need to use standard gas calibration during clinical use. The environment (temperature, atmospheric pressure,

humidity, etc) during measurement remained the same for all subjects.

FeNO measurements were performed strictly according to the technical standards published by ATS and ERS [2, 15]. Patients were abstained from foods, drinks, and alcohol for 1 h before the test, meanwhile smoking and vigorous exercise were forbidden. For patients who needed to have a pulmonary function test, they should take FeNO test first and then the pulmonary function test. Drugs used to treat coughs over the past 3 d were recorded. Before the test, the operator would explain the procedure and precautions to the subjects, consult and fill in the information of subjects. No more than five exhalations were taken for each subject, and if not, further attempts were abandoned and recorded as test failure.

CA2122: (a) Online: subjects were informed to inhale through a nitric oxide filter and exhale via a mouthpiece at constant flow rate of 50 ml s^{-1} for 10 s. Results were displayed after 70 s of analysis. The FeNO results were recorded in ppb. (b) Offline: Samples were obtained using the FeNO offline collection kit. Subjects were informed to inhale through a nitric oxide filter and exhale via a mouthpiece (sample was collected when expiratory flow rate reached 50 ml s^{-1}). After sampling finished, the sample bag was removed from the kit and connected it with the analyzer. Results were displayed after 70 s of analysis. The FeNO results were recorded in ppb. Offline measurement was taken after the online measurement.

VERO: The subjects took the sitting position, hold the inspiratory filter, exhaled the residual air, covered the mouth with the filter to inhale, inhaled first according to the test requirements, and then exhaled immediately to keep the exhalation flow rate at 50 ml s^{-1} (control the exhalation flow rate according to the prompts of the test interface), and started the automatic test and analysis after the exhalation meeting the requirements. Recorded after the results were displayed.

2.4. Statistical analysis
SPSS version 22.0 analysis software was used for data processing. For continuous variables, Kolmogorov–Smirnov normal test was performed. The data of normal distribution were expressed as mean ± standard deviation and analyzed by one-way ANOVA test. The data of non-normal distribution were expressed as median (interquartile range) and tested by nonparametric test. The difference of FeNO values measured by CA2122 and VERO in this study was compared by Wilcoxon test ($P < 0.05$ indicate significant difference).

The Pearson correlation analysis was carried out after the logarithm transformation of FeNO values measured by two devices. An equation to convert values was calculated by linear regression analysis. The agreement between the devices was evaluated

by Bland–Altman plots [16, 17]. According to the guideline published by ATS in 2011, clinically significant change in FeNO was >10 ppb (or 20%). So, the differences of <10 ppb for measured FeNO values of <50 ppb and of <20% for FeNO values ⩾50 ppb were considered within tolerance limits [18].

3. Results

3.1. Participants
A total of 287 outpatients participated in the study. Two hundred forty-four subjects successfully completed the FeNO measurement with two instruments. The basic information of 244 subjects was shown in table 1.

3.2. Device comparison
3.2.1. Agreement of FeNO values measured by two devices
For 244 subjects who finished measurements with both devices, FeNO values measured by CA2122 was significantly higher than VERO ($p < 0.001$, figure 1(A)), with median levels of 29.0 ppb (range: 9–271 ppb) and 25.5 ppb (range: 5–263 ppb), respectively. The range of difference between the two devices was −41–31 ppb (median: 2.0 ppb).

There was a strong positive correlation between FeNO values measured by two devices (Spearman correlation coefficient: $r = 0.929$, $p < 0.001$; figure 1(B)).

The Bland–Altman plot showed a moderate degree of agreement, with a mean difference of 2.6 [95% confidence interval (CI): −13.8 ∼ 19.0] (figure 1(C)). There were 17 (7.0%) values outside the 95% CI. Within the 95% CI, the absolute value of the difference was up to 16 ppb (VERO:76 ppb, CA2122: 91 ppb), 19% of the average value, which within the tolerance limits.

3.2.2. Agreement of FeNO values measured the first time and the second time
FeNO measured the first time ranged from 7 to 263 ppb (median:27.0 ppb), and FeNO measured the second time ranged from 5 to 271 ppb (median: 28.0 ppb). There was no significant difference between the two measurements ($p = 0.067$, figure 2(A)). The difference between the first time and the second time was −41–31 ppb (median: 2.0 ppb).

There was a strong positive correlation between FeNO values measured by the first time and the second time (Spearman correlation coefficient: $r = 0.953$, $p = 0.000$; figure 2(B)).

The Bland–Altman plot showed a moderate degree of agreement, with a mean difference of −1.2 ppb (95% CI: −18.2 ∼ 15.9 ppb) (figure 2(C)). There were 15 (7.1%) values outside the 95% CI. Within the 95% CI, the absolute value of the difference was up to 15 ppb (1st: 122 ppb, 2nd: 107 ppb), 13.1% of the average value, which within the tolerance limits.

