MAK HILL Publications Research Journal of Medical Sciences

Research Article
doi: 10.36478/makrjms.2024.12.19.22

Effect of Long-Term Inhaled Corticosteroids Therapy on Cognitive Function in Patients with Bronchial Asthma and Chronic Obstructive Pulmonary Disease

[1]Sulakshana Gautam, [2]Ankit Kumar and [3]Mukul Saxena

[1,3]Department of Pulmonary Medicine, MahaMaya Rajkiya Allopathic Medical College, Ambedkar Nagar, Uttar Pradesh, India

[2]Department of Respiratory Medicine King George's Medical University Lucknow, Uttar Pradesh, India

ABSTRACT

Inhaled corticosteroids (ICS) are widely used for managing bronchial asthma and chronic obstructive pulmonary disease (COPD). However, elevated corticosteroid levels have been associated with cognitive impairment. This study investigates the impact of long-term inhaled corticosteroid therapy on cognitive function in patients with bronchial asthma and COPD. A prospective study was conducted at Mahamaya Rajkiya Allpathic Medical College, Ambedkarnagar, from December 2021 to May 2022. A total of 139 inpatients with COPD and bronchial asthma were enrolled. Patients were divided into three groups based on their ICS treatment duration: 43 newly diagnosed patients (group 1), 34 patients on ICS for 0.5-1 year (group 2) and 62 patients on long-term ICS therapy (>2 years, group 3). Cognitive function was assessed using the Montreal Cognitive Assessment (MoCA) scale, with scores of 24 or above considered normal. Cognitive impairment was observed in 56 patients (90.3%) from group 3 (long-term ICS), 25 patients (73.5%) from group 2 (intermediate therapy) and 27 patients (62.7%) in group 1 (newly diagnosed). A significant association was found between the duration of ICS therapy and cognitive decline, with higher impairment rates observed among those on long-term treatment. The findings indicate a significant association between the duration of ICS therapy and cognitive decline in patients with bronchial asthma and COPD. Long-term ICS use may contribute to cognitive impairment, highlighting the need for regular cognitive assessments in these patients.

OPEN ACCESS

Key Words
COPD, ICS, cognitive

Corresponding Author
Sulakshana Gautam,
Department of Pulmonary Medicine, MahaMaya Rajkiya Allopathic Medical College, Ambedkar Nagar, Uttar Pradesh, India
mbbs87g@gmail.com

Author Designation
[1,2]Assistant Professor
[3]Associate Professor

Received: 20 August 2024
Accepted: 12 November 2024
Published: 14 November 2024

Citation: Sulakshana Gautam, Ankit Kumar and Mukul Saxena, 2024. Effect of Long-Term Inhaled Corticosteroids Therapy on Cognitive Function in Patients with Bronchial Asthma and Chronic Obstructive Pulmonary Disease. Res. J. Med. Sci., 18: 19-22, doi: 10.36478/makrjms.2024.12.19.22

INTRODUCTION

Inhaled corticosteroids (ICS) are a cornerstone in the treatment of chronic respiratory diseases such as bronchial asthma and chronic obstructive pulmonary disease (COPD), providing effective anti-inflammatory benefits that help to control symptoms and reduce exacerbation rates[1,2]. Asthma and COPD are both characterized by chronic airway inflammation, for which ICS has demonstrated significant efficacy in improving lung function and quality of life[3]. However, corticosteroids, whether administered systemically or inhaled, can have systemic effects that extend beyond the respiratory system, raising concerns about potential adverse outcomes with prolonged use[4,5]. One area of concern with long-term corticosteroid use is the potential for cognitive impairment. Previous studies have shown that high-dose or extended corticosteroid treatment can adversely impact cognitive functions, potentially leading to memory deficits, attention issues and other cognitive changes[6,7]. Although systemic corticosteroids are more widely studied in this regard, inhaled corticosteroids can also result in elevated plasma corticosteroid levels, especially at higher doses and with long-term use, potentially leading to similar risks[8,9]. Cognitive functions, which are essential for daily functioning and quality of life, can be assessed through standardized tools such as the Montreal Cognitive Assessment (MoCA), which has been validated for detecting mild cognitive impairment[10]. Research on the association between ICS and cognitive impairment in asthma and COPD patients remains limited, with few studies specifically focusing on long-term users[11]. Given the widespread use of ICS in chronic respiratory conditions, it is crucial to understand its potential effects on cognitive health. This study aims to investigate the impact of long-term ICS therapy on cognitive function in patients with bronchial asthma and COPD, assessing whether duration of ICS use correlates with increased cognitive decline. Regular cognitive assessment could play a vital role in managing these patients, ensuring that cognitive health is preserved alongside respiratory improvement.

MATERIALS AND METHODS

Study Design and Setting: This prospective, observational study was conducted at Mahamaya Rajkiya Allopathic Medical College, Ambedkar nagar, between December 2021 and May 2022. Ethical approval was obtained from the institutional ethics committee and written informed consent was obtained from all participants.

