Cardio Mag

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Dear Doctor,
*Greetings from Micro Labs Limited. We are happy to bring you "**Cardio Mag**", which contains latest and interesting news in the field of Cardiology.*

This issue contains

- ***A randomised trial on Bempedoic Acid Administration With Atherogenic Lipid Levels in Patients With Hypercholesterolemia..***
- ***Patriomer in chronic heart failure and reduced ejection fraction: A case report.***
- ***A novel AV Transcatheter Heart Pacer approved in Europe.***

Should you require any specific article or medical information, please feel free to contact us at ***medicalservices@microlabs.in***

Looking forward to your valuable feedback.
Best Regards,
Medical Team, Micro Labs Limited

1. A randomised trial on Bempedoic Acid Administration With Atherogenic Lipid Levels in Patients With Hypercholesterolemia.

Lipoprotein disorders are important clinically due to the of the role of lipoproteins in atherogenesis and the associated risk of atherosclerotic cardiovascular disease.

Bempedoic acid is a novel oral molecule that decreases LDL-C level as a consequence of competitive inhibition of adenosine triphosphate– citrate lyase, a key enzyme in the cholesterol biosynthesis pathway upstream of 3-hydroxy-3-methylglutaryl coenzyme A reductase.

Inhibition of cholesterol synthesis with bempedoic acid, similar to statins, upregulates hepatic LDL receptor expression, thus decreasing LDL-C blood levels by increasing clearance of circulating LDL-C.

Objective of the current study is to evaluate

Methods:

A double-blind placebo-controlled randomized clinical trials involving 4000 patients. Patients included were those with hypercholesterolemia receiving stable lipid-lowering therapy and high cardiovascular risk or hypercholesterolemia and statin intolerance.

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Patients were randomized 2:1 to bempedoic acid, 180mg (n = 2425), or placebo (n = 1198) once daily for 12 to 52 weeks.

Primary end points: Primary efficacy end point was percentage change from baseline in LDL-C level at week 12 in the intention-to-treat population.

Patients were divided into 2 groups

(1) patients with hypercholesterolemia and atherosclerotic cardiovascular disease (ASCVD) or with heterozygous familial hypercholesterolemia (HeFH) or with both and receiving statins and

(2) patients with hypercholesterolemia who were statin intolerant receiving maximally tolerated statins.

Results:

Baseline characteristics were comparable.

Amon g patients with patients with hypercholesterolemia and atherosclerotic cardiovascular disease (ASCVD) or with heterozygous familial hypercholesterolemia (HeFH), Mean LDL-C level was 107.6 (32.7)mg/dLAt the end of 12 weeks, the LDL-C level change from baseline was −16.0% with bempedoic acid vs 1.8 % with placebo (difference, −17.8%; 95%CI, −19.5%to −16.0%; P < .001).

Patients with statin intolerance had a mean (SD) baseline LDL-C level of 144.4 (38.8)mg/dL. The percentage changes in LDL-C levels at week 12 were −23.0% in the bempedoic acid group and 1.5%in the placebo group (difference, −24.5%; 95%CI, −27.8%to −21.1%; P < .001).

A sustained Decrease in LDL-C levels was seen with bempedoic acid on long-term follow-up in both pools (patients with ASCVD or HeFH or both receiving a maximally tolerated statin, difference of −12.7%at week 52; patients with statin intolerance, difference of −22.2%at week 24).

Also Decreases in non–high-density lipoprotein cholesterol, total cholesterol, apolipoprotein B, and high-sensitivity C-reactive protein levels were greater with bempedoic acid vs placebo.

Adverse events associated were more frequently with bempedoic acid than with placebo included increased blood uric acid level (2.1% vs 0.5%), gout (1.4%vs 0.4%), decreased glomerular filtration rate (0.7%vs <0.1%), and increased levels of hepatic enzymes (2.8%vs 1.3%).

Discussion:

Bempedoic acid is a non statin adjunct or alternative to statin therapy, it has the potential for use in a broad spectrum of patients.

