International Journal of Health Sciences and Research
Volume 14; Issue: 7; July 2024
Website: www.ijhsr.org
Research Protocol *ISSN: 2249-9571*

Comparison of Average Blood Gas Parameters Between Arterial Blood & Capillary Blood in Neonates: A Protocol for Systematic Review and Meta-analysis

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DOI: https://doi.org/10.52403/ijhsr.20240722

ABSTRACT

Blood gas sampling and acid-base determination are essential tools in evaluating, managing, and monitoring neonates with respiratory or circulatory issues, especially those receiving respiratory support. Arterial Blood Gas & Capillary Blood Gas are two types of blood gas tests done in the neonatal ICU. Arterial punctures are painful and may cause arterial injury, thrombosis with distal ischemia, haemorrhage and aneurysm formation. Capillary blood gas samples are easier to obtain and are a less invasive way of evaluating blood gas parameters in neonates. This study protocol outlines the methodology for collating evidence from multiple studies that compare capillary blood gas and arterial blood gas and will help to find out whether capillary blood gas could be used as a reliable alternative to arterial blood gas. The review will retrieve information from three major databases: PubMed, Scopus & Web of Science. Literature screening and data extraction will be completed by two authors independently. Authors will use Newcastle-Ottawa Scale & Joanna Brigg's Institute critical appraisal checklist to assess the included studies. Results will be visually represented through a forest plot, incorporating individual effect estimates, pooled estimates, and 95% confidence intervals. The EZR or STATA Software will be used to perform the meta-analysis. This systematic review will summarise the available evidence and contribute to our understanding in the controversy arising from conflicting studies on the reliability of capillary blood samples as a substitute to arterial samples.

Keywords: Blood gases; Meta-analysis; Neonates; Systematic review, pH, PCO2, PO2

INTRODUCTION

The cardiovascular system of the newborn undergoes many changes during the perinatal period [1]. Delayed cardiorespiratory transition leads to significant neonatal morbidity and mortality. Arterial blood gas (ABG) analysis is a common and vital invasive procedure

conducted in hospital intensive care units daily. It plays a crucial role in diagnosing and evaluating acutely ill patients. However, ABG sampling can be painful and distressing due to the highly innervated sampling locations and the need for multiple attempts to obtain samples. [2].

Capillary blood can be obtained through a nearly painless skin puncture using a lancet or automated incision device. This least-invasive, safest blood-collecting technique requires minimal training for healthcare personnel. Its simplicity, safety, and need for only small blood volumes (100 µL to 150 µL) make capillary blood a good substitute for arterial blood, especially in neonates where accessing arterial samples is challenging. The clinical value of capillary blood gas results hinges on how accurately the pH, PCO2, and PO2 of capillary blood mirror those of arterial blood [3].

Numerous studies have compared blood gas results from arterial and capillary samples, with mixed outcomes. In a 1990 study, Courtney et al. examined post-ductal arterial and capillary blood gas measurements and reviewed relevant literature. Their findings indicated that capillary blood gas measurements were not reliable predictors of arterial values in neonates [4]. There are conflicting results among studies regarding the reliability of the capillary blood gas method as a substitute for the arterial blood gas method. A systematic review, which addressed the comparison of arterial blood gas and capillary blood gas was previously done in adults. Compared to adults, neonates are more prone to severe complications of indwelling arterial catheters such as thrombosis, arterial injury and haemorrhage.

In summary, to prevent the possible complications and adverse effects of arterial catheters and puncture in neonates, it is important to investigate the reliability of capillary blood sampling method as a substitute to arterial blood sampling in blood gas analysis. However, the evidence investigating the reliability and accuracy of capillary blood gas method in previous studies seems to be inconsistent, warranting the present review. Therefore, this systematic review will summarise the best evidence and contribute to our understanding on the reliability of capillary blood samples as a substitute to arterial samples.

METHODOLOGY

This protocol was registered with PROSPERO [5] under the registration ID CRD42022335502 and was developed following the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocol (PRISMA-P).

Criteria for Included Studies

Types of Studies: Observational studies such as cohort studies, birth cohort studies and prospective case-control studies (1985 to 2022) will be included.

Types of Participants: Neonates, defined as infants in the first 4 weeks after birth, who were simultaneously subjected to both Arterial Blood Gas & Capillary Blood Gas analysis were included in the study. There were no restrictions on sex or nationality.

