

ORIGINAL ARTICLE

Asthma and delirium episodes during hospitalization

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Abstract

Background: Delirium incidences during hospitalization are an important problem in elderly patients. The problem of delirium episodes in patients with obstructive disease during hospitalization was investigated.

Material and Methods: From a total of 37,156 subjects, the following were randomly selected: 32,261 patients with asthma, 4896 with chronic obstructive pulmonary disease (COPD), and 5455 without obstructive disease. Their ages ranged from 65-95 years, and they were hospitalized between 2006 and 2015. Delirium incidences were monitored based on the International Classification of Disease (ICD)-10 codes and medical documentation.

Results: The delirium episodes during all hospitalizations were independently associated with asthma (odds ratio [OR] = 2.91, confidence interval [CI] = 1.62-5.84), with severe type of asthma (OR = 4.24, CI = 1.94-8.93), partim controlled asthma (OR = 3.1, CI = 1.29-8.46), and uncontrolled asthma (OR = 4.88, CI = 2.12-9.42). It was comparable with COPD as follows: all incidences of delirium during hospitalization (OR = 3.17, CI = 1.42-7.23) or severe COPD (III degree OR = 5.15, CI = 2.01-13.69). Elderly patients with asthma with uncontrolled or partially controlled asthma with a coincidence of advanced age, dementia, or smoking had a greater predisposition to delirium episodes, particularly after surgery. Additionally, delirium incidence caused death more frequently in patients with asthma than in those with COPD.

Conclusion: Elderly patients with asthma have a higher risk of delirium episodes during any hospitalization, and, frequently, it ends in death.

KEYWORDS

asthma, delirium

1 | INTRODUCTION

Delirium is a syndrome that is characterized by disturbances of consciousness and attention, perception, thinking, memory, psychomotor activity, emotions, and sleep-wake cycles.^{1,2} This is probably the most common form of organ failure, which goes unrecognized, despite the prevalence of Intensive Therapy

Units. According to the classification of mental disorders by the American Psychiatric Association Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), axial symptoms of delirium include (a) disturbances of consciousness (reduction in the perception of the environment, with a reduced ability to focus, and maintain or transfer attention), (b) cognitive dysfunction (memory deficits mainly concerning short-term memory and

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disorientation that are typically related to time or location and language disorders), and disorders of perception, which cannot be explained by pre-existing dementia (delusions or hallucinations, which are most often visual but may also involve other senses), and (c) development in a short period of time (hours and days), and a tendency to fluctuate during the day. Predisposing factors for delirium are advanced age, hypertension, alcoholism, a cognitive output impairment, previous dementia, possible depression, impaired vision and hearing, smoking, and genetic factors. Contributory factors associated with current acute diseases include sepsis, infection, fever, hypoxemia, metabolic, and electrolyte (hyperbilirubinemia, hyperamylasemia, hypocalcemia, and hyponatremia), metabolic acidosis, anemia, hypotension, and respiratory disease.²⁻⁴

Asthma is a common disease in elderly people. Elderly patients with asthma are relatively frequently hospitalized because of comorbidities.⁵ However, there is no information available about a possible association between incidences of asthma and delirium. Therefore, the primary end point of study is an estimation of delirium prevalence during any hospitalization in patients with asthma compared with non-asthmatics. The secondary end point is an assessment of the possible relationship between exacerbation of asthma (as a cause of hospitalization) and the occurrence of delirium and death as a consequence of it.

2 | MATERIALS AND METHODS

In a cross-sectional study, patients with asthma and patients with chronic obstructive pulmonary disease (COPD) aged 65-95 years were randomly selected from primary and secondary health care centers (37,156 patients screened in 5 centers). This was representative for age and sex according to the Polish demographic data. A diagnosis of asthma or COPD according to the International Classification of Disease (ICD)-10 code was determined, and the diagnosis was verified by a doctor (medical history and at least 12 months of treatment for asthma or COPD were documented). Using this method, 3261 patients with chronic asthma and 4896 with COPD were selected. Additionally, the remaining pool of 5455 randomly selected subjects (those without obstructive diseases) were used as a control group. These patients' characteristics are given in Table 1.

Subsequently, all hospitalizations of studied patients, their causes, and possible occurrence of delirium based on the relevant codes ICD-10 were analyzed. Delirium was assessed by the confusion assessment method for the Intensive Care Unit (CAM-ICU).⁶

Patients diagnosed with delirium were subjected to a detailed analysis containing the cause of hospitalization, duration of treatment, drug administration, and effect of hospitalization.

Descriptive statistics and standard parametric methods were performed by the use of Statistica version 8.1 software (StatPol).

