

Sepsis

Current Awareness Bulletin

March 2024

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1. Effect of oropharyngeal colostrum therapy on neonatal sepsis in preterm neonates: A systematic review and meta-analysis

Authors: Anne, Rajendra Prasad;Kumar, Jogender;Kumar, Praveen and Meena, Jitendra

Publication Date: Mar ,2024

Journal: Journal of Pediatric Gastroenterology & Nutrition 78(3), pp. 471-487

Abstract: Various studies have shown that oropharyngeal colostrum application (OPCA) is beneficial to preterm neonates. We performed a systematic review and meta-analysis to assess whether OPCA reduces the incidence of culture-proven neonatal sepsis in preterm neonates. Randomized controlled trials comparing OPCA with placebo or standard care in preterm neonates were included. Medline, Embase, Web of Science, Cumulated Index to Nursing and Allied Health Literature, Scopus, and CENTRAL were searched for studies published up to June 15, 2023. We used the Cochrane Risk of Bias tool, version 2, for risk of bias assessment, the random-effects model (RevMan 5.4) for meta-analysis, and Gradepro software for assessing the certainty of evidence. Twenty-one studies involving 2393 participants were included in this meta-analysis. Four studies had a low risk of bias, whereas seven had a high risk. Oropharyngeal colostrum significantly reduced the incidence of culture-proven sepsis (18 studies, 1990 neonates, risk ratio [RR]: 0.78, 95% confidence interval [95% CI]: 0.65, 0.94), mortality (18 studies, 2117 neonates, RR: 0.73, 95% CI: 0.59, 0.90), necrotizing enterocolitis (NEC) (17 studies, 1692 neonates, RR: 0.59, 95% CI: 0.43, 0.82), feeding intolerance episodes (four studies, 445 neonates, RR: 0.59, 95% CI: 0.38, 0.92), and the time to full enteral feeding (19 studies, 2142 neonates, mean difference: -2 to 21 days, 95% CI: -3.44, -0.99 days). There was no reduction in intraventricular hemorrhage, retinopathy of prematurity, bronchopulmonary dysplasia, ventilator-associated pneumonia, neurodevelopmental abnormalities, hospital stay duration, time to full oral feeding, weight at discharge, pneumonia, and duration of antibiotic therapy. The certainty of the evidence was high for the outcomes of culture-positive sepsis and mortality, moderate for NEC, low for time to full enteral feeding, and very low for feeding intolerance. OPCA reduces culture-positive sepsis and mortality (high certainty), NEC (moderate certainty), and time to full enteral feeding (low certainty) in preterm neonates. However, scarcity of data from extremely premature infants limits the generalizability of these results to this population. Copyright © 2023 The Authors. Journal of Pediatric Gastroenterology and Nutrition published by Wiley Periodicals LLC on behalf of European Society for Pediatric Gastroenterology, Hepatology, and Nutrition and North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition.

2. Early warning scores for sepsis identification and prediction of in-hospital mortality in adults with sepsis: A systematic review and meta-analysis.

Authors: Chua, W. L.;Rusli, K. D. B. and Aitken, L. M.

Publication Date: 2024

Journal: Journal of Clinical Nursing (pagination), pp. Date of Publication: 20 Feb 2024

Abstract: AIM: The early warning scores (EWS), quick Sequential Organ Failure Assessment (qSOFA) and systemic inflammatory response syndrome (SIRS) criteria have been proposed as sepsis screening tools. This review aims to summarise and compare the performance of EWS with the qSOFA and SIRS criteria for predicting sepsis diagnosis and in-hospital mortality in patients with sepsis. DESIGN: A systematic review with meta-analysis. REVIEW METHODS: Seven databases were searched from January 1, 2016 until March 10, 2022. Study quality was assessed using the Quality Assessment of Diagnostic Accuracy Studies 2 tool. Sensitivity, specificity, likelihood ratios and diagnostic odd ratios were pooled by using the bivariate random effects model. Overall performance was summarised by using the hierarchical summary receiver-operating characteristics curve. This paper adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses of Diagnostic Test Accuracy Studies (PRISMA-DTA) guidelines. RESULT(S): Ten studies involving 52,474 subjects were included in the review. For predicting sepsis diagnosis, the pooled sensitivity of

