Gout drug "could treat angina"

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NEW(S)

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A drug which has been used to prevent gout for more than 40 years has been found to be an effective treatment for patients with heart disease. Researchers discovered that angina patients who were given drug allopurinol were able to exercise longer and harder before they experienced chest pain. Professor of Cardiovascular Medicine at the University of Dundee, Dr. Allan Struthers, said that he hoped his team's findings would now help to increase the quality of life for angina sufferers.[1]

(RE)VIEW

Apart from the conventional risk factors (cigarette smoking, diabetes, hyperlipidemia, and hypertension) for coronary heart disease (CHD), it has been shown that hyperuricemia may independently increase the risk of CHD events marginally.[2]

In patients with chronic heart failure (CHF), hyperuricemia is a common finding and is associated with reduced vasodilator capacity and impaired peripheral blood flow. In hyperuricemic CHF patients, xanthine oxidase (XO) inhibition with allopurinol has been shown to improve blood flow both locally and systemically.[3] Experimental evidences also show that allopurinol improves myocardial function when it is hypoxic,[4] and normalizes endothelial dysfunction in heavy smokers,[5] hypercholesterolemic individuals,[6] diabetics,[7] etc.

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XO as such is a superoxide-generating enzyme that is upregulated in animal models of heart failure, which when inhibited, favorably affected the progression of postischemic cardiomyopathy in mice.[8] Thus, unlike in gout, the benefit of allopurinol in improving the endothelial function has been reported not due to reduction in the uric acid level, rather through an improved endothelial function.[9]

The reduction of myocardial oxygen consumption by allopurinol has been shown only in heart failure and that too in animal studies. However, the real beneficiary of a drug that decreases myocardial oxygen consumption will be the one with CHD. With this objective, researchers in UK investigated whether allopurinol prolongs exercise in patients with chronic stable angina pectoris.[10]

Allopurinol (600 mg per day) for 6 weeks was compared with placebo, in a crossover study in angiographically proven CHD patients (aged 18–85 years). Allopurinol was found to increase the median time to ST depression, median total exercise time, and the time to chest pain from a baseline compared to placebo, with no adverse effects. The magnitude of the anti-ischemic effect with allopurinol was suggested to be similar to that of other established antianginal drugs, such as amlodipine, nitrates, ivabradine, atenolol, and ranolazine. The authors have proposed the following mechanisms for the anti-ischemic effects of allopurinol:

a. By blocking XO, allopurinol might prevent oxygen wastage and thereby increase the supply of molecular oxygen in the ischemic tissue. This is because XO is known to use molecular oxygen to produce oxidative stress.
b. Substrates for ATP, such as AMP, are broken down by XO. The inhibition of XO augments high-energy phosphates, such as ATP, thereby supplying energy to ischemic tissues that are depleted of ATP.
c. Improved coronary and peripheral endothelial functions could also play a role in improving the local blood flow to

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heart as well as a reduction in the load to heart, the latter effect is like that of other antianginals like nitrates.

It was concluded that allopurinal is an inexpensive (compared to newer antianginals like ivabradine, ranolazine), a useful, well-tolerated (does not reduce the blood pressure or the heart rate unlike nitrates or beta blockers), and safe (already recorded for the treatment of gout) anti-ischemic drug for patients with angina.[10]

As usual to conclude, allopurinol's role in CHD needs further exploration. However, if established, it shall be more useful for countries like India where the burden of metabolic syndrome is catching at a faster pace than the annual economic inflation, or the endemic scams.

TAIL PIECE

Related news

"Beck's procedure"[11] is a surgical procedure to narrow the coronary sinus described in 1960s for the management of angina pectoris, but not practiced due to practical difficulties.

Based on this principle, "Neovasc Reducer," a stainless steel balloon-expandable stent shaped like an "hourglass," is implanted in the coronary sinus for the management of refractory angina pectoris, in persons who are not candidates for conventional revascularization. Mechanically reducing the cardiac venous blood flow (coronary sinus) causes a build-up in the capillary pressure, thereby increasing the perfusion of oxygenated blood (for a maximum extraction of oxygen) to areas of the heart muscle. The implantation is performed by a minimally invasive percutaneous procedure similar to placing the usual coronary stent. A significant reduction in the extent and severity of myocardial ischemia was noted.[12] Three years after the implantation of the Reducer, majority of patients continued to show measurable improvement in angina symptoms.

It is expected soon in the market, with an estimated price of $3000–5000.[13]

This news is presented with the following interrogation: Will there be any "cardioselective venoconstrictors" (medical preload enhancer) that may prop up in future?

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