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Original Article

Precision and accuracy of transcutaneous CO_2 monitoring in infants born at 32-36 weeks of pregnancy on respiratory support

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Abstract

Background Respiratory disorders in premature neonates often require respiratory support. Continous transcutaneous monitoring is an available non-invasive option to monitor CO_2 pressure, substituting the need for blood gas analysis as the gold standard evaluation in practice. Most studies have been conducted on very and extremely preterm neonates, but rarely in late and moderately preterm neonates.

Objective To determine the precision and accuracy of transcutaneous CO_2 pressure measuring devices compared to arterial blood gas analysis in neonates of 32-36 weeks gestational age who received respiratory support.

Methods This diagnostic, cross-sectional study was conducted on 35 late and moderately preterm neonates of 32-36 weeks gestation who received cardiopulmonary resuscitation (CPR) in the Neonatology Unit at Rumah Sakit Cipto Mangunkusumo, Jakarta. Subjects were monitored with a transcutaneous CO_2 monitor and blood gas analysis (BGA). The CO_2 pressure measurements were made three times from the two devices. Data were analyzed using Spearman's correlation and Bland-Altman tests to determine the precision and accuracy of transcutaneous monitoring by comparing its mean difference (MD) to BGA as the gold standard measurement.

Results Spearman's analysis revealed a significant positive correlation between BGA and transcutaneous CO_2 monitoring ($P<0.001$). However, the Bland-Altman test revealed a level of agreement between measuring devices was -14.46 to 6.9, with mean difference of -3.78; indicating poor precision of the transcutaneous evaluation regardless its high accuracy compared to its gold standard.

Conclusion The transcutaneous CO_2 monitoring device has low precision, but a strong positive correlation to BGA; underlining its high accuracy in practice. Transcutaneous CO_2 monitoring cannot replace BGA, the gold standard examination. **[Paediatr Indones. 2024;64:160-7; DOI: 10.14238/pi64.2.2024.160-7].**

Keywords: *transcutaneous CO2; respiratory support device; accuracy; precision; late and*

Premature neonates, especially those who are late and moderately preterm, often experience health issues, including respiratory system disorders, which among other things, contribute to high mortality rates.[1] A study assessing respiratory morbidity in late preterm neonates compared to mature neonates revealed that respiratory distress syndrome (RDS) was the main cause of neonatal morbidity, with an incidence of 10.5% in infants of 34 weeks' gestational age and that rate decreased to 0.3% at 40 weeks' gestational age. Transient tachypnea of the newborn (TTN) was the second leading cause of morbidity, with an incidence of 6.4% in neonates at 34 weeks' gestational age, followed by respiratory failure 1.6%, persistent apnoea and bradycardia 1.6%, pneumonia 1.5%, pulmonary hypertension 0.5%, and pneumothorax 0.8%.[2] Respiratory disorders in premature neonates often requires respiratory support via oxygenation and ventilation, which can be invasive or non-invasive.

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Non-invasive ventilation is a frequently used device among neonates with RDS, especially in premature birth conditions with higher risk of respiratory intervention.

Respiratory support via oxygenation and ventilation requires monitoring of oxygen and CO_2 pressures in order to assess the adequacy of ventilation. Blood gas analysis is the gold standard examination to monitor oxygenation and ventilation.[3] However, this test is expensive, impractical, invasive, must be performed by trained medical personnel, can cause iatrogenic anemia and infection, and only describe the condition at the time of the blood draw.[4] Blood gas analysis tests can also cause blood loss, thus increasing the need for blood transfusions. Apart from monitoring ventilation, oximetry can be used to monitor oxygenation, and is a non-invasive method used in the neonatal intensive care unit (NICU).[5]

Monitoring CO_2 pressure is also very important because it can have adverse effects, such as those caused by hypocarbia and hypercarbia conditions.[4] Arterial CO_2 pressures ($PaCO_2$) of less than 35 mmHg and greater than 60 mmHg should be avoided in ventilated low birth weight neonates. Hypocarbia in premature neonates has been associated with periventricular leukomalacia (PVL), cerebral palsy, impaired cognitive development, and hearing loss. Hypercarbia can cause interstitial cerebral edema, intracranial hypertension, intracranial hemorrhage, as well as reduced contractility of the myocardium and diaphragm, which can evolve into cardiovascular instability, arrhythmia, cardiac or respiratory attacks, or death.[6]