EWS (65%, 95% CI: 55, 75) was similar to SIRS ≥ 2 (70%, 95% CI: 49, 85) and higher than qSOFA ≥ 2 (37%, 95% CI: 20, 59). The pooled specificity of EWS (77%, 95% CI: 64, 86) was higher than SIRS ≥ 2 (62%, 95% CI: 41, 80) but lower than qSOFA ≥ 2 (94%, 95% CI: 86, 98). Results were similar for the secondary outcome of in-hospital mortality. CONCLUSION(S): Although no one scoring system had both high sensitivity and specificity, the EWS had at least equivalent values in most measures of diagnostic accuracy compared with SIRS or qSOFA. IMPLICATIONS FOR THE PROFESSION: Healthcare systems in which EWS is already in place should consider whether there is any clinical benefit in adopting qSOFA or SIRS. NO PATIENT OR PUBLIC CONTRIBUTION: This systematic review did not directly involve patient or public contribution to the manuscript. Copyright © 2024 The Authors. Journal of Clinical Nursing published by John Wiley & Sons Ltd.

3. Efficacy and safety of short- vs. standard-course antibiotics for culture-negative neonatal sepsis: a systematic review and meta-analysis.

Authors: Devi, Risha; Priyadarshi, Mayank; Singh, Poonam; Chaurasia, Suman and Basu, Sriparna

Publication Date: Feb 07, 2024

Journal: Journal of Tropical Pediatrics 70(2)

Abstract: OBJECTIVES: To conduct a systematic review and meta-analysis of evidence from randomized controlled trials (RCTs) comparing a short course of antibiotics (2-4 days), to a standard course (5-7 days), for the treatment of culture-negative neonatal sepsis. METHODS: Relevant databases were searched for RCTs comparing short- vs. standard-course of antibiotics for culture-negative sepsis. The primary outcomes were mortality and treatment failure, defined as the reappearance of clinical signs suggestive of sepsis within 7 days of stoppage of antibiotics. Secondary outcomes included neurological impairment, duration of hospital stay, need for oxygen, respiratory support and double-volume exchange transfusion (DVET). RESULTS: Seven RCTs were included in the review with 729 neonates >30 weeks gestational age at birth. No mortality occurred in either of the groups (2 studies; 276 neonates). Treatment failure rates were similar in the short- and standard-course antibiotic groups [7 studies; 729 neonates; risk ratio (RR) = 1.01; 95% confidence interval (CI), 0.55 to 1.86; very low certainty]. The short course of antibiotics resulted in a shorter hospital stay [3 studies; 293 neonates; mean difference (MD), -2.46 days; 95% CI, -3.16 to -1.75]. There was no difference in the need for oxygen supplementation (2 studies; 258 neonates; RR, 1.40; 95% CI, 0.40 to 4.91), any respiratory support (2 studies; 258 neonates; RR, 1.04; 95% CI, 0.92 to 1.17) or DVET (2 studies; 258 neonates; RR, 1.29; 95% CI, 0.56 to 2.95). CONCLUSION: Very-low certainty evidence suggests that a short antibiotic course, compared to a standard course, does not affect treatment failure rates in culture-negative neonatal sepsis. There is a need for well-designed RCTs powered enough to assess critical outcomes such as mortality and neurological sequelae to generate stronger evidence and inform guidelines. PROSPERO REGISTRATION NUMBER: CRD42023437199. Copyright © The Author(s) [2024]. Published by Oxford University Press. All rights reserved. For permissions, please email: journals.permissions@oup.com; plain-language-summary Prolonged antibiotic usage has been associated with increased mortality and morbidity in neonates. The standard practice in culture-negative neonatal sepsis has been to administer antibiotics for 5-7 days, based on expert consensus. In this systematic review, a short course of antibiotics (2-4 days), in comparison to a standard course (5-7 days), did not affect the treatment failure rates in culture-negative neonatal sepsis. However, the certainty of evidence was too low to make robust conclusions. There is a need for well-designed large trials to generate stronger evidence and inform guidelines. Language: English