3.2.3. Agreement of FeNO values in different value groups
The intra-subject difference of FeNO values ranged from −41 to 31 ppb, the mean intra-subject difference was 2.6 ppb (95% CI: 1.5 and 3.7 ppb). All subjects were divided into three groups according to the FeNO values measured by VERO: <25 ppb for group 1, 25–49 ppb for group 2, ⩾50 ppb for group 3. FeNO values measured by CA2122 was significantly higher than VERO in group 1 and group 2 ($p = 0.000$, $p = 0.017$). There was no significant difference for FeNO values in group 3 ($p = 0.200$) (table 2).

3.2.4. Agreement of FeNO values measured in various patients
In 83 patients with asthma, FeNO values measured by CA2122 were significantly higher than VERO, with median levels of 59.0 ppb (range: 14–271 ppb) and 55.0 ppb (range: 10–263 ppb) ($p = 0.001$, figure 3(A)).

There was a strong positive correlation between FeNO values measured by two devices (Spearman correlation coefficient: $r = 0.962$, $p = 0.000$; figure 3(B)). The Bland–Altman plot showed a high degree of agreement (figure 3(C)). There were 5 (6.0%) FeNO values outside the 95% CI. Within the 95% CI, the absolute value of the difference was up to 31 ppb (VERO: 208 ppb, CA2122: 239 ppb), 13.9% of the average value, which within the tolerance limits.

In 128 patients with chronic cough, there was no significant difference between FeNO values measured by CA2122 and VERO, with median levels of 23.5 ppb (range: 9–131 ppb) and 22.0 ppb (range: 5–135 ppb) ($p = 0.428$, figure 4(A)).

There was a strong positive correlation between FeNO values measured by two devices (Spearman correlation coefficient: $r = 0.907$, $p = 0.000$; figure 4(B)). The Bland–Altman plot showed a high degree of agreement (figure 4(C)). There were 8 (6.3%) FeNO values outside the 95% CI. Within the 95% CI, the absolute value of the difference was up to 10 ppb (VERO: 38 ppb, CA2122: 48 ppb), which within the tolerance limits.

In 33 patients with COPD, there was no significant difference between FeNO values measured by CA2122 and VERO, with median levels of 30.0 ppb (range: 12–212 ppb) and 28.0 ppb (range: 7–192 ppb) ($p = 0.074$, figure 5(A)).

There was a strong positive correlation between FeNO values measured by two devices (Spearman correlation coefficient: $r = 0.926$, $p = 0.000$; figure 5(B)). The Bland–Altman plot showed a high degree of agreement (figure 5(C)). There were 3

Table 1. Basic information of subjects.

Parameters		*n* (%)
Total, number (*n*)		244
Sex (Male/Female)		129/115
Age (years)		39.0 (29.0, 56.0)
Allergic rhinitis (*n*, %)		71 (29.1%)
Smokers (*n*, %)		44 (18.0%)
Asthma (*n*, %)		83 (34.0%)
Medications	Corticosteroid (inhaled, oral, or intravenous)	24 (28.9%)
	Antibiotics	16 (19.3%)
	Antitussives and expectorants (including traditional Chinese medicine)	10 (12.0%)
	Leukotriene receptor antagonist	6 (7.2%)
	Theophylline	1 (1.2%)
COPD (*n*, %)		33 (13.5%)
Medications	Corticosteroid (inhaled, oral, or intravenous)	8 (24.2%)
	Antibiotics	11 (33.3%)
	Antitussives and expectorants (including traditional Chinese medicine)	6 (18.2%)
	Leukotriene receptor antagonist	0
	Theophylline	4 (12.1%)
Chronic cough (*n*, %)		128 (52.5%)
Medications	Corticosteroid (inhaled, oral, or intravenous)	11 (8.6%)
	Antibiotics	54 (42.2%)
	Antitussives and expectorants (including traditional Chinese medicine)	30 (23.4%)
	Leukotriene receptor antagonist	3 (2.3%)
	Theophylline	0
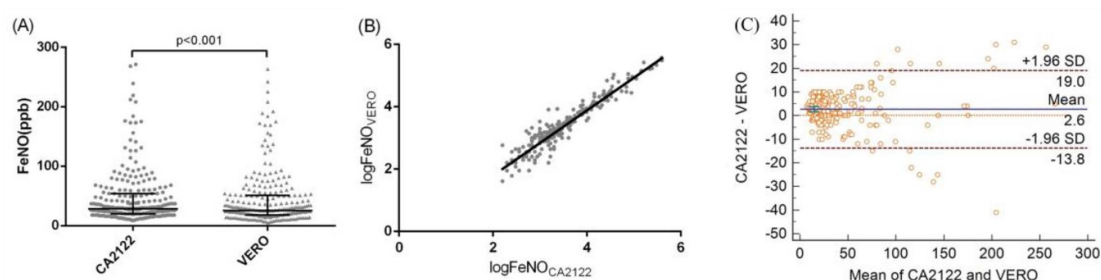
Figure 1. Comparison of FeNO values measured by two devices. (A) Scatter plot of FeNO values measured by both CA2122 and VERO. (B) Correlation between FeNO values measured with CA2122 or VERO. (C) The Bland–Altman plot showed the relationship between FeNO measured by CA2122 and VERO.
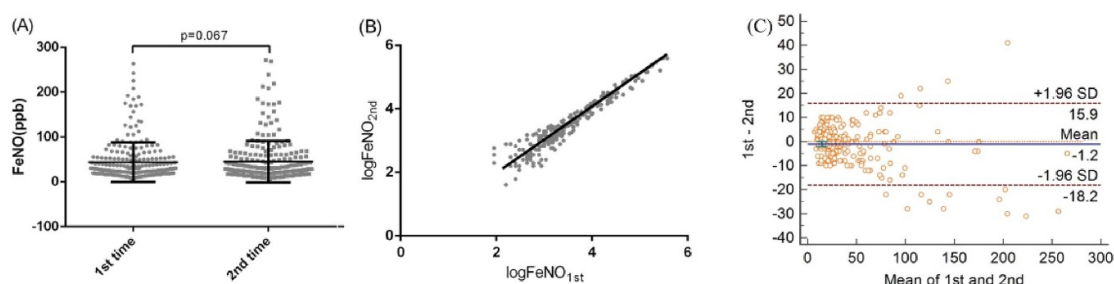
Figure 2. Comparison of FeNO values measured the first time and the second time. (A) Scatter plot of FeNO values measured the first time and the second time. (B) Correlation between FeNO values measured the first time and the second time. (C) The Bland–Altman plot showed the relationship between FeNO values measured the first time and the second time.