Neonates with respiratory support should be monitored for adequate ventilation and oxygenation in the absence of episodes of hypo/hypercarbia. Monitoring CO_2 pressure through transcutaneous CO_2 may be more precise, more reliable, and in accordance with the value of $PaCO_2$. Under certain circumstances, transcutaneous CO_2 can replace blood gas analysis.[7] However, a study on transcutaneous CO_2 monitoring in late and moderately preterm neonates has not been widely carried out; studies have been conducted on very and extremely preterm neonates. In Indonesia, a study on transcutaneous CO_2 monitoring has not been done, in late and moderately preterm neonates. Therefore, we aimed to assess the precision and accuracy of transcutaneous CO_2 pressure compared to arterial blood gas analysis in late and moderately preterm neonates (32-36 weeks of gestation) who received respiratory support.

Methods

This cross-sectional diagnostic study was performed in the Neonatology Unit, Rumah Sakit Umum Cipto Mangunkusumo, Jakarta. Subject sampling was conducted from July to December 2019, after the study was approved by the Ethics Committee, Faculty of Medicine, Universitas Indonesia. We included premature neonates with gestational age of 32-36 weeks and respiratory distress that required breathing support (continuous positive airway pressure/CPAP, nasal intermittent positive pressure ventilation/NIPPV, mechanical ventilation, and high frequency oscillatory ventilation/HFOV). Parents provided written informed consent. Neonates with major congenital abnormalities, unstable hemodynamic conditions, and allergic reactions to the transcutaneous CO_2 monitoring device material were excluded. Subjects underwent CO_2 pressure monitoring and blood specimens were taken for arterial BGA three times. Observed values of CO_2 pressure were obtained from both transcutaneous devices (*SenTec* AG, Switzerland), setted in 42cC electrodes' temperatures. Patients who met the inclusion criteria were considered as study subjects if they had undergone three CO_2 pressure readings through transcutaneous means and BGA according to medical indications.[8] The results obtained were analyzed to determine the accuracy and precision of the transcutaneous CO_2 pressure test device. Data were processed by using *SPSS version 22* software, using Spearman's correlation and coefficient realibility Bland-Altman tests to determine the precision and accuracy of test equipment pressure of transcutaneous CO_2. The term "Tc" or "Pa" were used to simplify the term which translated into 'transcutaenous pressure' and 'partial pressure', respectively; and was utilized on the following section e.g., $TcPO_2$ which meant transcutaneous oximetry findings. A P value <0.05 was considered as statistically significant. The subjects recruitment process can be seen in **Figure 1**.

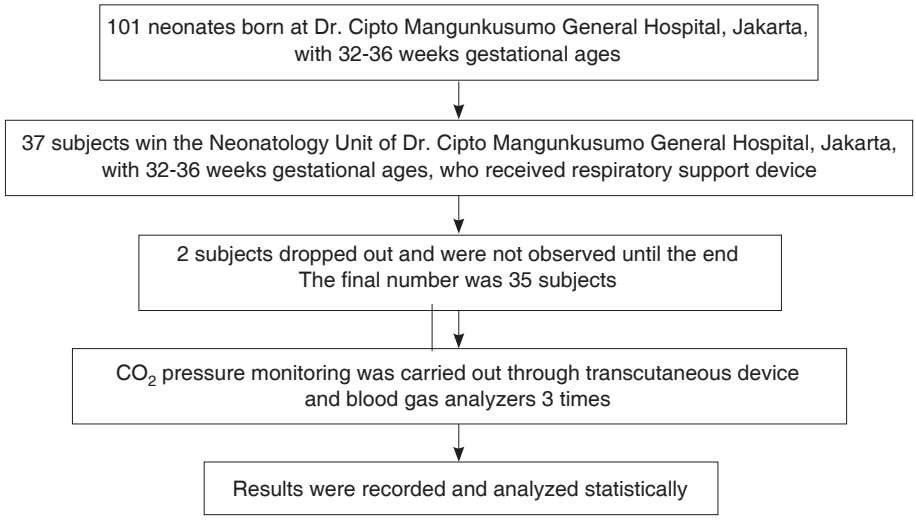

Figure 1. Schematic of study subjects

Results

There were 37 neonates admitted to the Neonatology Unit, Cipto Mangunkusumo General Hospital with gestational age of 32–36 weeks, and who received breathing support. Two infants dropped out and were not observed until completion because they failed to undergo the examination three times, so 35 neonates were included in the study. The characteristics of subjects are shown in **Table 1**.