4. Sepsis among Neonates Admitted to a Neonatal Intensive Care Unit in a Tertiary Care Centre.

Authors: Devkota, Kanchan; Kanodia, Piush and Joshi, Bibek

Publication Date: Feb 24, 2024

Journal: Jnma, Journal of the Nepal Medical Association 62(270), pp. 76-78

Abstract: Introduction: Neonatal sepsis is a condition that carries a high risk for mortality as neonates rapidly transition to extra-uterine life and are subjected to various risk factors. Sepsis prevalence can be reduced by good antenatal care, early detection and treatment of risk factors. The study aimed to find out the prevalence of sepsis among neonates admitted to a neonatal intensive care unit in a tertiary care centre. Methods: This is a descriptive cross-sectional study conducted among neonates admitted to the neonatal care unit of a tertiary care centre after obtaining ethical approval from the Institutional Review Committee. Data of patients admitted from 12 December 2022 to 30 June 2023 was collected from hospital records. Symptomatic patients admitted to the neonatal intensive care unit were included and those with incomplete data were excluded from the study. A convenience sampling method was used. The point estimate was calculated at a 95% Confidence Interval. Results: Among 379 neonates, the prevalence of sepsis was 138 (36.41%) (28.38-44.44, 95% Confidence Interval). A total of 98 (71.01%) had early-onset neonatal sepsis and 40 (28.99%) had late-onset neonatal sepsis. Conclusions: The prevalence of neonatal sepsis was found to be lower than other studies done in similar settings. Keywords: neonate; neonatal sepsis; prematurity; prevalence.

5. Balanced crystalloids versus isotonic saline in pediatric sepsis: a comprehensive systematic review and meta-analysis.

Authors: Mhanna, Asmaa;Beran, Azizullah;Srour, Omar;Mhanna, Mohammed;Assaly, Ahmad;Elsayed, Abdelrahman;Horen, Nicholas G. and Assaly, Ragheb

Publication Date: 2024

Journal: Baylor University Medical Center Proceedings 37(2), pp. 295-302

Abstract: Purpose: We conducted a comprehensive meta-analysis to compare the effects of balanced crystalloids (BC) and isotonic saline (IS) in pediatric sepsis. Methods: A systematic search was performed for studies comparing BC and IS in pediatric sepsis. Outcomes included mortality, acute kidney injury (AKI), need for renal replacement therapy (RRT), hospital length of stay (LOS), and pediatric intensive care unit (PICU) LOS. A random-effect models was used to calculated pooled odds ratios (OR) and mean differences (MD) with 95% confidence intervals (CIs). Results: The analysis included six studies with 8753 children. BC demonstrated significant reductions in overall mortality (OR 0.84, 95% CI 0.71 to 0.98, $P = 0.03$, $I^2 = 0\%$) and AKI (OR 0.74, 95% CI 0.57 to 0.96, $P = 0.03$, $I^2 = 37\%$) compared to IS. RRT need was similar between the BC and IS groups (OR 0.79, 95% CI 0.60 to 1.02, $P = 0.07$, $I^2 = 0\%$). Hospital and PICU LOS did not differ significantly. However, subgroup analysis of randomized controlled trials revealed significantly shorter hospital LOS in the BC group (mean difference -0.66 days, 95% CI -1.10 to -0.23, $P = 0.003$, $I^2 = 0\%$). Conclusion: Our meta-analysis demonstrates that using BC in pediatric sepsis is associated with reduced mortality, AKI, and hyperchloremia rates compared to IS, while maintaining similar hospital and PICU LOS. Large-scale randomized controlled trials are needed to validate these findings. Copyright © 2024 Baylor University Medical Center.

6. Medical Emergency Team call within 24 h of medical admission with a focus on sepsis: a retrospective review.

Authors: Nolan, J.;Mackay, I.;Nolan, T. and de Looze, J.