(9.1%) FeNO values outside the 95% CI. Within the 95% CI, the absolute value of the difference was up to 22 ppb (VERO: 134 ppb, CA2122: 156 ppb), 15.2% of the average value, which within the tolerance limits.

3.3. Agreement of FeNO values measured by CA2122 online and offline

For 244 subjects who finished FeNO measurement online and offline by CA2122, FeNO values measured online was higher than offline method ($p = 0.004$,

Table 2. Comparison of FeNO values in different groups based on FeNO values measured by VERO and CA2122.

Group	N	FeNO (VERO, ppb)	FeNO (CA2122, ppb)	Difference (ppb)	p
1 (FeNO: <25)	115	16.0 (12.0, 21.0)	20.0 (16.0, 24.0)	3.0 (0.0, 6.0)	0.000
2 (FeNO: 25–49)	61	31.0 (27.5, 36.5)	33.0 (29.0, 39.5)	1.0 (−1, 5.0)	0.017
3 (FeNO: ⩾50)	68	75.5 (56.0, 132.3)	79.5 (60.0, 122.8)	3.0 (−6.3, 12.0)	0.200

Figure 3. Comparison of FeNO values measured by two devices in patients with asthma. (A) Scatter plot of FeNO values measured by both CA2122 and VERO in patients with asthma. (B) Correlation between FeNO values measured with CA2122 or VERO in patients with asthma. (C) The Bland–Altman plot showed the relationship between FeNO measured by CA2122 and VERO in patients with asthma.

Figure 4. Comparison of FeNO values measured by two devices in patients with chronic cough. (A) Scatter plot of FeNO values measured by both CA2122 and VERO in patients with chronic cough. (B) Correlation between FeNO values measured with CA2122 or VERO in patients with chronic cough. (C) The Bland–Altman plot showed the relationship between FeNO measured by CA2122 and VERO in patients with chronic cough.