Twenty-four subjects used non-invasive breathing devices, consisting of CPAP (20) and NIPPV (4). Eleven subjects received invasive breathing support, consisting of HFOV (3) and mechanical ventilation (8).

Blood gas analysis were obtained only when the indications for its utilization were confirmed. **Figure 2** displayed the circumstances whereby the first BGA was drawn. For the first BGA, 25 subjects needed a baseline BGA post-birth and 6 subjects were undergoing observation. For the second data collection point, 21 subjects needed BGA while being observed and 14 were clinically worsening. On the third examination, 23 subjects had analyses while being observed, 7 subjects while being weaned from ventilation, and 5 subjects for worsening symptoms.

As a measure of precision, Spearman's correlation test was used to compare the paired CO_2 readings obtained by transcutaneous and BGA methods (**Table 2**). The total correlation coefficient value (R) was 0.738; $P<0.001$, indicating that the transcutaneous CO_2 pressure monitoring device had a moderate positive correlation with BGA, thus, higher levels of CO_2 by BGA tended to moderately correlate to an increase in the value read on the transcutaneous CO_2 monitoring device. This correlation was mapped by a scatter graph (**Figure 3**).

Figure 4 shows the relability coefficient, accuracy, and stability of the transcutaneous device compared to BGA, the gold standard used in this study. Bland-Altman test revealed a level of agreement of -14.46 to 6.9, with a mean difference of -3.78, which indicates that the mean difference scarcity in this study was observable; though the majority or trend of the findings were observed in between 0.0 to -5.0 range. Whilst its consistency only attainable by subjective assessment on the graph (**Figure 4**), it was apparent that the limit of agreement falls on the the latter range.

Discussion

The median age of our subjects at the time of data collection was 1 (range 1-30) days, while in a previous study the median age of the sample at the time of the study was 8.5 (1-44) days.[9] This findings was probably originated from changes in the texture and thickness of the skin and capillaries with increasing postnatal age, as well as a decrease in the oxygen permeability of

Table 1. Characteristics of study subjects

Characteristics	(N=35)
Gender, n	
Male	18
Female	17
Median gestational age (range), weeks	33 (32-36)
Median age at sampling, days	1.00 (1-30)
Mean birth weight (SD), gram	1,703.77 (420.59)
Mean birth length (SD), cm	39.43 (3.69)
Mean blood pressure (SD), mmHg	
Systolic	76.8 (13.45)
Diastolic	52.37 (9.72)
MAP	59.58 (9.69)
Median temperature (range), °C	37.00 (36.0-38.0)
Mean capillary refill time (SD), seconds	<3 (100)
Type of delivery	
Vaginal	6
Caesarean section	29
Ventilation supporT	
Invasive	11
Non-invasive	24
Measurement of PCO_2	
Mean BGA (SD), mmHg	33.61 (8.71)
Non-invasive ventilation support	33.19 (7.30)
Invasive ventilation support	34.52 (7.31)
Mean transcutaneous CO_2 (SD), mmHg	37.39 (8.78)
Non-invasive ventilation support	36.69 (6.36)
Invasive ventilation support	38.79 (9.69)