Publication Date: 2024

Journal: Internal Medicine Journal (pagination), pp. Date of Publication: 2024

Abstract: Background and Aims: Clinical deterioration within the first 24 h of patient admission triggering a Medical Emergency Team (MET) call is a common occurrence. A greater understanding of these events, with a focus on the recognition and management of sepsis, could lead to quality improvement interventions. Method(s): A retrospective observational review of general and subspecialty medical admissions triggering a MET call within 24 h of admission at a quaternary Australian hospital. Result(s): 2648 MET calls occurred (47.9/1000 admissions), 527 (20% of total MET

events, 9.5/1000 admissions) within 24 h of admission, with the trigger more likely to be hypotension (odds ratio: 1.5, P = 0.0013). There were 263 MET calls to 217 individual medical patients within 24 h of admission, of which 84 (38.7%) were admitted with suspected infection, 69% of which fulfilled sepsis criteria. Of these, 36.2% received antimicrobial therapy within the recommended timeframe and 39.6% received antibiotics in line with hospital guidelines. Sepsis was initially missed in 11% of patients. Afferent limb failure occurred in 29% of patients with 40.5% experiencing a failure of the ward-based response to deterioration prior to MET call. Median hospital length of stay was increased in patients admitted with suspected infection (7 vs 5 days, P = 0.015) and in those with sepsis not receiving antimicrobial therapy within guideline timeframes (9 vs 4 days, P = 0.017). Conclusion(s): There is a significant opportunity to improve care for patients who trigger a MET within 24 h of admission. This study supports the implementation of a hospital sepsis management guideline. Copyright © 2024 The Authors. Internal Medicine Journal published by John Wiley & Sons Australia, Ltd on behalf of Royal Australasian College of Physicians.

7. Sepsis among Adults Admitted to Intensive Care Unit of a Tertiary Care Centre

Authors: Shrestha, Kundu;Vaidya, Sagun Ram;Shrestha, Keny;Shrestha, Surendra Man;Rawal, Prabhat and Dangol, Shova

Publication Date: Feb 24 ,2024

Journal: Jnma, Journal of the Nepal Medical Association 62(270), pp. 85-88

Abstract: Introduction: Sepsis is a syndrome that starts with an infection, causes organ dysfunction, and leads to death is a global health issue in critically ill patients. While its epidemiology is well-known in high-income countries, it is poorly understood in low- and middle-income countries, including Nepal. This study aimed to find out the prevalence of sepsis among adults admitted to the intensive care unit of a tertiary care centre. Methods: This descriptive cross-sectional study was conducted among adults admitted to the intensive care unit after obtaining ethical approval from the Ethical Review Board. Data was collected from 11 January 2022 and 29 December 2022 from hospital records. A convenience sampling method was used. The point estimate was calculated at a 95% Confidence Interval. Results: Among 195 patients, the prevalence of sepsis was seen in 74 (37.95%) (31.14-44.76, 95% Confidence Interval). Septic patients had a median age of 44 (interquartile range: 33.75+/-60.25) years. A total of 40 (54.05%) were male. A total of 28 (37.84%) septic patients were identified with ≥ 2 diagnoses, while 9 (12.16%) had ≥ 2 comorbidities. Conclusions: The prevalence of sepsis among adult patients admitted to the intensive care unit was higher as compared to other studies done in other international studies. Keywords: intensive care units; prevalence; sepsis.

8. Role of corticosteroids in the treatment of critically ill sepsis patients: a meta-analysis review.

Authors: Song, Y.;Hao, J. and Liu, Y.

Publication Date: 2024

Journal: Inflammopharmacology (pagination), pp. Date of Publication: 2024

Abstract: Objective: It was to systematically evaluate the effect of corticosteroids on 28d all-cause mortality (ACM), in-hospital death rate, and ICU death rate in critically ill sepsis patients. Method(s): PubMed, Embase, and Medline databases were used to screen the published literatures on the therapeutic effect of corticosteroids in the treatment of critically ill sepsis patients. After evaluating the quality of the included literatures, RevMan 5.3 software was used for meta-analysis. 4524 literatures regarding the application of corticosteroids to treat critically ill sepsis patients were preliminarily searched. After screening was carried out, 9 literatures were finally included. 2,850 patients were treated with corticosteroids and 2867 patients were treated with placebo. Result(s): The meta-analysis of the effect of corticosteroids versus placebo on 28dACM showed [OR = 0.87, 95% CI 0.78-0.98, Z = 2.22, P = 0.03], P Result(s): The meta-analysis of the effect of corticosteroids versus placebo on 28dACM showed [OR = 0.87, 95% CI 0.78-0.98, Z = 2.22, P = 0.03], P Result(s): The meta-analysis of