Figure 5. Comparison of FeNO values measured by two devices in patients with COPD. (A) Scatter plot of FeNO values measured by both CA2122 and VERO in patients with COPD. (B) Correlation between FeNO values measured with CA2122 or VERO in patients with COPD. (C) The Bland–Altman plot showed the relationship between FeNO measured by CA2122 and VERO in patients with COPD.
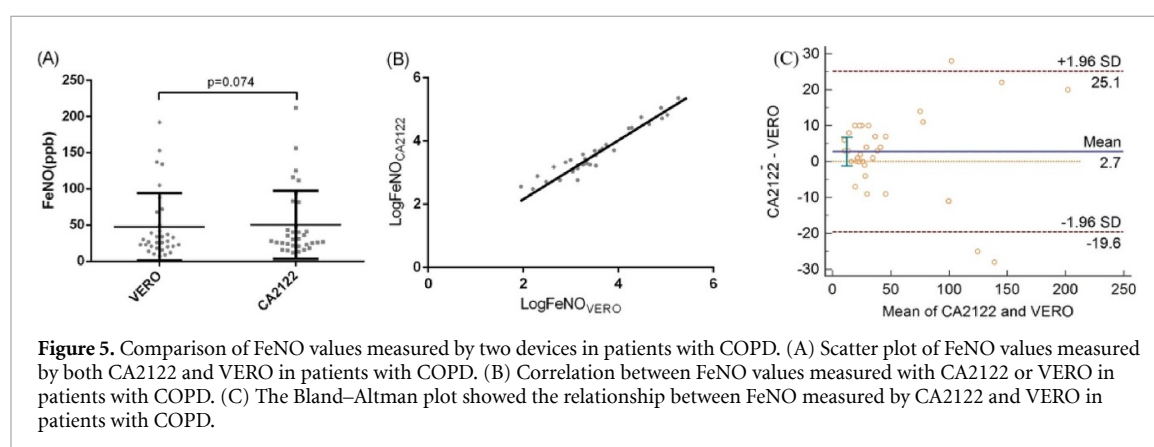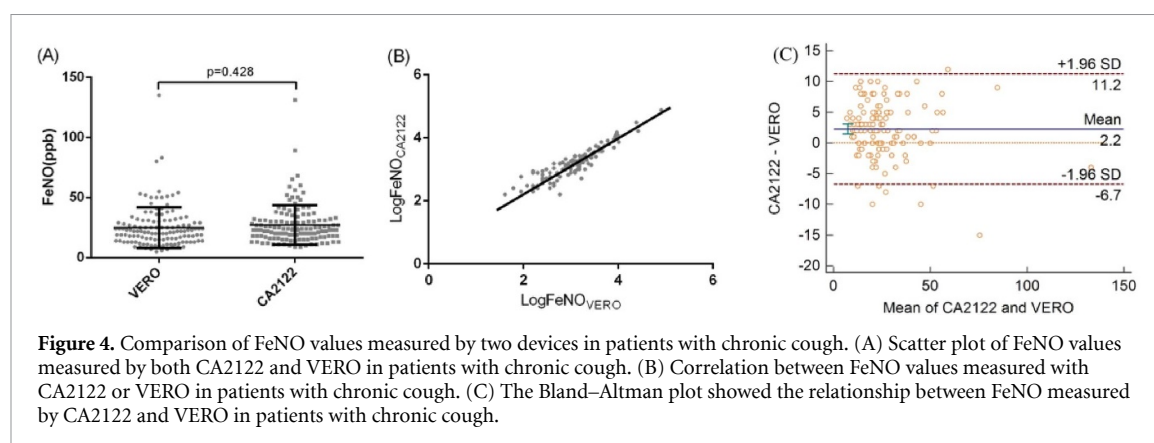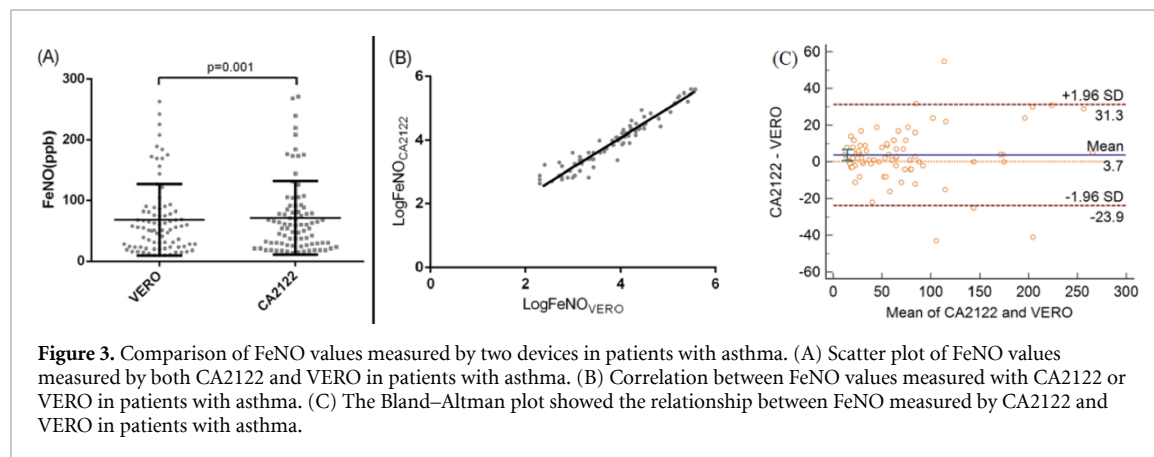
figure 6(A)), with median levels of 29.0 ppb (range: 9–271 ppb) and 28.0 ppb (range: 2–290 ppb), respectively. The range of difference between the two devices was −32–142 ppb (median: 1.0 ppb).

There was a strong positive correlation between FeNO values measured online and offline (Spearman correlation coefficient: $r = 0.932$, $p = 0.000$; figure 6(B)).