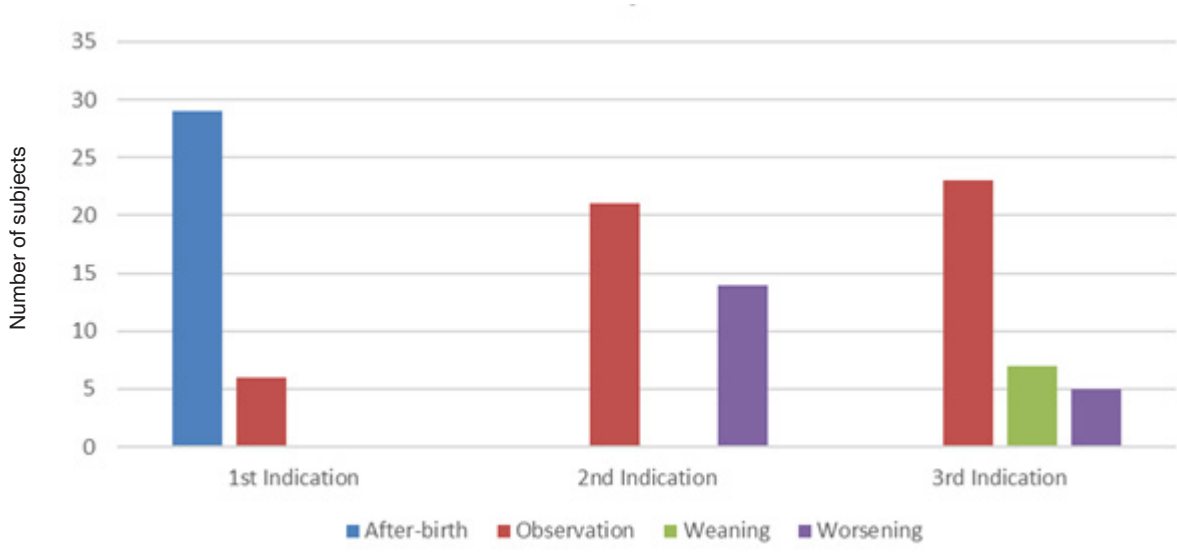

Figure 2. Indications for the 3 data collection points

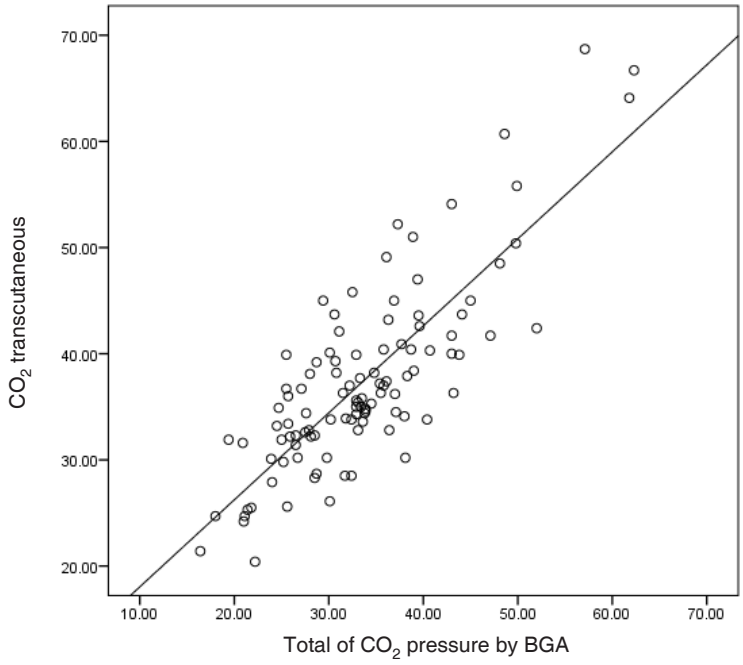

Figure 3. Scatter graph of Spearman's correlation for CO_2 pressure by BGA and CO_2 transcutaneous device

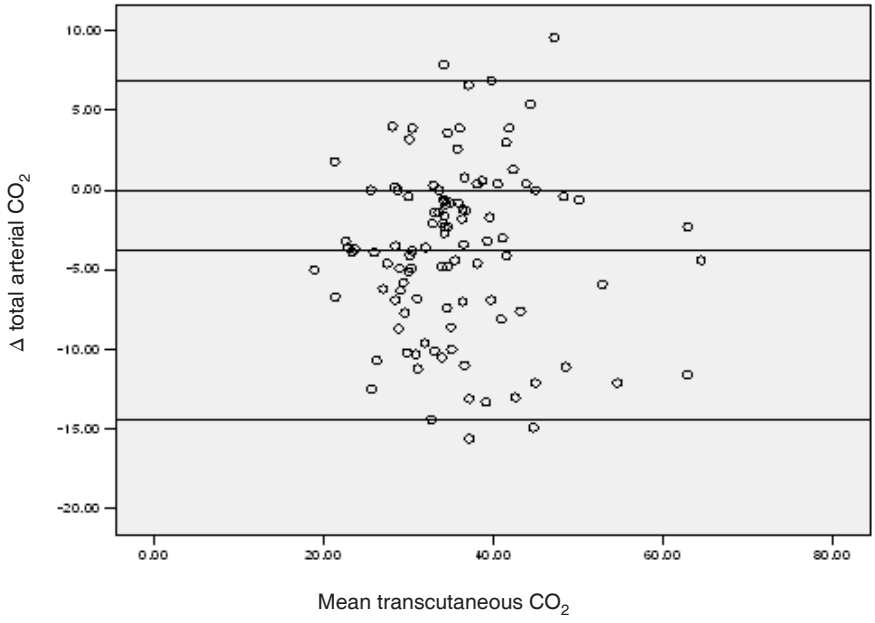

Figure 4. Bland-Altman test from the value of CO_2 in examination by BGA and CO_2 transcutaneous device