the effect of corticosteroids versus placebo on 28dACM showed [OR = 0.87, 95% CI 0.78-0.98, Z = 2.22, P = 0.03], P Result(s): The meta-analysis of the effect of corticosteroids versus placebo on 28dACM showed [OR = 0.87, 95% CI 0.78-0.98, Z = 2.22, P = 0.03], P Conclusion(s): In summary, corticosteroids can reduce the death rate of critically ill sepsis patients to a certain extent and have good clinical application value. Copyright © The Author(s), under exclusive licence to Springer Nature Switzerland AG 2024.

9. Maresins as novel anti-inflammatory actors and putative therapeutic targets in sepsis

Authors: Sun, Yan;Sun, Shujun;Chen, Pu;Dai, Yan;Yang, Dong;Lin, Yun and Yi, Lisha

Publication Date: Apr ,2024

Journal: Pharmacological Research 202, pp. 107113

Abstract: Sepsis, a complex clinical syndrome characterized by an exaggerated host response to infection, often necessitates hospitalization and intensive care unit admission. Delayed or inaccurate diagnosis of sepsis, coupled with suboptimal treatment strategies, can result in unfavorable outcomes, including mortality. Maresins, a newly discovered family of lipid mediators synthesized from docosahexaenoic acid by macrophages, have emerged as key players in promoting inflammation resolution and the termination of inflammatory processes. Extensive evidence has unequivocally demonstrated the beneficial effects of maresins in modulating the inflammatory response associated with sepsis; however, their bioactivity and functions exhibit remarkable diversity and complexity. This article presents a comprehensive review of recent research on the role of maresins in sepsis, aiming to enhance our understanding of their effectiveness and elucidate the specific mechanisms underlying their actions in sepsis treatment. Furthermore, emerging insights into the management of patients with sepsis are also highlighted. Copyright © 2024 The Authors. Published by Elsevier Ltd.. All rights reserved.

10. Effect of delayed antibiotic use on mortality outcomes in patients with sepsis or septic shock: A systematic review and meta-analysis

Authors: Tang, Fajuan;Yuan, Hongxiu;Li, Xihong and Qiao, Lina

Publication Date: Mar 10 ,2024

Journal: International Immunopharmacology 129, pp. 111616

Abstract: BACKGROUND: The use of antibiotics is essential in the treatment of sepsis and septic shock, and delaying their administration may impact patient mortality outcomes. However, there is currently a controversial debate surrounding this issue. In this meta-analysis, we aimed to explore the association between delayed antibiotic use and mortality in patients with sepsis and septic shock. METHODS: A systematic search was conducted on PubMed, EMBASE, Web of Science, and Cochrane Library to identify relevant studies published from 2013 to 2023. These studies focused on patients with sepsis or septic shock and provided information on various antibiotic administration times and mortality rates. Two independent reviewers screened and extracted the data. The quality of each study was assessed using the Newcastle-Ottawa Scale, and the collected data were analyzed using STATA 15.1 software. RESULTS: A total of 29 studies were included, consisting of 17 prospective cohort studies and 12 retrospective cohort studies. The meta-analysis showed that compared to administration of antibiotics within 1 h, each hour of delay in antibiotic administration increased the in-hospital mortality (IHM) (OR = 1.041, 95 % CI: 1.021-1.062), and ministration of antibiotics after 1 h increased the IHM (OR = 1.205, 95 % CI: 1.123-1.293). There was no significant change in the 28-day mortality (OR = 1.297, 95 % CI: 0.882-1.906), 90-day mortality (OR = 1.172, 95 % CI: 0.846-1.622), and 1-year mortality (OR = 0.986, 95 % CI: 0.422-2.303). Administration of antibiotics within 3 h may reduce the IHM (OR = 1.297, 95 % CI: 1.011-1.664, p = 0.041), while administration of antibiotics within 6 h showed no significant association with the IHM. CONCLUSION: The administration of antibiotics beyond 1 h after emergency triage or disease identification is strongly associated with an increased