The Bland–Altman plot showed a moderate degree of agreement, with a mean difference of 2.6 (95% CI: −23.1 ~ 28.2) (figure 6(C)). There were 15 (7.1%) values outside the 95% CI. Within the
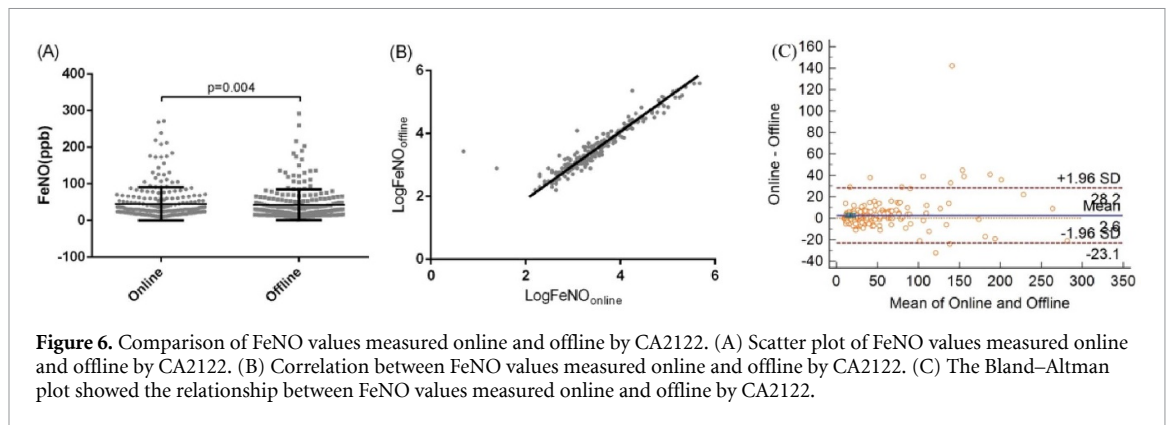
Figure 6. Comparison of FeNO values measured online and offline by CA2122. (A) Scatter plot of FeNO values measured online and offline by CA2122. (B) Correlation between FeNO values measured online and offline by CA2122. (C) The Bland–Altman plot showed the relationship between FeNO values measured online and offline by CA2122.

95% CI, the absolute value of the difference was up to 22 ppb (VERO: 239 ppb, CA2122: 217 ppb), 9.6% of the average value, which within the tolerance limits.

3.4. Success rates and attempts of two devices

A total of 287 patients participated in the study, of which 37 failed to use VERO, with a success rate of 87.1%; 19 failed in the CA2122 online measurement, with a success rate of 93.4%; only one failed in the CA2122 offline measurement, with a success rate of 99.7%. The success rates of online and offline measurement of FeNO by CA2122 were higher than that of VERO.

A comparison of the attempts required for the successful measurement by two devices was shown in figure 7. The mean attempts needed for the successful measurement by VERO was higher than that by CA2122, with the mean attempts of 2.4 and 2.1, respectively.

Two hundred forty-four patients completed measurements both by VERO and CA2122. The average time required for a successful measurement by CA2122 was 110.5 ± 35.7 s, and that of VERO was 117.5 ± 48.1 s. The time required for successful measurement by VERO was higher than CA2122 (figure 8).

4. Discussion

As an indicator of airway inflammation, exhaled nitric oxide (eNO) can reflect the level of eosinophilic inflammation in the airway and predict the responsiveness of corticosteroid therapy, at present, FeNO is more and more widely used in clinical practice [1, 18]. FeNO can be measured by several available analyzers, which differ in the methods of measurements. Stationary chemiluminescence NO analyzers have been widely used and was regarded as the gold standard for FeNO measurement. However, because of its large volume and high price, the stationary analyzer is mainly used in clinical research. The handheld electrochemical NO analyzer is small and easy to operate and have been widely used in clinical routine measurement [19, 20]. VERO (Aerocrine,

Sweden) and CA2122 (SUNVOU, China) are currently the two most commonly used electrochemical analyzers in China. There were many reports on the clinical application of VERO [21–24], but few reports on the clinical application of CA2122, meanwhile there was less research on the agreement between VERO and CA2122 in the measurement of FeNO. A previous study had compared CA1222 with VERO, but the subjects were all asthmatic patients and thus could not represent other respiratory diseases [12]. In this study, by far the largest sample size, FeNO values of 244 subjects, not only asthma patients, but also COPD and chronic cough patients, were measured by CA2122 and VERO. The results showed that FeNO values measured by CA2122 were slightly higher than VERO, and the average difference was 2.6 ppb. Although there was a significant difference, the FeNO values measured by the two instruments were highly correlated ($r = 0.964$). In addition, the Bland–Altman plot analysis further suggested a high degree of agreement between FeNO values measured by CA2122 and VERO. Our results were consistent with Huang T's [12], and our larger sample size and more disease types further proved the reliability of the FeNO values measured by CA2122. Although the difference of 2.6 ppb might be considered as not clinically meaningful in a single patient, and the difference of 2.6 ppb did not exceed the manufacture's specifications, nevertheless it might significantly influence the management of asthmatic patients, especially those with severe asthma. The cut-off point of FeNO value measured by different device might be different [25–27]. The reference value of FeNO for CA2122 in respiratory diseases needs further study. Whether the difference between the two devices is related to the difference of sensors used by the two devices also required to be further studied.