Types of comparison: The comparison groups are arterial blood gas (ABG) and capillary blood gas (CBG). ABG involves testing a blood sample collected from the artery of the newborn, while CBG is obtained by a skin puncture on the neonatal heel using a lancet or automated incision device.

Types of Outcomes: The primary outcomes are Acid-Base balance in blood (pH), Partial pressure of carbon dioxide (PCO_2) and Partial pressure of oxygen (PO_2)

Exclusion Criteria

Studies which were carried out in animal population and pregnant mothers in labour will be excluded. Studies which reported blood gas values using either of the two methods will be excluded. Studies which reported blood gas values obtained from the foetal scalp or cerebrospinal fluid will be excluded. Studies which did not provide sufficient data of the outcome measures will also be excluded. Case reports, case series

and other qualitative studies will be excluded.

Search Strategy

All relevant articles published in English will be searched for and retrieved from three databases: PubMed, Scopus, and Web of Science using comprehensive search terms. The search strategies will include both medical subject headings (MeSH) and free-text terms, tailored to each database. The PubMed search strategy is detailed in Table 1. Additionally, the reference lists of selected articles will be reviewed to identify pertinent studies not found in the database search. Other resources such as google scholar will also be searched for relevant articles that meet the criteria for inclusion.

Table 1. Search strategy developed in PubMed

Category	Search Term
Population	(((neonates) OR (infants [MeSH Terms])) OR (newborns[MeSH Terms])) OR (neonat*) OR newborn babies OR newborn baby OR baby OR infant
Control group	Artery
Comparator group	Capillary
Outcomes	(("Blood gases" OR "pH" OR "PO2" OR "PCO2" OR "PaCO2" OR "PcapCO2" OR "PaO2" OR "PcapO2") OR ("blood gas analysis")) OR ("Blood Gas Analysis"[Mesh])

Selection of Studies

The initial electronic database search will be performed to obtain all eligible studies based on our topic. First, duplicate literature will be excluded. At least two reviewers will independently screen the titles and abstracts to identify potentially eligible studies and exclude irrelevant ones. Any disagreements will be resolved through discussion and consensus between the two reviewers, or with the involvement of a third reviewer. Eligibility criteria will be based on the PECO approach, an acronym representing the population, exposure, comparator and outcome. P (population) of interest are neonates, the E (exposure) is arterial blood gas method, the C (comparator) is the capillary blood gas method & the O (outcomes) of interest are blood gas parameters: pH, PCO_2, & PO_2. Thereafter, the full text will be retrieved for those literatures that meet the standards and reviewed independently by the two reviewers for a final selection of studies for inclusion into the review. Figure 1 shows the process of literature screening in this review (PRISMA Flowchart).

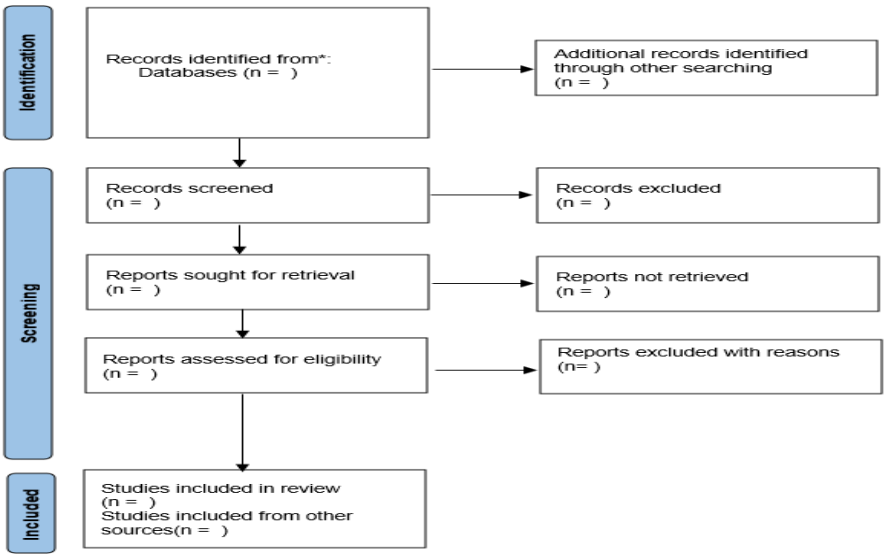

Figure 1: PRISMA Flowchart

Data Extraction.

