LETTER TO THE EDITOR

In Reference to "Optimizing Non-cardiac Prescription in a Cardiac Patient"

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Sir/Ma'am,

This letter is in reference to "Optimizing Non-cardiac Prescription in a Cardiac Patient." The article is very well written and is very apt in the current era when optimization of noncardiac medications for cardiac patients poses a challenge to the treating physician. Many of these patients have multiple comorbidities and seek specialist advice for each one of them, who in turn, treat only the part related to their own specialty. Thus, the patient ends up with a complex regimen with contributions from Sall specialists from whom he seeks advice.

Therefore, it becomes a challenge to treat the patient holistically and integrate all the prescriptions and simplify the regimen that may be best suited for the patient, addressing all of his comorbidities, without letting any of his problems being left uncovered. It is here that optimization of the prescription becomes crucial; such as using drugs that may address multiple comorbidities, avoiding serious drug interactions, and modifying the dosage, if their concomitant use becomes inevitable.

Fifty percent of all heart failure patients suffer from iron deficiency with resultant reductions in functional capacity, quality of life, and life expectancy. This is independent of left ventricular ejection fraction or presence of anemia. However, the AFFIRM–AHF trial showed that treatment with ferric carboxymaltose reduced the risk of heart failure hospitalizations but did not reduce the risk of cardiovascular death.[1]

Sometimes gastrointestinal (GI) bleed is only suspected with progressive decline in hemoglobin levels without an obvious bleeding source. Endoscopy is often crucial. While aspirin causes GI bleeding by direct inhibition of cyclooxygenase-1, and thus reducing the protective effect of prostaglandins, P2Y12 inhibitors are believed not to be directly ulcerogenic, but to impair ulcer healing by blocking platelet aggregation, angiogenesis, and endothelial proliferation. Clopidogrel carries a lesser risk of GI bleed compared to ticagrelor and prasugrel.[2] While the development of an antidote for ticagrelor, PB2452, a monoclonal antibody fragment, is in progress,[3] the TWILIGHT trial showed ticagrelor monotherapy was associated with a lower incidence of clinically relevant bleeding in high-risk patients who have completed 3 months of dual antiplatelet therapy, than ticagrelor plus aspirin, with no higher risk of death, myocardial infarction, or stroke.[4]

The 2020 ESC guidelines for the management of ACS suggests that in patients with NSTE-ACS and stent implantation who are at high risk of bleeding (e.g., PRECISE-DAPT>_25 or ARC-HBR criteria met), discontinuation of P2Y12 receptor inhibitor therapy after 3 to 6 months should be considered and aspirin continued after completion of dual antiplatelet therapy. In patients at very high-risk of bleeding, defined as a recent bleeding episode in the past month or planned, not deferrable surgery in the near future, 1 month of aspirin and clopidogrel should be considered with clopidogrel monotherapy to be continued beyond 1 month.

In renal disease, ACE inhibitors or ARBs should be started at low doses after checking baseline blood pressure, urea, creatinine, potassium, and sodium levels. After initiation, serum creatinine and potassium should be checked at days 4 and 10, after dose increase or increase in diuretic dose. A small rise of creatinine level is common and expected, but a rise of 20–30% above baseline within 4 weeks of initiation of treatment is considered significant and warrants no further up-titration or, sometimes, down-titration. The potassium levels should be maintained below 5 mmol/L and hypotension avoided. The increase can be made every week and titrated to the highest approved dose that is tolerated.[5] Though aldosterone receptor antagonists are usually avoided in renal disease, finerenone, a nonsteroidal, selective mineralocorticoid receptor antagonist, reduces albuminuria and has been shown to lower risks of CKD progression and cardiovascular events than placebo in patients with CKD and type 2 diabetes.[6] Sometimes, treatment with GI cation exchangers, such as patiromer or sodium zirconium cyclosilicate, may be used to treat hyperkalemia associated with RAS blockade therapy for up to 12 months.[7]

In patients with diabetes and heart failure, in addition to carvedilol, nebivolol may be preferred because of their ability to improve insulin sensitivity, with no negative effects on glycaemic control.[8]

In patients with diabetes and coronary artery disease, trimetazidine could significantly improve clinical outcomes in patients with angina or heart failure and diabetes. In patients with diabetes undergoing revascularization, administering trimetazidine could also provide significant clinical benefits. Trimetazidine reduces the number of weekly angina attacks, mean nitroglycerin consumption per week, and time to 1-mm ST-segment depression. When used early as an adjunct to other agents, trimetazidine improved ventricular function in patients with DM and stable CAD.[9]

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It should be appreciated that not all DPP-4 inhibitors are associated with higher rates of heart failure. In the SAVOR-TIMI 53 trial, saxagliptin was associated with an increase in the risk of hospitalization for HF, compared with a numerical, nonsignificant increase with alogliptin in EXAMINE, and no HF signal with sitagliptin in TECOS and with linagliptin in CARMELINA. Nevertheless, despite differences in results among the four DPP-4 inhibitor trials, the U.S. Food and Drug Administration continues to recommend avoidance of this class in the setting of heart failure.[8,10,11]

In addition to patients with diabetes, in patients without diabetes mellitus, SGLT2 inhibitors showed positive metabolic outcomes in weight and blood pressure control and improve cardiovascular outcomes.[12] The glucagon-like peptide-1 receptor agonists (GLP-1RAs) have also been demonstrated to reduce cardiovascular events in at-risk individuals with type 2 diabetes. GLP-1RAs have demonstrated a mean relative risk reduction in MACE by 12%, cardiovascular death by 12%, all-cause mortality by 12%, stroke by 16%, myocardial infarction by 9%, and composite kidney events by 17% (driven by improvements in albuminuria). Concurrent use of SGLT2 inhibitors and GLP-1 agonist may provide incremental advantages, given their distinct mechanisms of action, nonoverlapping adverse effect profiles, and unique target cardiovascular effects.[13]

The term mental stress-induced myocardial ischemia (MSIMI) is coined to describe objective signs of myocardial ischemia (such as ST-segment depression on an electrocardiogram) during a mental stress task. MSIMI has been associated with death and cardiovascular events. The REMIT trial (responses of MSIMI to escitalopram treatment), showed that a greater proportion of patients treated with the selective serotonin-reuptake inhibitor escitalopram (5 mg daily for 6 weeks) were free of MSIMI compared to patients treated with a placebo ($p = 0.04$). Escitalopram did not have any effect on exercise-induced ischemia but rather improved anxiety and emotional reactions to mental stress. Because of increased suicidal risk in subsets of patients, escitalopram should be used cautiously in patients suffering from concomitant major depression.[14]

In conclusion, this enlightening article will enrich the readers a lot and enable them to better manage patients in their day-to-day clinical practice.

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