In addition, some studies have reported that FeNO values might be affected by some external factors, such as lung function test, repeated exhalations, etc. Some studies have shown that if the pulmonary function test is performed before FeNO measurement, FeNO value would be reduced [28–30]. So in this study, all subjects were informed to take
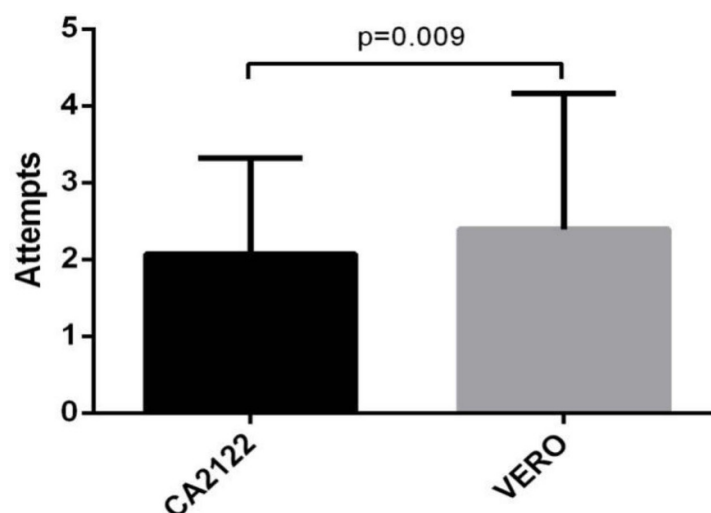
Figure 7. Comparison of attempts needed for the successful measurement by VERO and CA2122.
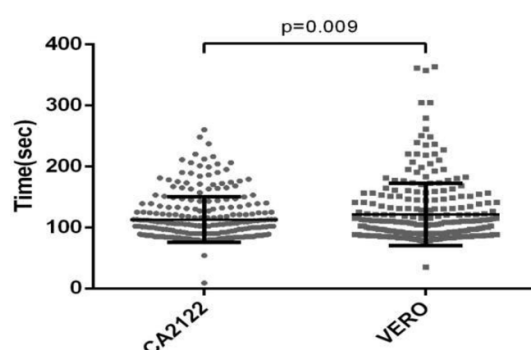

Figure 8. Comparison of time required for the successful measurement by VERO and CA2122.

the FeNO measurement before the pulmonary function test. Each subject performed no more than five exhalations. If the subject failed after five exhalations, the attempt would be stopped and recorded as failure. At the same time, we studied whether the sequence of measurements would affect the test results. The results showed that there was no statistical difference between the FeNO results of the first and second measurement. FeNO values measured the first and the second time were correlated, and Bland–Altman plot analysis showed a high agreement between the FeNO values measured the first and the second time. The study showed that the values of FeNO measured by CA2122 and VERO had good repeatability and consistency. The study also demonstrated that the repeatability of FeNO test was reliable and the results of one measurement using CA2122 or VERO could meet the needs of clinical work [20].

We divided the patients into three groups according to ATS clinical guideline. There were 115 patients of FeNO < 25 ppb, 61 patients of FeNO between 25 and 50 ppb, and 68 patients of FeNO > 50 ppb.

For patients with FeNO less than 50 ppb, the mean value of FeNO measured by CA2122 was about 3 ppb higher than that measured by VERO, and the difference between the two groups was significant. For patients with FeNO greater than 50 ppb, there was no significant difference in FeNO values between the two devices. Our results were consistent with Huang T's [12]. It was further suggested that the results of FeNO at different level measured by CA2122 was reliable. Nevertheless, whether the cut-off point of FeNO value measured by different device needs to be adjusted needs further study [25–27]. In clinical practice, when FeNO values obtained by different analyzers are deviated, the clinical background (such as symptoms, pulmonary function, asthma control, etc) should be considered [2].

In this study, 244 patients with common respiratory diseases (asthma, COPD, chronic cough, including rhinitis) took FeNO measurement by CA2122 and VERO. The results showed that FeNO measured by CA2122 was higher than VERO in 83 patients with asthma and 128 patients with chronic cough. The difference was significant. Correlation analysis and Bland–Altman plot analysis showed a high degree of agreement between the FeNO values measured by two devices. In 33 patients with COPD, there was no significant difference between the FeNO values measured by two devices. Correlation analysis and Bland Altman plot analysis showed a high agreement between the FeNO values. These results indicated that there was a high degree of agreement between the FeNO values measured by CA2122 and VERO in patients with different respiratory diseases. This further demonstrates the application prospect of CA2122 in respiratory diseases [31].

Online measurement of FeNO is still the main method nowadays. There are advantages and disadvantages in online and offline measurement of FeNO.

There are still lack of studies concerning offline measurement of FeNO in patients until now. FeNO can only be measured online by NIOX in China, while FeNO can be measured both online and offline by CA2122. This study found that the FeNO measured by CA2122 online was about 2.6 ppb higher than that of offline measurement, which was consistent with Shimizu *et al's* study [14], and the difference was significant. Correlation analysis and Bland–Altman plot analysis showed a high degree of agreement between FeNO values measured online and offline. In addition, we found that the success rate of offline measurement (99.7%) was significantly higher than online measurement (93.4%), suggesting that for patients who fail or might fail in online measurement, offline method could be used [32]. These results show that CA2122 is supposed to have a broader prospect in clinical application.