the skin.[10] A study reported an interclass correlation coefficient for transcutaneous carbon dioxide gas pressure ($TcPCO_2$) and partial presure of carbon dioxide ($PaCO_2$) was 0.45, 0.73, and 0.53, in the three inspections at ages 4, 12, and 24 hours after birth in 27 ventilated neonates. This correlation coefficient value decreased with the increasing postnatal age, which was thought to be influenced by the thinning of the epidermal layer in newborns, especially neonates who were born prematurely.[11]

Most of our subjects used non-invasive breathing support. Similarly, a study on 52 neonates in Sweden, of whom 24 neonates received breathing support using a mechanical ventilator, [27] neonates used nCPAP, and one neonate used a nasal cannula,[12] while another study on 50 neonates born prematurely showed that 40% used bCPAP breathing support, 16% used NIPPV, 18% used mechanical ventilators, 24% used HFOV, and one neonate did not use any breathing support.[13]

Subjects' BGA specimens had mean CO2 pressure of 33.61 (SD 8.71) mmHg. The mean CO2 pressure using a transcutaneous device was 37.39 (SD 8.78) mmHg. A previous study reported mean CO2 measurements of 51.3 (SD 16) mmHg by transcutaneous device and 49.1 (SD 13.7) mmHg by BGA. The variation between this report to ours might be originated from difference, e.g., the utilization of very low birth weight infant on their study compared to the late-moderate preterm in our study. Moreover, difference of the electrodes' temperature (42^{o}C *vs.* 41^{o}C in their study). Nevertheless, that study observed similar conclusion with a positive correlation was confirmed between transcutaneous measurement and BGA outputs.[13]

Spearman's correlation analysis of transcutaneous and BGA CO_2 measurements revealed a total correlation coefficient value of 0.738, indicating a strong correlation between both modalities, hence the accuracy of transuctaneous evaluation is considerable. Hence, using BGA as the gold standard, the transcutaneous CO_2 pressure readings, though generally higher than BGA, showed high accuracy in infants of 32-36 weeks gestational age. Moreover, the precision of the transcutaneous measurement may be subjectively estimated by the Bland-Altman plot, which indicates a similarity between mean difference findings in the range between 0.00 and -5.00. The scatter graph showed a positive correlation (**Figure 3**), showing that the greater the CO_2 pressure obtained from transcutaneous CO_2 measurements, the greater the CO_2 pressure measurement using the BGA will be. Similarly, Hirata *et al.*[14] noted a significant positive correlation between TcPCO2 and PaCO2 (R 0.751; P=0.001), as did Aly *et al.*[13] (R 0.6; P=0.001).

Bland–Altman analysis revealed a discrepancies between BGA and $PtCO_2$ with the estimated value of 3,785 mmHg, with a predictive precision of 10.68 mmHg, implying that the limit of agreement was -14.46 to 6.9 mmHg. The findings are close to the value of 0 as the expected accurate point. Thus, transcutaneous CO_2 measurement can be classified as a fairly accurate tool. Hirata et al. discovered a mean difference of 5.87 mmHg (95%CI 5.25 to 6.49), with a limit of agreement ranging from -4.11 to 15.84 mmHg.[14]

However, our Bland-Altman analysis also revealed that this tool had poor precision, despite the fairly strong positive correlation and accuracy as a measurement tool, as seen from the mean difference, standard deviation, and limits of agreement. To simplify the findings, this trancutaneous tool offers similarly high accuracy as the gold standard, but its precision thorough several tests is generally poor since the finding often scattered around the Bland-Altman plot. Yet, its accuracy is statistically considerable since there is a positive correlation based on the Spearman correlation test between the transcutaneous findings and BGA, indicating its favorable accuracy.

