Un-Suggested Prescriptions of Non-Cardio-Selective Beta-Blockers for Heart Failure in Patients with Concurrent Chronic Obstructive Pulmonary Disease.

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Since 2008, the use of non-cardio-selective beta-blockers (NCSBB) in patients with chronic obstructive pulmonary disease (COPD) has been discouraged by European Society of Cardiology (ESC) clinical management guidelines for acute and chronic heart failure because of the lack of pharmacological selectivity for the beta-1 receptor that could result in adverse respiratory reactions such as bronchoconstriction and worsening of lung function. To date, it is unknown to which extent the international guidelines have been followed in Denmark and therefore it is unknown whether adherence to guidelines needs to be reinforced. To overcome this gap in knowledge, we conducted a nationwide study to evaluate the use and persistence in treatment of NCSBB for heart failure in patients with COPD and concurrent heart failure in the period 2009-2012, the factors important for their selection and their impact on the risk of being hospitalized for COPD. All patients with a diagnosis of COPD in the period from January 1st 2009 to December 31st 2012 were identified in Danish registries. The year 2009 was chosen to have a grace period from the release of ESC guidelines that we considered necessary to allow dissemination of recommendation into routine clinical practice. A patient was defined as being in treatment with NCSBB with an authorized indication for heart failure if redeemed prescriptions of carvedilol. Similarly, we defined a patient as treated with cardio-selective beta-blockers with an authorized indication for heart failure if redeemed prescriptions of metoprolol, bisoprolol, or nebivolol. Those beta-blockers represent the only beta-blockers used in Denmark in the period 2009-2012 for heart failure. The persistence in treatment with NCSBB was estimated by evaluating the time in treatment without discontinuation. For each patient that received a claimed prescription of NCSBB, we compared the odds of being hospitalized for COPD 60 days prior and 60 days after the redemption of the first prescription of NCSBB by using a conditional logistic regression. In all, 90,179 patients with a diagnosis of COPD were identified, of which 24,999 patients had a concurrent diagnosis of heart failure, and 14,898 out of the 24,999 (59.6%) had at least one claimed prescription of beta-blockers. In total, 3902 out of 14,339 (27.2%) received a claimed prescription of NCSBB indicated for heart failure, or rather carvedilol, contributing with a follow-up period of 23,938 person-years. Among patients receiving NCSBB, 1156 out of the 3902 (29.6%) started for the first time the pharmacological treatment with NCSBB in the period 2009-2012 with a restricted mean time persistence of 507 days, which evidenced a protracted period of un-suggested treatment with NCSBB. Chronic kidney disease was found to be positively associated with claimed prescription of NCSBB used for heart failure. Hypertension and atrial fibrillation instead, were found to be negatively associated with claimed prescription of NCSBB used for heart failure. Of 3902 patients treated with NCSBB, 1729 (44.4%) were hospitalized 5272 times for COPD during treatment with NCSBB. The 3902 patients that received claimed prescriptions of NCSBB had, during the 60 days following the redemption of the first prescription, an odds ratio of 1.38

(95%CI 1.23-1.56) for being hospitalized for the COPD compared to themselves in an equivalent period prior to the redemption of the prescription. A call for action is needed to increase the awareness of the Danish physicians on the risk associated with the administration of NCSBB for heart failure in presence of COPD as well as on the importance of adhering clinical guidelines given the severity of clinical implications connected to their neglecting.