In this study, the success rate of FeNO measurement by two devices was also analyzed. If measurement was unsuccessful for five exhalations, it was recorded as a failure. In this study, the success rate of measurement by CA2122 was significantly higher than that of VERO, with 99.7% for online method by CA2122, 93.4% for offline method by CA2122 and 87.1% for online method by VERO, respectively. Korn S measured the success rates of three devices (CLD 88, NIOX VERO, and Vivatmo pro) in testing FeNO, which were 81%, 85% and 86%, respectively [33]. Our success rate was slightly higher than their results. For the first time, we also compared the number of attempts and the total time required for a successful measurement by two devices. The results showed that the number of attempts and the total time required of CA2122 was significantly lower than VERO. The shortening of FeNO measurement time was very important to improve the efficiency of pulmonary function room staff [34]. In this study, we defined more than five exhalations as failure. If we increased this number, the difference between the number of attempts and the time required by the two devices would increase accordingly. Of course, our results needed to be further confirmed by other studies. At present, no studies have been reported on the difference between the two devices in terms of success rate, number of attempts and total time required for a successful measurement. The researchers believe that it may be related to the use of the mouth holder of the two devices, the filter used by the two devices, the different measurement interface of exhalation, etc. Whether there are other factors remains to be further studied.

The limitations of this study: (a) subjects in this study were patients with chronic cough. Of all, 52.5% of the patients with chronic cough did not get their final clinical diagnosis because they did not carry out other relevant clinical examinations. Therefore, the application value in other respiratory diseases needs to be further studied. (b) In this study, we conducted a single measurement by each device on the subjects and compared the FeNO values. Whether there was still a good agreement between the two devices when two or three measurements were taken by each device needed further research. (c) This study was a single center study, the sample size was not large, follow-up research was needed to further verify our conclusions.

In conclusion, our results showed that FeNO values measured by CA2122 was slightly higher than VERO in patients with chronic cough, asthma, and COPD. There was a high degree of agreement between FeNO values measured by CA2122 and VERO, online method and offline method by CA2122. The success rate of measurement by CA2122 test was significantly higher than VERO, and the number of attempts and total time required for a successful measurement by CA2122 were lower than VERO. The results suggested that the new handheld device CA2122 has an excellent reproducibility for FeNO and might have a broader prospect in clinical or epidemiological research. However, this conclusion needs to be further confirmed by multicenter, large sample, randomized controlled study.

Funding

Conflict of interests

The authors declare that they have no competing interests.

ORCID iD

Wei Lei ⬦ https://orcid.org/0000-0001-8498-7161

References

[1] Bjermer L *et al* 2014 Current evidence and future research needs for FeNO measurement in respiratory diseases *Respir. Med.* **108** 830–41
[2] Horváth I *et al* 2017 A European Respiratory Society technical standard: exhaled biomarkers in lung disease *Eur. Respir. J.* **49** 1600965
[3] Högman M, Thornadtsson A, Bröms K, Janson C, Lisspers K, Ställberg B, Hedenström H and Malinovschi A 2019 Different relationships between FENO and COPD characteristics in smokers and ex-smokers *COPD* **16** 227–33
[4] Naderi M and Sabour S 2020 Diagnostic value of FeNO and MMEF for predicting cough variant asthma in chronic cough patients: methodological issues *J. Asthma* 1–2

[5] Ricciardolo F L, Sorbello V and Ciprandi G 2015 FeNO as biomarker for asthma phenotyping and management *Allergy Asthma Proc.* **36** 1–8

[6] Csoma B, Bikov A, Nagy L, Tóth B, Tábi T, Szűcs G, Komlósi Z I, Müller V, Losonczy G and Lázár Z 2019 Dysregulation of the endothelial nitric oxide pathway is associated with airway inflammation in COPD *Respir. Res.* **20** 156

[7] Cameli P, Bergantini L, Salvini M, Refini R M, Pieroni M, Bargagli E and Sestini P 2019 Alveolar concentration of nitric oxide as a prognostic biomarker in idiopathic pulmonary fibrosis *Nitric Oxide* **89** 41–45

[8] Furukawa K *et al* 2011 Increase of nitrosative stress in patients with eosinophilic pneumonia *Respir. Res.* **12** 81

[9] Cameli P, Bargagli E, Bergantini L, Refini R M, Pieroni M, Sestini P and Rottoli P 2019 Evaluation of multiple-flows exhaled nitric oxide in idiopathic and non-idiopathic interstitial lung disease *J. Breath Res.* **13** 026008

[10] Kis A, Meszaros M, Tarnoki D L, Tarnoki A D, Lazar Z, Horvath P, Kunos L and Bikov A 2019 Exhaled carbon monoxide levels in obstructive sleep apnoea *J. Breath Res.* **13** 036012

[11] Cakmak S, Kaur L, Mahmud M, Shutt R, Liu L, Rigden M, Kumarathasan P, Vincent R, Thomson E M and Dales R 2020 Effect of industrial point-source air pollutants on fractional exhaled nitric oxide in healthy volunteers *Environ. Res.* **181** 108965

[12] Huang T, Liu B, Yang D and Liu C 2019 Fractional exhaled nitric oxide measurement: comparison between the Sunvou-CA2122 analyzer and the NIOX VERO analyzer *J. Asthma* 1–8

[13] Barbara S, Juerg H, Juerg B and Daniel T 2009 Comparability of a hand-held nitric oxide analyser with online and offline chemiluminescence-based nitric oxide measurement *Pediatr. Allergy Immunol.* **20** 679–85

