ASPECTS OF DIAGNOSIS AND THERAPY IN PATIENTS WITH ISCHEMIC HEART DISEASE AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Mariana Tudoran¹, Rodica Avram¹, Cristina Tudoran¹, Simona Macesan³

SUMMARY:
Chronic obstructive pulmonary disease (COPD) increases the risk of coronary artery disease (CAD) to 2-3-fold. Cigarette smoking and aging were considered long time as responsible factors, but recent epidemiologic evidence supports the importance of systemic inflammatory response. Noninvasive assessment of coronary disease in patients with COPD is problematic because they are often ventilatory limited in exercise, and pharmacologic stress testing (including adenosine and dipyridamole) may be associated with bronchospasm. Therapy remains an important problem: although beta-blockade plays a pivotal role in the management of CAD, there has been concern that it precipitates bronchospasm in COPD. Despite the clinical benefits of long-acting beta-agonist agents in the treatment of COPD, patients may have an increased risk of tachyarrhythmia and angina due to beta-adrenergic stimulation. This paper presents aspects related to diagnosis and therapy of 43 patients with CAD and COPD admitted in the Clinic of Cardiology of the County Hospital Timişoara, between 2006-2009.

Key Words: chronic obstructive pulmonary disease, coronary artery disease, betablockade.

DIAGNOSTICUL ŞI TERAPIA PACENTILOR CU CARDIOPATIE ISCHEMICĂ ASOCIATĂ CU BOALA PULMONARĂ OBRUCTIVĂ

Rezumat:
În prezenţa bronhopneumopatiei cronice obstrucive (BPCO) riscul de boală coronariană (BC) este de 2-3 ori mai crescut. Fumatul şi procesul de îmbătrânire au fost consideraţi mult timp factorii principali responsabili pentru această asociere, însă conform noilor date epidemiologice este implicat şi un răspuns inflamator. Diagnosticul neinvaziv al bolii coronariene este dificil la bolnavi cu BPCO deoarece aceştia prezintă frecvent disfuncţie ventilatorie la efort, iar testele farmacologice (cu adenosină sau dipiridamol) pot induce bronchospasm. Tratamentul acestor bolnavi ridică o serie de probleme, astfel beta-blocantele care reprezintă o terapie de ecolie în BC pot precipita bronhospasmusul la bolnavii cu BPCO, iar β-stimulatoarele adrenergice benefice în tratamentul BPCO pot induce tăhiriitmii şi angină. În lucrarea următoare sunt prezentate particularităţile de evaluare şi terapie la un lot de 43 bolnavi coronarieni cu BPCO asociată internaţii în Clinica de Cardiologie a Spitalului Clinic Judeţean Timişoara în perioada 2006-2009.

1. University of Medicine and Pharmacy Timisoara, Department of Cardiology of the County Hospital Timisoara

PATHOPHYSIOLOGICAL BACKGROUNDS

Patients with chronic obstructive pulmonary disease and ischemic heart disease have increased risk of developing cardiovascular events compared with those without COPD. As a general aspect, for every 10% decrease of FEV1 overall mortality increases with 14%, cardiovascular mortality with 28% and rate of nonfatale coronary events increases with 20%. The causal link between these diseases has historically been considered cigarette smoking, but the exact mechanisms have only recently been studied. Epidemiologic evidence supports the importance of systemic inflammation in the pathogenesis of atheroma formation and recent studies have indicated that patients with COPD have a prominent systemic inflammatory response. Various studies have

Correspondence to: Mariana Tudoran, e-mail: mariana.tudoran@gmail.com
reported a strong link between the occurrence of COPD and the presence of CAD. C-reactive protein (CRP), a known marker of systemic inflammation, is elevated in patients with both stable COPD and during exacerbation. Because elevations in CRP have been linked to CAD, it appears as though the pathogenesis of both COPD and CAD may stem from enhanced systemic inflammation. Positive diagnosis of CAD in patients with COPD is difficult in most cases. The patients have low tolerance to physical exercise due to respiratory dysfunction, echocardiographic examination is difficult because of hyperinflation and pharmacologic stress testing (including adenosine and dipyridamole) may be associated with bronchospasm.

**MATERIAL AND METHODS**

43 patients with CAD and COPD were admitted in the Clinic Cardiology of County Hospital in the period January 2006 - September 2009. 36 patients were male (83.72%) and 7 women (16.27%), aged between 45 and 74 years (mean age 63.3 ± 7.1 years). Regarding the diagnosis, 19 had old myocardial infarction (44.18%) and 24 angina pectoris (55.81%): 33 of them (76.74%) were hospitalized as medical emergency, for chest pain or arrhythmias; 10 patients (23.25%), known with CAD, were admitted for evaluation. Investigations consisted in chest radiography, respiratory functional tests, repeated electrocardiograms, biological tests, including assessment of risk factors and determination of C-reactive protein performed in all patients. In 40 patients (93%) echocardiographic examination M mode, 2D and Doppler was performed. Stress test (bicycle ergometry) was performed at 39 patients (90.69%) and at 33 (76.74%) ECG Holter monitoring was done. Despite call these methods of exploration, in 5 patients we could not determine the exact diagnosis of CAD. 2 of them were further explored by noninvasive 64-slice multidetector computed tomography coronary angiography and 3 were referred for invasive coronary angiography. Treatment consisted in administration of antiplatelet therapy (aspirin, clopidogrel), statins and nitroglycerin; therapy with beta-blockade agents raised questions in some patients with exacerbated COPD. However in 29 of them, with stable COPD, this medication could be administered, but in sub-optimal doses.