TABLE 1 Characteristics of the studied patients

	Asthma N = 3261	COPD N = 4896	Control N = 5455	P value
Mean age ± SD, y	68.31 ± 6.82	70.34 ± 5.22	67.12 ± 5.01	NS
Women	2008 (61.6%)	1202 (24.6%) ^a	3120 (57.2%)	0.02
The mean time of disease duration ^b	43.2 ± 11.5	52.4 ± 9.12	—	NS
Smoking	1144	4237 ^a	1987	0.007
Asthma control ^c	C - 1451 PC - 1045 UC - 765 SA - 445	—	—	—
COPD degree ^d	—	I degree - 1911 II degree - 1211 III degree - 1683	—	—
Comorbidity				
Heart disease	1455 (44.6%)	2150 (43.9%)	2378 (43.6%)	NS
Hypertension	1783 (54.7%)	2870 (58.6%)	3487 (63.9%) ^a	0.03
Dementia	231 (7.1%)	458 (9.9%)	567 (10.4%)	NS
Depression	344 (10.5%)	423 (8.6%)	455 (8.3%)	NS
Diabetes	987 (30.3%)	1698 (34.7%)	1767 (32.4%)	NS

Abbreviations: C, controlled asthma; COPD, chronic obstructive pulmonary disease; NS, not statistically significant; PC, partially controlled asthma; SA, severe asthma; UC, uncontrolled asthma.

^aSignificant in analysis of variance.

^bObstructive disease.

^cAccording to Global Initiative for Asthma (GINA).

^dAccording to Global Initiative for Chronic Obstructive Lung Disease (GOLD).

Differences between groups for continuous data were tested using Student's *t* test or analyses of variance. Differences in proportions were assessed using the chi-square test. Multiple logistic regression was used in the multivariate analyses. In these analyses, patients with partially and uncontrolled asthma were combined into one group. Independent variables that were statistically significantly ($P < 0.05$) associated with asthma control in the univariate analyses were included in the multivariate analyses. Interaction analyses were performed for effect modification by sex and smoking history.

The study was performed in accordance with the Declaration of Helsinki and with the approval of the Ethics Committee at the Medical University of Silesia in Katowice Poland (registration site Medical University of Silesia, Katowice, Poland, no. NN-6501--115/I/04). Patients were included in the study only after informed written consent was obtained.

3 | RESULTS

During 2006-2015, there were 1417 patients with asthma and 1882 patients with COPD among all hospital admissions, and the remaining 2187 formed the control group. The most common causes of hospitalization were cardiac disease, sepsis, surgical surgery (surgery and/or oncology), metabolic decompensation, asthmatic condition, trauma, and others. The number of delirium episodes during hospitalization is shown in Figure 1.

The delirium episodes during all hospitalizations were independently associated with asthma OR = 2.91 (CI = 1.62-5.84), severe type of asthma OR = 4.24 (CI = 1.94-8.93), partim controlled asthma OR = 3.1 (CI = 1.29-8.46), and uncontrolled asthma OR = 4.88 (CI = 2.12-9.42).

The delirium episodes in patients with COPD were comparable with patients with asthma as follows: all incidences of delirium during hospitalization OR = 3.17 (CI = 1.42-7.23) or severe COPD (III degree) OR = 5.15 (CI = 2.01-13.69).

The delirium episodes were independently associated with asthma exacerbation as a cause of hospitalization OR = 2.64

(CI = 1.11-9.39) and with COPD exacerbation OR = 3.56 (CI = 1.34-11.08).

The delirium episodes were also associated with polypragmasy (more than 5 drugs used in chronic therapy), as found for both patients with asthma (OR = 3.92, CI = 0.77-9.34) and patients with COPD (OR = 3.43, CI = 0.88-11.76).

There was no association among delirium and sex, FEV1, or the types of drug used in obstructive diseases other than beta2mimetics. There was an association between incidences of delirium and usage of short beta2mimetics (more than 10 times per month) in patients with asthma (OR = 4.76, CI = 0.93-11.22) and a mild association with COPD (OR = 1.21, CI = 0.99-3.78). Additional risk factors for delirium episodes in patients with asthma are presented in Table 2.

Death as a consequence of a delirium episode was independently associated with asthma (OR = 2.99, CI = 0.56-5.97) but was not associated with COPD.

4 | DISCUSSION

These are first data presented on the relationship between hospitalization and delirium in patients with asthma. Observing delirium during hospitalization is difficult, particularly in specific subgroups, including patients with asthma and COPD.^{1,2} It is extremely difficult to determine the cause of delirium in patients with comorbidities.² However, based on the obtained results, the incidence of delirium during hospitalization in patients with obstructive pulmonary disease was more frequent than that observed in a standard population. There is no information in the literature about incidences of delirium in patients with asthma. However, some authors have emphasized that COPD could be a risk factor for delirium.^{7,8} However, there are no detailed data that have confirmed this opinion. Aghanwa et al⁹ emphasized the problem of psychiatric morbidity (including delirium) among patients with COPD.