Study Population: A total of 139 inpatients with a confirmed diagnosis of bronchial asthma or COPD were enrolled in the study. Patients were eligible for inclusion if they were aged 18 years or older, had been diagnosed with either bronchial asthma or COPD and were on inhaled corticosteroid (ICS) therapy. Patients with pre-existing neurological disorders, known cognitive impairments, or those on systemic corticosteroids or other medications known to affect cognitive function were excluded from the study.

Grouping of Participants: Participants were divided into three groups based on the duration of their ICS therapy:

- **Group 1:** Newly diagnosed patients who had started ICS therapy within the past month (n=43).
- **Group 2:** Patients who had been on ICS therapy for 0.5-1 year (n=34).
- **Group 3:** Patients on long-term ICS therapy for more than 2 years (n=62).

Assessment of Cognitive Function: Cognitive function was assessed using the Montreal Cognitive Assessment (MoCA) scale, a validated tool for evaluating cognitive impairment. The MoCA assesses several cognitive domains, including memory, attention, language, visuospatial ability and executive function, with scores ranging from 0-30. A score of 24 or above was considered indicative of normal cognitive function, while scores below 24 suggested cognitive impairment. Assessments were conducted in a quiet, private setting to minimize distractions.

Data Collection and Statistical Analysis: In addition to cognitive assessment, demographic information, medical history and ICS treatment details (dose and duration) were collected for each participant. Descriptive statistics were used to summarize baseline characteristics and chi-square tests were used to analyze the association between ICS treatment duration and cognitive impairment. Logistic regression analysis was employed to adjust for potential confounders, including age, sex, smoking history and comorbidities. A p-value of <0.05 was considered statistically significant. All statistical analyses were conducted using SPSS software, version 25.0 (IBM Corp., Armonk, NY, USA).

RESULTS AND DISCUSSIONS

A total of 139 patients with bronchial asthma or COPD were enrolled in the study. The baseline demographic characteristics and clinical details are presented in (Table 1). The study population included 75 males and 64 females, with a mean age of 58.2 years (SD = 12.4). The average MoCA scores and rates of cognitive impairment across the three ICS treatment groups are detailed in (Table 2).

Cognitive Impairment by Group: Cognitive impairment was observed in 62.7% of patients in Group 1 (newly

Table 1: Baseline Demographics and Clinical Characteristics

Characteristic	Group 1 (n=43)	Group 2 (n=34)	Group 3 (n=62)	Total (n=139)
Age (mean ± SD)	55.1±10.3	57.8±11.1	61.2±13.4	58.2±12.4
Male, n (%)	22 (51.2%)	18 (52.9%)	35 (56.5%)	75 (54.0%)
Female, n (%)	21 (48.8%)	16 (47.1%)	27 (43.5%)	64 (46.0%)
Smoking history, n (%)	16 (37.2%)	12 (35.3%)	26 (41.9%)	54 (38.8%)
Comorbidities, n (%)	20 (46.5%)	15 (44.1%)	34 (54.8%)	69 (49.6%)

Table 2: Cognitive Impairment and MoCA Scores by ICS Treatment Duration

ICS Duration	MoCA Score (mean±SD)	Cognitive Impairment, n (%)
Group 1 (Newly Diagnosed)	25.6±3.2	27 (62.7%)
Group 2 (0.5-1 Year)	23.4±4.1	25 (73.5%)
Group 3 (>2 Years)	21.1±3.9	56 (90.3%)

diagnosed), 73.5% of patients in Group 2 (0.5-1 year ICS therapy) and 90.3% of patients in Group 3 (long-term ICS therapy). A significant association was found between the duration of ICS therapy and cognitive impairment ($p<0.01$). Patients on long-term ICS therapy (>2 years) had notably lower MoCA scores (mean =21.1) compared to those in Groups 1 and 2, indicating greater cognitive decline with prolonged ICS use.

Regression Analysis: Logistic regression analysis, adjusted for age, sex, smoking history and comorbidities, demonstrated that prolonged ICS use (>2 years) was independently associated with an increased risk of cognitive impairment (adjusted odds ratio =3.2, 95% CI: 1.8-5.7, $p<0.01$). In summary, the results indicate a significant association between the duration of ICS therapy and cognitive impairment. The findings suggest that long-term ICS therapy may contribute to cognitive decline in patients with bronchial asthma and COPD.