An additional LDL-C level decrease was achieved when bempedoic acid was added to background statin therapy was greater than the anticipated LDL-C level decrease of 5% to 6% that is achieved after doubling the statin dose.

Bempedoic acid is associated with modest increases in blood uric acid levels. This is due to the fact that Bempedoic acid inhibits the organic anion transporter 2.

Bempedoic acid is also associated with an increased risk of tendon rupture.

Conclusion:

Bempedoic acid effectively decreased LDL-C levels when added to maximally tolerated statins, and was associated with hyperuricaemia and tendon rupture.

Reference:

Banach M et al. Association of Bempedoic Acid Administration With Atherogenic Lipid Levels in Phase 3 Randomized Clinical Trials of Patients With Hypercholesterolemia. JAMA Cardiol. 2020; E1-E11.

2. Patriomer in chronic heart failure and reduced ejection fraction: A case report.

Chronic heart failure (CHF) is a growing public health problem. Cornerstone of medical therapy in these patients is the inhibition of the renin–angiotensin–aldosterone system (RAAS).

RAAS blockade leads to development of hyperkalaemia (defined as serum potassium levels > 5.0mmol/L) a condition which often prevents optimizing Class I pharmacotherapies such as angiotensin-converting enzyme inhibitors (ACEIs)5 or mineralocorticoid receptor antagonists (MRAs).

Latest treatments for hyperkalaemia such as patiromer or sodium zirconium cyclosilicate provide an opportunity to ameliorate this issue.

Current is a case of chronic heart failure and reduced ejection fraction for which patriomer was used.

Case presentation:

A 70-year-old male with Type 2 diabetes mellitus, hypertension, hypercholesterolaemia, former tobacco use, chronic pulmonary obstructive disease, and chronic kidney disease (CKD) Stage 3].

Past history of atrial fibrillation and ischaemic heart disease with an acute myocardial infarction (AMI) in 2009; the angiography showed coronary disease: chronic total occlusion of the right coronary artery and severe stenosis of the proximal left anterior descending artery, treated percutaneously with a drug-eluting stent.

Subsequent to AMI, the patient's LVEF was <40%, and he developed HFrEF. He presented several acute decompensations requiring hospital admissions .

In latter admission, echocardiography showed a dilated left ventricle (end-diastolic volume: 67mL/m^2), LVEF 34%, moderate functional mitral regurgitation, normal right ventricle without pulmonary hypertension.

Stress echocardiography was normal. He was discharged in a New York Heart Association (NYHA) functional Class IIb, with suboptimal medical therapy.

Patient was added on low doses of an ACEI (enalapril), a beta-blocker (nebivolol), and MRA (eplerenone) were initiated sequentially, as per current clinical practice guidelines.

Then Up-titration of beta-blockers up to 10mg/day was successfully achieved after 2 months.

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Enalapril and eplerenone were discontinued 2 weeks after initiating eplerenone due to deterioration of renal function and hyperkalaemia (eGFR 30mL/min, Kþ6.3mmol/L).

No clinical manifestations, no significant arrhythmias and both T wave and the QRS complex remained unaltered in the electrocardiogram.

Blood tests showed a recovery of renal function and potassium levels 1 week after (eGFR 39mL/min, Kþ4.9mmol/L).

After few weeks as second attempt to use ACEIs, low doses of ramipril (1.25mg/24 h) were initiated. Despite the very low dose, potassium levels raised again up to 6.1mmol/L (eGFR unchanged).

Ramipril was discontinued, and the patient was questioned about dietary habits, with no evidence of intake of potassium-rich foods, supplements, or other preventable causes of hyperkalaemia.

To optimally inhibit the RAAS, calcium polystyrene sulphonate was introduced. Nevertheless, the patient spontaneously abandoned treatment due to self-reported gastric intolerance.

patient suffered a new acute decompensation of CHF in the context of a respiratory infection leading to acute pulmonary oedema.

Patiromer 8.4 g/24 h and ramipril 2.5mg/24 h were initiated simultaneously after discharge (eGFR 50mL/min, Kþ4.6mmol/L) .