IHM in patients with sepsis or septic shock, and each hour of delay in antibiotic administration may be associated with an increase in the IHM. Furthermore, the use of antibiotics identification beyond 3 h after emergency triage / sepsis or septic shock may also increase the IHM. Copyright © 2024. Published by Elsevier B.V.

11. Advances in metabolic reprogramming of renal tubular epithelial cells in sepsis-associated acute kidney injury

Authors: Wang, Tiantian;Huang, Ying;Zhang, Xiaobei;Zhang, Yi and Zhang, Xiangcheng

Publication Date: 2024

Journal: Frontiers in Physiology 15, pp. 1329644

Abstract: Sepsis-associated acute kidney injury presents as a critical condition characterized by prolonged hospital stays, elevated mortality rates, and an increased likelihood of transition to chronic kidney disease. Sepsis-associated acute kidney injury suppresses fatty acid oxidation and oxidative phosphorylation in the mitochondria of renal tubular epithelial cells, thus favoring a metabolic shift towards glycolysis for energy production. This shift acts as a protective mechanism for the kidneys. However, an extended reliance on glycolysis may contribute to tubular atrophy, fibrosis, and subsequent chronic kidney disease progression. Metabolic reprogramming interventions have emerged as prospective strategies to counteract sepsis-associated acute kidney injury by restoring normal metabolic function, offering potential therapeutic and preventive modalities. This review delves into the metabolic alterations of tubular epithelial cells associated with sepsis-associated acute kidney injury, stressing the importance of metabolic reprogramming for the immune response and the urgency of metabolic normalization. We present various intervention targets that could facilitate the recovery of oxidative phosphorylation-centric metabolism. These novel insights and strategies aim to transform the clinical prevention and treatment landscape of sepsis-associated acute kidney injury, with a focus on metabolic mechanisms. This investigation could provide valuable insights for clinicians aiming to enhance patient outcomes in the context of sepsis-associated acute kidney injury. Copyright © 2024 Wang, Huang, Zhang, Zhang and Zhang.

12. The 'analysis of gene expression and biomarkers for point-of-care decision support in Sepsis' study; temporal clinical parameter analysis and validation of early diagnostic biomarker signatures for severe inflammation and sepsis-SIRS discrimination.

Authors: Szakmany, Tamas;Fitzgerald, Eleanor;Garlant, Harriet N.;Whitehouse, Tony;Molnar, Tamas;Shah, Sanjoy;Tong, Dong Ling;Hall, Judith E.;Ball, Graham R. and Kempself, Karen E.

Publication Date: 2023

Journal: Frontiers in Immunology 14, pp. 1308530

Abstract: Introduction: Early diagnosis of sepsis and discrimination from SIRS is crucial for clinicians to provide appropriate care, management and treatment to critically ill patients. We describe identification of mRNA biomarkers from peripheral blood leukocytes, able to identify severe, systemic inflammation (irrespective of origin) and differentiate Sepsis from SIRS, in adult patients within a multi-center clinical study. Methods: Participants were recruited in Intensive Care Units (ICUs) from multiple UK hospitals, including fifty-nine patients with abdominal sepsis, eighty-four patients with pulmonary sepsis, forty-two SIRS patients with Out-of-Hospital Cardiac Arrest (OOHCA), sampled at four time points, in addition to thirty healthy control donors. Multiple clinical parameters were measured, including SOFA score, with many differences observed between SIRS and sepsis groups. Differential gene expression analyses were performed using microarray hybridization and data analyzed using a combination of parametric and non-parametric statistical tools. Results: Nineteen high-performance, differentially expressed mRNA biomarkers were identified between control and combined SIRS/Sepsis groups ($FC > 20.0$, $p < 0.99$). Twenty entities, termed 'SIRS or Sepsis' (SdegreeS) biomarkers, were differentially expressed between sepsis and SIRS ($FC > 2.0$, p -value < 0.99). Twenty entities, termed 'SIRS or Sepsis' (SdegreeS)

