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Review Article

Glucocorticoid Treatment and Hyperglycaemia in People Living with Chronic Obstructive Pulmonary Disease: Systematic Review and Meta-analysis

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Abstract

Chronic Obstructive Pulmonary Disease (COPD) is a significant global health concern, often requiring systemic glucocorticoid treatment during acute exacerbations. However, glucocorticoid use is associated with the development of hyperglycaemia. This study aimed to assess the prevalence of hyperglycaemia in COPD patients treated with systemic glucocorticoids. A comprehensive search of electronic databases was conducted, yielding 18 studies for meta-analysis. The pooled prevalence of hyperglycaemia was 42% (95% CI: 31%-53%), with substantial heterogeneity among studies (I^2=97.4%, p<0.001). Subgroup analysis suggested varying prevalence based on study design, publication year, age, BMI, and baseline diabetes status. These findings underscore the importance of monitoring and managing hyperglycaemia in COPD patients receiving glucocorticoid therapy.

Keywords: Chronic Obstructive Pulmonary Disease (COPD); Glucocorticoid; Randomised Controlled Trials (RCTs)

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a major public health problem and the third leading cause of death globally in 2022. Acute exacerbations of COPD are treated with systemic glucocorticoids among other therapies. Glucocorticoid treatment is associated with new-onset hyperglycaemia.

The aim was to assess the prevalence of hyperglycaemia in people treated with systemic glucocorticoids for COPD (Kholis FN, 2023).

LITERATURE REVIEW

We searched the following electronic databases: PubMed, EMBASE, Cochrane Library and ClinicalTrials.gov until 9 Nov 2023 (Koarai A, 2024).

Inclusion criteria were: adults (aged ≥ 18 years) diagnosed with COPD, with or without documented diabetes at baseline, systemic use of glucocorticoids equivalent to prednisolone ≥ 5 mg daily for ≥ 3 days with or without a concomitant use of topical glucocorticoids, Randomised Controlled Trials (RCTs) and observational analyses of

RCTs, any observational studies and peer-reviewed publications. Hyperglycaemia was defined as a blood glucose concentration above a study-specific cut-off. We extracted data on study and participant characteristics, exposure, and outcome of interest (Abroug F, 2014).

We performed a random-effects meta-analysis to calculate a pooled estimate of study-specific prevalence estimates of hyperglycaemia. Prevalence was expressed as the proportion of people who developed hyperglycaemia (new or worsening in those with diabetes at baseline) among all people exposed to systemic glucocorticoids.

Estimates were not reported by diabetes status in included studies (Hu HS, 2022). We estimated heterogeneity using I2 statistic for overall and, X^2 and p-value for heterogeneity between subgroups (Aldibbiat AM, 2020).

RESULTS

We included 18 studies (11 RCTs,7 observational studies). The majority (56%) were conducted in North America or Europe. There were N=2861 participants in all meta-analysed studies; all were exposed to systemic glucocorticoids, and N=1165 (41%) developed new or worsening hyperglycaemia in those who had diabetes at baseline. Median follow-up ranged from 4 days to 5 years. The pooled period prevalence of hyperglycaemia was 42% (95%CI:31%-53%).

There was a high heterogeneity between studies, I^2=97.4%, p<0.001 (Mao Y, 2022). The prevalence by subgroup was: study design, 29% (16%-44%) *vs.* 49% (35%-64), observational *vs.* RCTs, p=0.058 ; year of publication, 27% (9%-45%) *vs.* 46% (35%-57%), before 2010 *vs.* in/after 2010, p=0.080; age, 44% (29%-59%) *vs.* 39% (29%-53%), age<69.6 years (median across studies) *vs.* ≥ 69.9 years, p=0.629; Body Mass Index (BMI) 46% (37%-54%) *vs.* 100% (95%CI 85%-100%), BMI<30 kg/m^2 *vs.* ≥ 30 kg/m^2 and proportion of people with diabetes at baseline 33% (21%-45%) *vs.* 51% (33%-68%), <19.4% (median across studies) *vs.* ≥ 19.4%, p=0.106 (**Figure 1**).