3 days later , laboratory tests showed serum potassium levels of 5.4mmol/L, eGFR 53mL/min. Ramipril was maintained, and the dose of patiromer was doubled (16.8 g/24 h); subsequent blood test showed serum potassium levels back to normal (4.9mmol/L).

Ramipril was then up-titrated to 5mg/24 h, without evidence of hyperkalaemia in the subsequent controls. MRAs were then reintroduced.

Initially 12.5 mg/24 h of eplerenone, potassium levels being persistently <5mmol/L, followed by up-titration to 25 mg/24 h. The patient's subjective tolerance was excellent, and blood tests consistently showed stable eGFRs and potassium levels.

Ramipril was replaced by an angiotensin receptor blocker neprilysin inhibitor (sacubitril/valsartan 24/26mg), with no recurrence of significant hyperkalaemia.

No substantial differences in renal function or electrolytes before and after patiromer initiation, except potassium levels. Creatinine and eGFR levels ranged 130–150 mmol/L and 40–50mL/min, respectively, and phosphate levels ranged 1.1–1.2mmol/L.

It has not been possible to further up-titrate RAAS inhibitors due to arterial hypotension (persistent asymptomatic systolic blood pressure below 90mmHg).

After 3months under optimal medical therapy, follow-up echocardiography showed no significant changes: the left ventricle remained dilated, with an LVEF of 35%. Patient is planned for implantable cardioverter-defibrillator.

Discussion:

Patiromer is an oral non-absorbed polymer that exchanges calcium and K^+ in the colon, resulting in increased K^+ excretion.

Not quite common, Drug–drug interactions and there are no significant systemic side effects.

Most frequent adverse effects include gastrointestinal symptoms (i.e. diarrhoea, constipation) and

non-serious electrolyte abnormalities (i.e. hypomagnesaemia).

Sodium zirconium cyclosilicate is an inorganic cation that eliminates excess potassium in the gastrointestinal tract.

Potassium binders among CKD, there were encouraging outcomes in maintaining normokalaemia and RAAS inhibitors in patients with eGFR between 15 and 60mL/min. Also some positive real-world data in patients in haemodialysis under patiromer.

Conclusion:

A case of hyperkalaemia in heart failure with reduced ejection fraction with CKD was successfully managed with Patriomer.

Reference:

Marrero SJ et al. Use of potassium-binder patiromer for up-titration of renin–angiotensin–aldosterone system inhibition therapy in a patient with chronic heart failure and reduced ejection fraction followed in a multidisciplinary integrated chronic care management programme: a case report. Eur Heart Jl - Case Rep.; 2020: 1-3.

IN FOCUS

3. A novel AV Transcatheter Heart Pacer

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European Union has cleared an novel AV pacemaker as a minimally invasive transcatheter procedure. The device is indicated for patients suffering from AV block. This AV pacemaker addresses this condition by continuously monitoring the physical movement of the heart, using a built-in accelerometer, and adjusting the pace of ventricle at every heartbeat.

It not only stimulates but is also able to recognize the electrical activity of the whole heart.

MARVEL 2 (Micra Atrial Tracking Using A Ventricular accelerometer) study evaluated the safety and effectiveness of accelerometer-based atrial sensing algorithms.

Study evaluated the ability of the internal sensor to monitor and detect atrial contractions and enable coordinated pacing between the atrium and ventricle, thereby providing AV synchrony.

Primary efficacy objective was met significantly greater percentage of complete heart block patients with normal sinus rhythm having >70% AV synchrony during algorithm-mediated AV synchronous pacing (38 of 40 patients, 95%) than VVI pacing (0 patients, P<0.001 for proportion of patients with >70% synchrony). The study's primary safety objective was also met, with no pauses or episodes of pacing-induced tachycardia reported during algorithm mediated AV synchronous pacing.

Reference:

Available at : https://www.medgadget.com/2020/06/medtronic-micra-av-transcatheter-heart-pacer-cleared-in-eu.html. Accessed on 03-07-2020.