[14] Shimizu H, Obase Y, Ikeda M, Kurose K, Abe M, Mouri K, Katoh S, Miyashita N, Kobashi Y and Oka M 2011 Stability of sealed-bag samples for off-line measurement of fractional exhaled nitric oxide *Ann. Allergy Asthma Immunol.* **106** 378–80

[15] American Thoracic Society; European Respiratory Society 2005 ATS/ERS recommendations for standardized procedures for the online and offline measurement of exhaled lower respiratory nitric oxide and nasal nitric oxide *Am. J. Respir. Crit. Care Med.* **171** 912–30

[16] Bland J M and Altman D G 1986 Statistical methods for assessing agreement between two methods of clinical measurement *Lancet* **1** 307–10

[17] Dong F, Zhu C, Xu H, Wang J, Zhu Y, Fan Q, Huang J and Lei W 2017 Measuring endotracheal tube depth by bedside ultrasound in adult patients in an intensive care unit: a pilot study *Ultrasound Med. Biol.* **43** 1163–70

[18] Dweik R A, Boggs P B, Erzurum S C, Irvin C G, Leigh M W, Lundberg J O, Olin A C, Plummer A L and Taylor D R American Thoracic Society Committee on Interpretation of Exhaled Nitric Oxide Levels (FENO) for Clinical Applications 2011 An official ATS clinical practice guideline: interpretation of exhaled nitric oxide levels (FENO) for clinical applications *Am. J. Respir. Crit. Care Med.* **184** 602–15

[19] Mandon J, Högman M, Merkus P J, van Amsterdam J, Harren F J and Cristescu S M 2012 Exhaled nitric oxide monitoring by quantum cascade laser: comparison with chemiluminescent and electrochemical sensors *J. Biomed. Opt.* **17** 017003

[20] Cristescu S M, Mandon J, Harren F J, Meriläinen P and Högman M 2013 Methods of NO detection in exhaled breath *J. Breath Res.* **7** 017104

[21] Alving K, Anolik R, Crater G, LaForce C F and Rickard K 2017 Validation of a new portable exhaled nitric oxide analyzer, NIOX VERO®: randomized studies in asthma *Pulm. Ther.* **3** 207–18

[22] Endo Y, Shirai T, Akamatsu T and Asada K 2017 Comparison of fractional exhaled nitric oxide levels measured using the NIOX VERO and NOA 280i *Ann. Allergy Asthma Immunol.* **119** 383–5

[23] Inoue Y, Sato S, Manabe T, Makita E, Chiyotanda M, Takahashi K, Yamamoto H, Yanagida N and Ebisawa M 2018 Measurement of exhaled nitric oxide in children: a comparison between NObreath® and NIOX VERO® analyzers *Allergy Asthma Immunol.* **105** 478–89

[24] Tanabe Y *et al* 2019 Difference between two exhaled nitric oxide analyzers, NIOX VERO® electrochemical hand-held analyzer and NOA280i® chemiluminescence stationary analyzer *J. Asthma* **56** 167–72

[25] Bushe C, Kamada A and Hafnera R 2020 FeNO variability when using different analyzers at the joint ATS/ERS guideline cutoff *Respiration* **99** 93

[26] Molino A, Fuschillo S, Mosella M, Accardo M, Guida P, Motta A and Maniscalco M 2019 Comparison of three different exhaled nitric oxide analyzers in chronic respiratory disorders *J. Breath Res.* **13** 021002

[27] Saito J *et al* 2019 Comparison of fractional exhaled nitric oxide levels measured by different analyzers produced by different manufacturers *J. Asthma* 1–11

[28] Mauro M, Carolina V, Alessandro V, Antonio M, Andrea B and Gennaro M 2016 Fractional exhaled nitric oxide-measuring devices: technology update *Med. Devices* **9** 151–60

[29] Duong-Quy S 2019 Clinical utility of the exhaled nitric oxide (NO) measurement with portable devices in the management of allergic airway inflammation and asthma *J. Asthma Allergy* **12** 331–41

[30] Haccuria A, Michils A, Michiels S and Van Muylem A 2014 Exhaled nitric oxide: a biomarker integrating both lung function and airway inflammation changes *J. Allergy Clin. Immunol.* **134** 554–9

[31] Zeng J, Chen Z, Hu Y, Hu Q, Zhong S and Liao W 2018 Asthma control in preschool children with small airway function as measured by IOS and fractional exhaled nitric oxide *Respir. Med.* **145** 8–13

[32] van der Heijden H H, Brouwer M L, Hoekstra F, van der Pol P and Merkus P J 2014 Reference values of exhaled nitric oxide in healthy children 1–5 years using off-line tidal breathing *Pediatr. Pulmonol.* **49** 291–5

[33] Korn S, Wilk M, Voigt S, Weber S, Keller T and Buhl R 2020 Measurement of fractional exhaled nitric oxide: comparison of three different analysers *Respiration* **99** 1–8

[34] Li F, Huang Z W, Wang X F, Xu H W, Yu H, Chen Y B, Huang J A, Wang J J and Lei W 2019 Safety and use of pulmonary function tests: a retrospective study from a single center over seven years' clinical practice *BMC Pulm. Med.* **19** 259