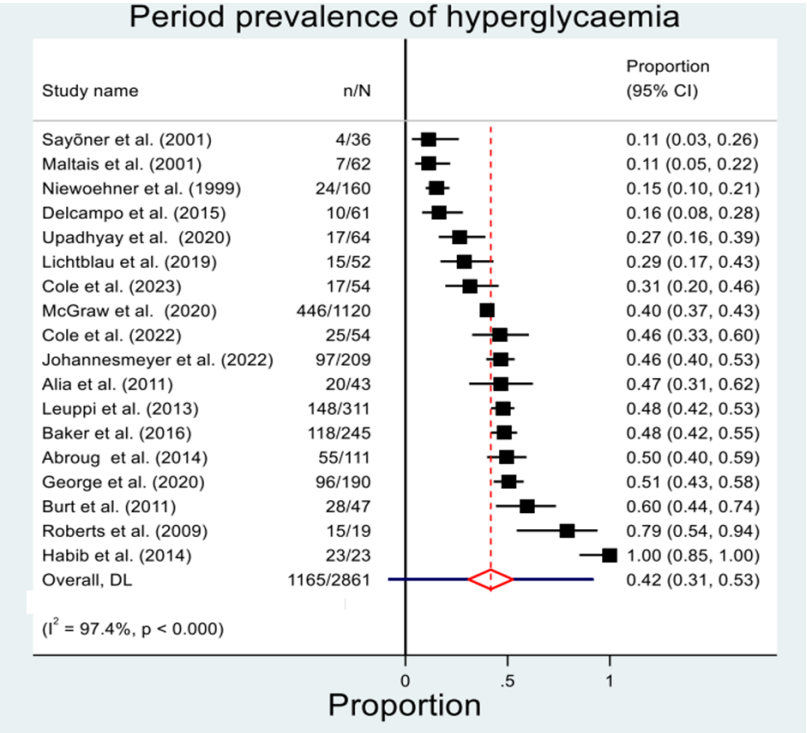

Figure 1. Period prevalence of glucocorticoid-induced hyperglycaemia in patients with COPD.

DISCUSSION

The findings of this study highlight the significant prevalence of hyperglycaemia among patients with COPD who undergo treatment with systemic glucocorticoids during acute exacerbations. The pooled prevalence of hyperglycaemia was found to be substantial, with 42% of individuals developing new or worsening hyperglycaemia.

This underscores the importance of monitoring glucose levels in COPD patients receiving glucocorticoid therapy.

One notable aspect of the study was the considerable heterogeneity observed among the included studies. This variability may stem from differences in study design, patient demographics, glucocorticoid dosing regimens, and other factors. Such diversity underscores the complexity of managing COPD exacerbations and the need for personalized approaches to treatment.

Subgroup analyses revealed potential factors influencing the prevalence of hyperglycaemia. Observational studies tended to report higher prevalence rates compared to Randomized Controlled Trials (RCTs), suggesting a need for

cautious interpretation of observational data. Additionally, there was a trend towards higher prevalence rates in studies published after 2010, possibly indicating changes in clinical practice or patient populations over time.

Age, Body Mass Index (BMI), and baseline diabetes status also appeared to influence hyperglycaemia prevalence to some extent, although the differences were not statistically significant in all cases. Older age and higher BMI were associated with slightly higher prevalence rates, consistent with known risk factors for glucose dysregulation. Furthermore, a higher proportion of individuals with diabetes at baseline correlated with increased prevalence, highlighting the interplay between pre-existing metabolic conditions and glucocorticoid-induced hyperglycaemia.

Despite these insights, several limitations should be considered when interpreting the findings. The reliance on study-specific definitions of hyperglycaemia and variability in glucose monitoring protocols may have introduced measurement bias. Additionally, the duration of follow-up varied widely across studies, potentially impacting the detection of hyperglycaemic events.

CONCLUSION

In conclusion, this study provides valuable insights into the prevalence of hyperglycaemia in COPD patients treated with systemic glucocorticoids. Clinicians should be vigilant for glucose dysregulation in this patient population, particularly in those with pre-existing diabetes or other risk factors. Future research should aim to elucidate optimal strategies for managing glucocorticoid-induced hyperglycaemia while minimizing adverse effects on COPD outcomes.

The pooled prevalence of hyperglycaemia in patients with COPD and exposed to systemic glucocorticoids was 42% with a high heterogeneity between the studies.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest related to this research.

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