Cholesterol drug shows benefits for kidney patients

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(PhysOrg.com) -- A combination drug that lowers levels of 'bad' cholesterol in the blood can benefit people with chronic kidney disease and is safe, a study led by the Clinical Trial Service Unit at Oxford University has found.

Patients receiving the daily pill - a combination of simvastatin and ezetimibe produced by Merck - had one-sixth fewer heart attacks, strokes or operations to unblock arteries than those receiving a placebo 'dummy' pill. The study findings were reported at an American Society of Nephrology conference in Denver, USA.

Chronic kidney disease is very common, affecting up to one in twenty of the middle-aged population, and substantially more of those who are older. Although people with chronic kidney disease are known to have an increased risk of a stroke or heart attack, it has been very unclear what treatments could prevent these conditions in this group of patients.

Dr Martin Landray, co-principal investigator at Oxford's Clinical Trial Service Unit, said: 'Over the past couple of decades, we have increasingly recognized that chronic kidney disease is associated with a high risk of cardiovascular complications, and have realised that kidney disease is common. But we have failed so far to identify any treatments that are effective in reducing that risk.

'The SHARP trial results now provide clear evidence that lowering cholesterol with ezetimibe/simvastatin safely reduces the risk of major atherosclerotic events. This is the first trial that has demonstrated that the high risk of heart attacks, strokes and other vascular diseases can be reduced in these patients.'

The Study of Heart and Renal Protection (SHARP) involved almost 9,500 volunteers aged 40 or over with chronic kidney disease. Those taking part came from 380 hospitals in 18 countries and had lost more than 50% of their normal kidney function, with a third of them requiring dialysis treatment. None had had a previous heart attack or needed bypass surgery or 'stents' to unblock their heart arteries.

Volunteers in this double-blind placebo-controlled trial were randomly allocated to take either cholesterol-lowering therapy with a tablet containing ezetimibe 10mg daily and simvastatin 20mg daily, or matching placebo tablets. Study treatment and follow-up continued for an average of 5 years.

In that time, 11.3% of patients (526 out of 4650) taking the drug had a heart attack, stroke or needed an operation to unblock an artery compared with 13.4% (619 of 4620) in the placebo group. That's a reduction of a sixth in the likelihood of these events.

Professor Colin Baigent of the Clinical Trial Service Unit at Oxford University, the trial's principal investigator, said: 'This is excellent news for patients who have kidney disease.

'It was already known that cholesterol-lowering could reduce the risk of heart attacks, strokes and the need for surgery to unblock arteries in people with normal kidney function. But this trial now shows that cholesterol-lowering has similar effects in people with chronic kidney disease, irrespective of the severity of their illness.'

During the 5-year period of the trial, the proportion of patients who stopped taking their allocated treatment was about one third, but this was not generally due to side-effects and was the same for both real and dummy treatments. If taken without interruption, however, ezetimibe plus simvastatin could have even larger effects than were seen in SHARP, the researchers note. Taking ezetimibe plus simvastatin long-term could avoid around one

quarter of heart attacks, strokes and operations to unblock arteries, leading to their prevention in at least 250,000 people with kidney disease worldwide each year.

Importantly there were no safety concerns with the drug, which is already being taken by many people with normal kidney function to lower their cholesterol.

There was no support for previous concerns with ezetimibe about possible adverse effects on cancer, and no evidence of an increased risk of muscle or liver problems.

Dr Landray said: 'There was no evidence of any serious adverse effects and, in particular, no support for earlier concerns that ezetimibe might cause cancer. SHARP shows clearly that the large cholesterol reduction produced with this treatment is safe, and provides similar benefits to those seen in people with normal kidney function.'

The SHARP trial was designed, conducted and analysed independently of all funding sources by the Clinical Trial Service Unit at Oxford University, with guidance from an independent steering committee that included many of the world's leading kidney specialists.

The study was supported by Merck (known as MSD outside the US and Canada), who also supplied the study tablets. Additional support came from the Australian National Health and Medical Research Council (NHMRC), the British Heart Foundation (BHF) and the UK Medical Research Council (MRC).

Merck now plans to seek regulatory approvals for the use of Vytorin (the commercial name for the drug in the US) in patients with chronic kidney disease, based on the results from the SHARP study.

Provided by Oxford University