biomarkers, were differentially expressed between sepsis and SIRS ($FC > 2.0$, p -value Discussion: The best performing signature for discriminating sepsis from SIRS was CMTM5/CETP/PLA2G7/MIA/MPP3 ($AUC = 0.9758$). The I_{deg} and S_{deg} signatures performed variably in other independent gene expression datasets, this may be due to technical variation in the study/assay platform. Copyright © 2024 Szakmany, Fitzgerald, Garland, Whitehouse, Molnar, Shah, Tong, Hall, Ball and Kempell.

13. Unraveling the impact of nitric oxide, almitrine, and their combination in COVID-19 (at the edge of sepsis) patients: a systematic review.

Authors: Wang, Ying; Yu, Qian; Tian, Yuan; Ren, Shiyong; Liu, Liping; Wei, Chaojie; Liu, Renli; Wang, Jing; Li, Dong and Zhu, Kun

Publication Date: 2023

Journal: Frontiers in Pharmacology 14, pp. 1172447

Abstract: Introduction: During the coronavirus disease 2019 (COVID-19) pandemic, a large number of critically ill and severe COVID-19 patients meet the diagnostic criteria for sepsis and even septic shock. The treatments for COVID-19 patients with sepsis are still very limited. For sepsis, improving ventilation is one of the main treatments. Nitric oxide (NO) and almitrine have been reported to improve oxygenation in patients with "classical" sepsis. Here, we conducted a systematic review and meta-analysis to evaluate the efficacy and safety of NO, almitrine, and the combination of both for COVID-19 (at the edge of sepsis) patients. Method: A systematic search was performed on Embase, PubMed, the Cochrane Library, the Web of Science, Wanfang Data, and China National Knowledge Infrastructure. Randomized clinical trials, cohort studies, cross-sectional studies, case-control studies, case series, and case reports in COVID-19 patients with suspected or confirmed sepsis were performed. Study characteristics, patient demographics, interventions, and outcomes were extracted from eligible articles. Results: A total of 35 studies representing 1,701 patients met eligibility criteria. Inhaled NO did not affect the mortality (OR 0.96, 95% CI 0.33-2.8, $I^2 = 81\%$, very low certainty), hospital length of stay (SMD 0.62, 95% CI 0.04-1.17, $I^2 = 83\%$, very low certainty), and intubation needs (OR 0.82, 95% CI 0.34-1.93, $I^2 = 56\%$, very low certainty) of patients with COVID-19 (at the edge of sepsis). Meanwhile, almitrine did not affect the mortality (OR 0.44, 95% CI 0.17-1.13, low certainty), hospital length of stay (SMD 0.00, 95% CI -0.29-0.29, low certainty), intubation needs (OR 0.94, 95% CI 0.5-1.79, low certainty), and SAEs (OR 1.16, 95% CI 0.63-2.15, low certainty). Compared with pre-administration, the PaO_2/FiO_2 of patients with NO (SMD -0.87, 95% CI -1.08-0.66, $I^2 = 0\%$, very low certainty), almitrine (SMD -0.73, 95% CI -1.06-0.4, $I^2 = 1\%$, very low certainty), and the combination of both (SMD -0.94, 95% CI -1.71-0.16, $I^2 = 47\%$, very low certainty) increased significantly. Conclusion: Inhaled NO, almitrine, and the combination of the two drugs improved oxygenation significantly, but did not affect the patients' mortality, hospitalization duration, and intubation needs. Almitrine did not significantly increase the patients' SAEs. Well-designed high-quality studies are needed for establishing a stronger quality of evidence. Systematic Review

Registration: https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=367667, identifier CRD42022367667. Copyright © 2024 Wang, Yu, Tian, Ren, Liu, Wei, Liu, Wang, Li and Zhu.

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