Two authors will independently do the data extraction work from full text using a pre-structured data extraction sheet in e Microsoft Excel software. The data extraction form includes the first Authors' names, Year of study, Type of study (Study design), Place of study, Sample size, mean difference (MD), Standard deviation of MD, and Standard error of MD. If discrepancies arise in the data extraction results, they will be discussed or referred to a third party for adjudication.

Quality assessment and risk of bias

Quality assessment and risk of bias will be measured using the Newcastle Ottawa scale for cohort and case-control studies [6]. Cohort and case-control studies will be assigned a maximum score of nine stars. Studies scoring 7 or higher will be classified as high quality, while those scoring below 7 will be considered low quality. The Joanna Briggs Institute critical appraisal checklist will be used for observational cross-sectional studies [7]. Two authors will independently assess the quality of the studies, resolving any disagreements through discussion or consultation with a third reviewer.

Dealing with Missing Data

If necessary, data is missing, the author of the article will be contacted for relevant information. If the data remains unavailable, the study with missing data will be excluded from the analysis.

Data synthesis

Results will be visually represented through a forest plot, incorporating individual effect estimates, pooled estimates, and 95% confidence intervals. The I^2 statistic will be used to investigate heterogeneity [8]. When the estimate of heterogeneity I^2 is greater than 50%, it indicates a high level of heterogeneity, and a random effect model will be used. STATA /EZR software will be used for data analysis.

Assessment of publication biases

When more than ten articles are included, the assessment of reporting bias can be conducted by examining the symmetry of the funnel plot and Egger's test [8].

Subgroup Analysis

Subgroup analysis will be conducted based on clinical characteristics if there is significant heterogeneity among the included studies, considering factors like gestational age, health condition, and blood sample collection site.

Sensitivity Analysis

A sensitivity analysis will be conducted to evaluate the robustness of the pooled estimate by altering systematically removing the included studies based on the quality, sample size etc.

DISCUSSION

Blood gas analysis in neonates is the process of analysing blood gas parameters such as pH, partial pressure of oxygen, partial pressure of carbon dioxide and acid-base balance in blood. Blood gas analysis is frequently performed on neonates by medical professionals in order to monitor respiratory, circulatory and metabolic disorders in the perinatal and neonatal period. Blood can be drawn from either an artery or from capillary to perform blood gas analysis. Arterial blood gas (ABG) sampling is considered the gold standard for assessing a patient's acid-base and ventilatory status [9]. However, it is associated with several complications, including pain, arterial injury, thrombosis leading to distal ischemia, hemorrhage, and aneurysm formation. These risks are higher with repeated arterial punctures, especially in infants with small arteries. Neonatal blood gas parameters can be easily obtained through less invasive Capillary blood gas samplings.

In Germany, Capillary blood gas analysis is frequently used to assess blood gases in pediatric patients and is the primary method for adult patients. However, it is not utilized in only two scenarios: when the patient is in

shock or when continuous monitoring requires arterial catheter insertion [10].

This review has certain limitations such as there is a chance of heterogeneity among the studies due to changes in technologies and advancement in the equipment used for blood gas analysis. A subgroup analysis will also be done to address the heterogeneity due to different methods of blood sampling for analysis. The overall result of meta-analysis depends on the quality of the included studies so, if the study does not contain sufficient good-quality primary literature, meta-analysis results may be affected.

CONCLUSION

This protocol outlines methods for a systematic review and meta-analysis to summarize the best evidence, contributing to our understanding of the reliability of capillary blood samples as substitutes for arterial samples in neonates.

Declaration by Authors

Ethical Approval: Not applicable

Acknowledgement: We would like to thank Dr. Leela Kamath, Professor and Head of the Department of Neonatology at M.O.S.C Medical College, Kolenchery, Kerala, India, for her support.

Source of Funding: None

Conflict of Interest: The authors declare no conflict of interest.

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How to cite this article: Pooja S, Kalesh M Karun, Roseline K Madathil, Deepthy M S, Sheethal Joseph, Lintu M K. Comparison of average blood gas parameters between arterial blood & capillary blood in neonates: a protocol for systematic review and meta-analysis. *Int J Health Sci Res.* 2024; 14(7):170-174. DOI: *https://doi.org/10.52403/ijhsr.20240722*

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