**RESULTS AND DISCUSSIONS**

Regarding the study group most of the patients had multiple risk factors. All of them were exsmokers (10 of them, 23.25%, current smokers), 11 (25.58%) had diabetes mellitus and 28 (65.11%) dyslipidemia. 37 patients (86.04%) had an elevated circulating CRP level sustaining the importance of inflammation in this disease.

**NONINVASIVE ASSESSMENT OF CAD**

Moderate and severe airflow obstruction was associated with increased occurrence of ischemic changes on electrocardiograms. Hyperinflation, accompanying COPD, has limited in many cases the diagnostic accuracy of transthoracic echocardiography for detecting wall motion abnormalities. Stress testing was performed in 39 (90.69%) patients, but only 18 (46.15%) could finish the test so that it was conclusive for CAD. 21 patients (53.84%) abandoned the test at 25, 50 or 75 Watt claiming dyspnea and the test was inconclusive. Holter monitoring was performed in 33 (76.74%) patients, but only in 29 (87.87%) ST segment depressions suggestive of CAD have been obtained. Average frequency was increased (86 + 17 b/min). At 21 patients (63.63%) the monitoring revealed arrhythmias: 17 supraventricular premature beats, TPSV or episodes of paroxysmal atrial fibrillation, and 9 had ventricular extrasystoles. In 5 patients (11.62%) the diagnosis of CAD could not be certified with the noninvasive tests mentioned above. 2 of them had computer tomographic angiography of coronary arteries and 3 were referred for invasive angiocoronarography.

**TREATMENT**

Although beta-blockade plays a pivotal role in the management of CAD, there has been longstanding concern that it may precipitate bronchospasm in COPD. However, the use of cardioselective beta-blockers such as bisoprolol, nebivolol and metoprolol, appears to be safe. In our study at 29 (67.44%) patients, with stable COPD, therapy with selective beta-blockers could be initiated without any adverse effects: thus, 17 patients received bisoprolol, 7 nebivolol and 5 metoprolol succinate, but at 17 of them the administered dose was suboptimale. 14 patients had exacerbated COPD, 9 of them could be treated with small doses of bisoprolol, but in 3 of the 5 with severe COPD long-acting calcium channel blockers, like diltiazem, was preferred. In addition to their role in CAD, the use of beta-blockers has become standard of care for most patients with left ventricular dysfunction. Cardioselective beta-blockers, given as a single dose even for longer duration, produced no change in FEV1. The use of this drugs in patients with moderate COPD (mean FEV1, 50% of predicted) had no
evidence of adverse respiratory effects. 32 patients had indication for concomitant therapy either with angiotensin converting enzyme inhibitors (IEC), 27 of them patients, or angiotensin receptor blockers (ARB), 5 patients as illustrated in table 1.

An important problem was the concomitant therapy of COPD. All patients were treated with inhalatory corticoids (fluticason or budesonid). 23 of the patients, with increased cardiovascular risk, were treated with beta-adrenergic stimulators (salbutamol and salmeterol). Despite the clinical benefits of long-acting beta-agonist agents in the treatment of COPD, some patients had increased incidence of tachyarrhythmias on Holter monitoring due to cardiovascular toxicity and beta-adrenergic stimulation. 20 patients were treated with tiotropium, 2 of those, claimed palpitations.

<table>
<thead>
<tr>
<th>THERAPY OF PATIENTS WITH CAD AND COPD</th>
<th>SEVERITY OF COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mild 21p</td>
</tr>
<tr>
<td>beta-blockers: bisoprolol</td>
<td>15</td>
</tr>
<tr>
<td>Nebivolol</td>
<td>2</td>
</tr>
<tr>
<td>Metoprolol succinat</td>
<td>4</td>
</tr>
<tr>
<td>Diltiazem</td>
<td>-</td>
</tr>
<tr>
<td>IEC</td>
<td>17</td>
</tr>
<tr>
<td>ARB</td>
<td>-</td>
</tr>
<tr>
<td>Statins</td>
<td>21</td>
</tr>
<tr>
<td>Tiotropium</td>
<td>5</td>
</tr>
<tr>
<td>beta-adrenergic stimulators</td>
<td>7</td>
</tr>
</tbody>
</table>

CONCLUSIONS

1. Chronic obstructive pulmonary disease is a major risk factor that increases morbidity and mortality at patients with coronary artery disease;
2. Multiple risk factors association and low-grade systemic inflammation is present in patients with mild to severe airflow obstruction and is associated with increased risk of cardiac injury;
3. The use of beta-blockers in patients with exacerbations of COPD is well tolerated and do not induce adverse effects in patients with moderate or mild ventilatory dysfunction;
4. Tiotropium provides symptomatic benefits in patients with COPD and is not associated with evidence of electrocardiographic changes;
5. Patients with COPD, treated with beta-adrenergic stimulators have an increased risk of tachyarrhythmia due to beta-adrenergic stimulation.

REFERENCES