Several studies have been carried out to assess the accuracy and reliability of transcutaneous CO_2 pressure devices, with results still debated.[15] Several studies have shown poor correlation between CO_2 pressure measured by BGA when compared to transcutaneous CO_2 devices, but some studies have shown good results.[12,16-18]

A study on 27 ventilated neonates who were of 28-week gestational age reveals the interclass correlation coefficients in 3 examinations at the ages of 4, 12, and 24 hours after birth for $TcPCO_2$ and $PaCO_2$ were 0.45, 0.73, and 0.53, respectively and for $PetCO_2$ and $PaCO_2$ were 0, 61, 0.56, and 0.57, respectively.[10] Their results provided a bias value (scarcity of the mean difference findings, indicating poor precision of the evaluated diagnostic tool) and high limit of agreement, so it was considered to have poor precision.[10]

The transcutaneous CO_2 measuring instrument provides results with good precision and accuracy when performed at the recommended electrode temperature of 38°C; though the 38-42oC range remains considerable.[16,17] Another study reported that TcPO2 and TcPCO2 measurements were similar to those by BGA.[12] The discrepancies of the estimated means obtained from this study is still relatively small and is still clinically acceptable to apply to the management of neonates in the NICU. This device can also be recommended for neonates with very low birth weight during intensive care.[12]

In our study, the value of transcutaneous CO2 pressure appeared to be approximately 3.78 mmHg higher when compared to the BGA result. In Bland-Altman analysis of a study on 25 infants with gestational ages of 23 to 41 weeks, the bias between BGA and $TcCO_2$ was 0.30 ± 7 kPa, the precision was ±1.47 kPa, and the difference in values between $TcCO_2$ and BGA was 1 kPa in 19 of 25 samples (76%). Similarly, another study showed that transcutaneous CO2 meter reading was 5.78 mmHg higher than the measurement via BGA.[14]

Body weight, postnatal age, and FiO_2 can influence the transcutaneous CO_2 measurement. In general, such measurements tend to be higher in neonates with postnatal age > one week and body weight <1 kg compared BGA measurement.[12] In addition, the temperature of the transcutaneous probe can also affect the results.[3,12,13] Lower probe temperature of the transcutaneous device is associated with a decrease in the accuracy and precision of the instrument. The difference of the mean difference from the comparison of the transcutaneous measuring instrument with the BGA will increase as the electrode temperature decreases.[13] Measurements at a room with the temperature of 40 or 41°C can provide a correction of 12 to 15%,[17] while the standard deviation increased by about 5 mmHg when the setted electrode temperature on control monitor was lowered to 38, 39, and 40°C, indicating low reliability, i.e., reduced precision.[14]

Another factor that can affect the transcutaneous CO_2 pressure reading is the skin condition of the subject. Neonates' skin is immature, and especially so in premature neonates. The workings of the transcutaneous CO_2 pressure device can be influenced by imperfect skin keratinization process, considerable water loss through the skin, temperature instability, capillary blood flow and unstable skin metabolism, of premature neonates compared to babies born full term.[11,18-20] Other non-medical conditions that are thought to affect the results of the study are lack of instrument calibration between patients, not replacing parts and membranes in a timely manner, and an improperly connected attachment ring. In addition, relocation of the electrodes used during the examination also gave an unstable value during the stabilization time, as well as disturbing the infants.[17]

Blood gas analysis allows the clinician to assess pH, base excess, and HCO_3 as well as the metabolic condition of the neonate. The CO_2 obtained from examination using BGA taken at the same time as the transcutaneous CO_2 reading can be a reference for monitoring CO_2 pressure continuously.[14] However, the use of a transcutaneous CO_2 pressure device can minimize the need for blood draws, thereby reducing the risk of anemia and need for tranfusion.[3,17] The device is also useful for assessing continuous ventilation without causing excessive blood loss and excessive manipulation of the neonate's condition. A past study noted that the frequency of BGA examinations per day decreased from 3.9 to 2.9 times after monitoring with transcutaneous CO_2 (P=0.002), in 123 neonates intubated for > 48 hours and mean gestational age of 28.6 (SD 4.3) days.[3]

Although several related studies provide an overview of the factors that affect the accuracy and precision of the use of this transcutaneous CO_2 measuring instrument in neonates, our study had limitations in being able to test these factors, so our findings were limited to determining the accuracy and precision of the transcutaneous CO_2 device compared to BGA as the gold standard.

In conclusion, the transcutaneous CO_2 pressure device has good accuracy but poor precision based on our investigation. Despite its low precision, this tool can still be utilized therapeutically in regular medical practice because it has several flaws and a pretty broad bias. BGA remains the gold standard for measuring CO_2 pressure, thus, the transcutaneous device can be used in conjunction with treatment in the NICU. This technique can be used to continually measure CO_2 pressure, but it is not a substitute for BGA.[3]

Conflict of interest

None declared.

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