

Introduction

Depending on the patient subgroup studied, epidemiological surveys suggest that 2-37% of people with chronic obstructive pulmonary disease (COPD) are affected by type 2 Diabetes mellitus (T2DM). In population studies, COPD is consistently associated with a 1.4-2.0-fold increased risk of T2DM.

Pathophysiologic mechanisms that connect these diseases are complex and still unclear. Possible explanations include obesity, reduced physical activity, smoking, oxidative stress. Also, COPD increases insulin resistance due to chronic inflammation (its effect on signal transmission through insulin receptor), hypoxia and corticosteroid treatment.

On the other hand, insulin as an anabolic hormone stimulates post-prandial protein synthesis and regulates mitochondrial oxidative phosphorylation in skeletal muscle, a process that generates adenosine triphosphate (ATP) which is essential for muscle contraction and other cellular activities. That is why insulin resistance is associated with mitochondrial dysfunction which is an important factor in the development of muscle weakness. Other mechanisms that may affect respiratory muscle strength and dysfunction in patients with T2DM and COPD include altered muscle blood flow and neuropathy.

In COPD patients skeletal muscle strength declines by 4.3% over 1 year so that skeletal muscle weakness is common (32%) compared with 1-2% in a healthy ageing population. This is a significant determinant of poor health status, frequency of exacerbations, hospitalisation, need for mechanical ventilatory support and mortality.

We aimed to assess the influence of metformin treatment on lung function and its potential clinical benefit in patients with T2DM and COPD considering the hypothesis that, as oral insulin-sensitising agent increases respiratory muscle strength.

Methodology

Retrospective study included patients with both T2DM and COPD who were hospitalized in Department of Pulmology, Clinical Centre of Montenegro for acute exacerbation of COPD (AECOPD) defined following Anthonisen criteria. COPD exacerbation was treated according to American Thoracic and European Respiratory Society guidelines, T2DM with pre-existing antidiabetic therapy. Spirometric parameters and length of hospital stay were compared conforming to presence or absence of metformin therapy.

Unpaired t-test was used for statistical analysis.

Table 1. Anthonisen classification of AECOPD

Type I (most severe)	Type II	Type III
All three symptoms (i.e., increased sputum volume, increased sputum purulence and increased dyspnea).	Any two symptoms present	One symptom present plus at least one of the following: <ul style="list-style-type: none"> • An upper respiratory tract infection in the past 5 days • Increased wheezing • Increased cough • Fever without an obvious source • A 20% increase in respiratory rate • Heart rate above baseline

Results

34 patients were enrolled of whom 23 (67.6%) treated with metformin (mean age 67.3 ± 10.0 years; 52.2% males) and 11 (32.4%) with sulfonylureas and/or insulin (mean age 68 ± 7.7 years; 63.6% males).

Patients in metformin group had highly significantly better FEV1 (t=2.868, df=32, p=0.007) and Tiffneau index (t=2.511, df=32, p=0.017) while the difference in FVC showed a considerable trend toward significance (t=1.925, df=32, p=0.063).

Among these patients, single dose of metformin 500mg turned out to be sufficient for the beneficial effect on FEV1; further improvement in FEV1 with increased dosage was insignificant (p>0.05).

Patients treated with metformin had the lower stages of disease according to Global Initiative for Chronic Obstructive Lung Disease (GOLD) classification.

However, there was no significant difference concerning length of stay among them: median 10.8 days in metformin group vs 13.5 in non-metformin group (p=0.129).

Conclusion

Treatment with metformin was associated with improvements in spirometric examinations in patients with both T2DM and COPD.

References

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