Analyzing patients with asthma draws attention to the problem of the high rate of morbidity caused by delirium in elderly

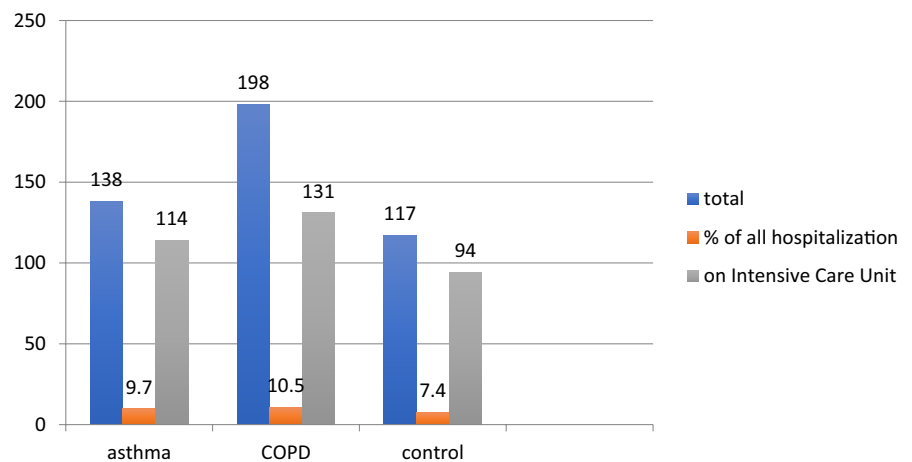


FIGURE 1 Hospitalizations of studied patients. COPD, chronic obstructive pulmonary disease

TABLE 2 Risk factors for delirium incidence during hospitalization

	Partially controlled or uncontrolled asthma OR (95% CI) n = 1810	Controlled asthma OR (95% CI) n = 1451
Age group		
65-<75	1.14 (0.67-4.19)	1.02 (0.69-3.78)
75-<85	1.83 (0.87-4.91)	1.12 (0.69-2.92)
≥85	3.09 (1.14-7.92)	2.94 (0.98-8.02)
BMI (kg × m ⁻²)		
<20	2.98 (1.18-4.97)	1.43 (0.92-4.05)
20-<25	1.1 (0.87-3.92)	1.03 (0.88-3.14)
25-<30	1.07 (0.79-3.01)	1
≥30	1.34 (0.83-5.02)	1.27 (0.79-4.02)
Atopy	1.09 (0.98-3.21)	1.18 (0.86-2.96)
Smoking or ever smoked	3.89 (1.85-8.93)	1.45 (0.88-4.56)
Heart disease	2.14 (1.05-4.98)	2.01 (1.07-5.23)
Hypertension	1.58 (0.77-4.89)	1.46 (0.78-5.91)
Dementia	4.57 (1.01-12.84)	3.64 (0.95-11.76)
Depression	1.21 (0.87-3.88)	1
Diabetes	1.29 (0.79-4.98)	1.15 (0.95-3.22)
Operation with anesthesia	3.65 (1.55-14.71)	3.56 (1.12-13.01)

Abbreviations: BMI, body mass index; CI, confidence interval; OR, odds ratio.

patients with asthma. This phenomenon may be explained in different ways. It could be related to the abuse of short-acting beta-agonists. Evidence of this includes the strong dependence between the use of short beta agonists and an increased risk of delirium in the obtained results. Arrhythmias and hypokalemia, which is the increased conversion of thyroid hormone T4-T3 as a consequence of beta2 receptor stimulation, can possibly explain this.¹⁰ However, there are also possible interactions between beta2 agonists and other used drugs. Moss et al described a case report in which the combination of inhaled corticosteroid and bronchodilator induced delirium in an elderly patient with COPD.¹¹ The author did not specify which of these drugs had a main role in the induction of delirium. In contrast, there are some reports about a stimulatory role of glucocorticosteroid in delirium incidence in patients with obstructive lung diseases. High doses of oral or inhaled steroids were involved. However, the mechanism has not been explained.^{12,13}

It is noteworthy that the degree of control of asthma is important in the induction of delirium. The relationship between uncontrolled asthma and age, cigarette smoking, and previous dementia increases the risk of delirium during hospitalization. These patients should be under special observation. In these patients, surgery brings a significant risk of delirium. There are no data on this subject in the literature.

Despite the different causes of hospitalization, it should be emphasized that an exacerbation of asthma (eg, COPD) has a very

large role in the generation of delirium. This implies the need for adequately treating these diseases, with a special emphasis on older patients. Evidence for the improvement of mental functions in improving the treatment of asthma was confirmed.¹⁴

The main limitation of the work is the small group of studied patients and the evaluation of delirium based on ICD-10 codes and medical records. This may have caused an underestimation of the number of delirium incidents. The nonrecognition of delirium during hospitalization is still a frequent occurrence.²

Another limitation is the lack of a precise assessment of the impact that drugs have on delirium episodes and the quite diverse causes of hospitalization. However, this is the only system that has allowed the observation group to perform an adequate analysis.

5 | CONCLUSION

Elderly patients with asthma have a higher risk of delirium episodes during hospitalizations. They also have an increased risk of death in such a situation. Such patients require adequate preparation and caution during surgical procedures and other hospitalizations.

CONFLICTS OF INTEREST

Nothing to disclose.

AUTHOR CONTRIBUTIONS

Conceptualization, project administration, and supervision: Bożek. Investigation, Resources, and writing – review and editing: Fiolka. Formal analysis and methodology: Zając.

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