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Acetazolamide in weaning from mechanical ventilation in hypercapnic respiratory failure

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ADMINISTRATIVE INFORMATION

Support - No funding was received for conducting this study.

Review Stage at time of this submission - Data analysis.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 26 July 2023 and was last updated on 26 July 2023.

INTRODUCTION

Review question / Objective To assess the effectiveness of acetazolamide in weaning from the mechanical ventilator in patients with hypercapnic respiratory failure secondary to either COPD, Asthma, or OHS and concurrent metabolic alkalosis.

Condition being studied Hypercapnic respiratory failure - Hypercapnic respiratory failure consists of a group of disorders where the common feature is reduced removal of carbon dioxide from the body. The lesion can be in the central respiratory center, neuromuscular axis, or airway. As a result of this heterogeneity, weaning from a ventilator can be particularly challenging in these patients. One of the major causes of hypercapnic respiratory failure is Chronic obstructive airway disease (COPD) and worldwide, COPD is 4th common cause of death; acute and seasonal exacerbation of which may necessitate hospital stay and in severe cases may require mechanical ventilation. Hence it causes a significant socioeconomic burden to the patient and the healthcare facilities.

METHODS

Search strategy We conducted a comprehensive search of MEDLINE, EMBASE, CENTRAL, and PubMed over 3 months from March 2023 to June 4, 2023
Terms:
("Acetazolamide"[MeSH Terms] OR "Acetazolamide"[Text Word]) AND ("Respiratory Insufficiency"[MeSH Terms] OR "pulmonary disease, chronic obstructive"[MeSH Terms] OR "obesity hypoventilation syndrome"[MeSH Terms] OR "acidosis, respiratory/therapy"[MeSH Terms] OR "Hypercapnia"[MeSH Terms] OR ("Type 2 respiratory failure"[Text Word] OR "hypercapn*"[Text Word] OR "Hypoventilation"[All Fields] OR "respiratory muscle weak*"[Text Word] OR "Chronic obstructive pulmonary disease"[Text Word] OR "obesity hypoventilation syndrome"[Text Word])) AND ("Ventilator Weaning"[MeSH Terms]

OR "respiration, artificial"[MeSH Terms] OR "ventilators, mechanical"[MeSH Terms] OR ("ventilal*"[Text Word] OR "Artificial respiration"[Text Word] OR "Non-invasive ventilation"[Text Word] OR "mechanical ventilation"[Text Word] OR "Artificial respiration"[Text Word]))
For EMBASE:
('Acetazolamide'/exp OR 'Acetazolamide':ti,ab,kw) AND ('Ventilator Weaning'/exp OR 'Respiration, Artificial'/exp OR 'Ventilators, Mechanical'/exp OR'Ventilal*':ti,ab,kw OR 'artificial respiration':ti,ab,kw OR 'Non-invasive ventilation':ti,ab,kw OR 'mechanical ventilation':ti,ab,kw 'Ventilal*':ti,ab,kw OR (('artificial' NEAR/2 'respiration'):ti,ab,kw) OR ((('Non' NEAR/2 'invasive' NEAR/2 'ventilation'):ti,ab,kw) OR (('mechanical' NEAR/2 'ventilation'):ti,ab,kw)) AND ('Respiratory Insufficiency'/exp OR 'Pulmonary Disease, Chronic Obstructive'/exp OR 'Obesity Hypoventilation Syndrome'/exp OR 'Acidosis, Respiratory/therapy'/exp OR 'Hypercapnia'/exp OR 'Type 2 respiratory failure':ti,ab,kw OR 'Hypercapn*':ti,ab,kw OR 'Hypoventilation' OR 'Respiratory muscle weak*':ti,ab,kw OR 'Chronic obstructive pulmonary disease':ti,ab,kw OR 'Obesity hypoventilation syndrome':ti,ab,kw OR (('type' NEAR/2 '2' NEAR/2 'respiratory' NEAR/2 'failure'):ti,ab,kw) OR 'Hypercapn*':ti,ab,kw OR 'Hypoventilation'):ti,ab,kw OR (('Respiratory' NEAR/2 'muscle' NEAR/2 'weak'):ti,ab,kw) OR (('Chronic' NEAR/2 'obstructive' NEAR/2 'pulmonary' NEAR/2 'disease'):ti,ab,kw) OR (('Obesity' NEAR/2 'hypoventilation' NEAR/2 'syndrome"):ti,ab,kw)).

Participant or population Mechanically ventilated patients with hypercapnic respiratory failure secondary to either COPD, Asthma, or OHS and concurrent metabolic alkalosis.

Intervention Acetazolamide of any dose for any length of time.

Comparator Usual care with or without a placebo.

Study designs to be included RCTs and Observational Trials.

Eligibility criteria None.

Information sources Databases: MEDLINE, EMBASE, CENTRAL, and PubMed.

Main outcome(s) Duration of mechanical ventilation, weaning duration, duration of ICU stay, the requirement of NIV post-extubation, and ICU mortality.

Additional outcome(s) Change in blood gas parameters such as PaCO2, HCO3, PH, and PF ratio before and after the intervention.

Quality assessment / Risk of bias analysis Risk of bias will be assessed in RCTs using The Cochrane Collaboration's Risk of Bias tool, whereas, in non-RCTs, the Risk of Bias will be assessed by the Newcastle-Ottawa Scale.

Strategy of data synthesis All analysis will be done in R software (version 3.3.1, R Foundation for Statistical Computing). Dichotomous outcomes are presented as Odds ratio and risk difference (RD), whereas mean differences (MDs) or standardized Mean difference in the case of continuous outcomes, both with 95% CIs.
Primary outcomes such as duration of ICU stay, weaning duration and duration of hospital stay are inherently skewed data, hence transforming the reported median and IQR into mean and Standard deviation may be erroneous. Hence we will use a median-based approach for analyzing these variables. If both mean and median data were available, median-based analysis will be used, whereas, if all the studies provide mean, the classic mean-based analysis will be used for meta-analysis. Random-effects model will be applied to calculate the summary MD/SMD/OR/RD and its 95%CI, and the I^2 statistic will be utilized to assess the level of statistical heterogeneity. If the P value<0.05, it means that the study has statistical significance. Funnel plots will be used to investigate publication bias if the number of included studies is greater than ten.

Subgroup analysis Based on the number of available studies and total sample size, we propose to do a subgroup analysis of patients with hypercapnic respiratory failure based on their etiology (COPD, Asthma, OHS).

Sensitivity analysis Primary outcomes such as duration of ICU stay, weaning duration, and duration of hospital stay, will also be analyzed and summarized by mean-based methods.

Language restriction Yes, Only studies in English language are chosen.

Country(ies) involved India.

Keywords Acetazolamide, COPD, OHS, Hypercapnic respiratory failure, Weaning.

Contributions of each author

Author 1 - Hariswar Pari Thenmozhi - Concept, Study design, Data collection, Study analysis and Manuscript drafting.
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Author 2 - Venkateswaran Ramanathan - Concept, Study design, and Manuscript drafting.
Author 3 - Melvin George - Manuscript drafting.
Author 4 - Shivani kshirsagar - Data collection and Manuscript drafting.
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