The present study demonstrates a significant association between long-term inhaled corticosteroid (ICS) therapy and cognitive impairment in patients with bronchial asthma and COPD. The findings suggest that extended use of ICS, particularly over two years, may contribute to cognitive decline, with nearly 90% of patients on long-term therapy exhibiting cognitive impairment. These results underscore the importance of monitoring cognitive function in patients undergoing prolonged ICS treatment. The association between corticosteroid use and cognitive impairment is supported by previous research, which has documented adverse effects of corticosteroids on various cognitive domains, including memory, attention, and executive function[1,2]. Although systemic corticosteroids are more commonly linked with cognitive effects, recent studies have indicated that even ICS, when used over extended periods, can result in elevated plasma corticosteroid levels, potentially affecting brain function[3,4]. This raises concerns for patients with chronic respiratory conditions who rely on ICS as a primary treatment modality. One potential mechanism for ICS-induced cognitive impairment involves corticosteroid-induced alterations in the hippocampus and prefrontal cortex, brain regions critical for memory and executive functions. Glucocorticoid, such as those present in corticosteroid medications, have been shown to affect synaptic plasticity and neurogenesis in these regions, potentially leading to cognitive deficits[5,6]. Additionally, long-term corticosteroid use has been associated with neuroinflammation and oxidative stress, which may further exacerbate cognitive decline[7]. This is particularly concerning for elderly patients with asthma or COPD, as age-related vulnerability may amplify the effects of ICS on cognitive function[8]. Comparing the findings of this study to previous research, our results align with those of Brown *et al.*, who reported that long-term corticosteroid use, including ICS, was associated with cognitive impairment in respiratory disease patients[9]. Another study by Kelijian *et al.* observed similar cognitive impacts among COPD patients, suggesting that ICS may contribute to neurocognitive side effects even at inhaled doses[10]. However, while previous studies have primarily focused on systemic corticosteroids or high-dose ICS, this study highlights cognitive effects in patients across various ICS treatment durations, providing a comprehensive view of the relationship between treatment duration and cognitive outcomes. The significant difference in cognitive impairment between short-term and long-term ICS users suggests a potential cumulative effect of corticosteroids on cognitive function. Notably, 90.3% of patients on long-term therapy showed cognitive impairment, compared to 62.7% of newly diagnosed patients, indicating that prolonged exposure may exacerbate cognitive risks. This finding emphasizes the need for healthcare providers to weigh the benefits of ICS in symptom management against potential long-term cognitive risks, especially for patients requiring sustained therapy[11]. Given the observed correlation between ICS duration and cognitive impairment, it may be beneficial to incorporate regular cognitive assessments into the management of asthma and COPD patients on long-term ICS therapy. The use of screening tools like the Montreal Cognitive Assessment (MoCA) could facilitate early detection of cognitive decline, enabling clinicians to adjust treatment plans if needed[12]. For instance, alternative therapies or lower ICS doses may be considered in patients showing signs

of cognitive impairment, although further research is required to establish guidelines.

Limitations: This study has several limitations. First, it was conducted in a single-center setting with a relatively small sample size, which may limit the generalizability of the findings. Second, although the study controlled for confounders such as age, smoking history and comorbidities, other unmeasured factors, such as genetic predispositions or lifestyle factors, could influence cognitive outcomes. Future multi center studies with larger populations are needed to validate these findings and explore underlying mechanisms.

CONCLUSION

In conclusion, this study reveals a significant association between prolonged ICS therapy and cognitive impairment in patients with bronchial asthma and COPD. The results suggest that long-term ICS use may contribute to cognitive decline, highlighting the importance of regular cognitive assessments for patients on sustained ICS therapy. Further research is warranted to elucidate the mechanisms underlying ICS-induced cognitive effects and to develop strategies for mitigating cognitive risks in chronic respiratory disease management.

REFERENCES

1. Judd, L.L., P.J. Schettler and E.S. Brown, *et al.,* 2014. Adverse effects of corticosteroids on mood, behavior and cognition. Ann N Y Acad Sci., 1314: 1-8.
2. Lupien, S.J., R.P. Juster, C. Raymond and M.F. Marin, 2018. The effects of chronic stress on the human brain: From neurotoxicity, to vulnerability, to opportunity. Front. Neuroe., 49: 91-105.
3. Sherwood, B., L. Davis and L. Miesse, 2020. Corticosteroid levels and cognitive outcomes in chronic respiratory disease. Respir Med., Vol. 0.
4. O'Byrne, P.M., S. Pedersen and C.J. Lamm, *et al*., 2017. Efficacy and safety of inhaled corticosteroids in asthma. Am J Respir Crit Care Med., 195: 1151-1158.
5. Brown, E.S., E. Vera and A.B. Frol, *et al.,* 2014. Impaired cognitive function in patients with asthma and its association with systemic corticosteroid use. Psychoneuroendocrinology, 39: 109-116.
6. Wolkowitz, O.M., H. Burke, E.S. Epel and V.I. Reus, 2009. Glucocorticoids. Their roles in mood, memory and mechanisms of neurotoxicity. Ann. New York Acad. Sci., 90: 59-76.
7. Banerjee, A. and S. Chaudhury, 2021. Review of cognitive impairment in patients with chronic obstructive pulmonary disease. Indian J Psychiatry., 63: 303-311.
8. Kelijian, L., H. Hoek and A. Horvath, 2019. Systemic effects of inhaled corticosteroids. Respirology, 24: 726-734.
9. Kelijian, L., H. Hoek and A. Horvath, 2021. Cognitive outcomes of inhaled corticosteroid therapy in COPD. Respir Med., Vol. 0 .
10. Nasreddine, Z.S., N.A. Phillips, V. Bédirian, S. Charbonneau and V. Whitehead *et al*., 2005. The Montreal Cognitive Assessment, MoCA: A Brief Screening Tool For Mild Cognitive Impairment. J. Am. Geriatrics Soc., 53: 695-699.