Double duty for blood pressure drugs: how they could revolutionize how we treat valve disease

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A type of medication known as angiotensin-receptor blockers could reduce risk of mortality in people with a heart disease called calcific aortic stenosis (AS) by 30 per cent over an eight-year period, Heart and Stroke Foundation researcher Dr. Philippe Pibarot told delegates at the Canadian Cardiovascular Congress. The condition is currently managed with open heart surgery.

"Our discovery shifts how we think about AS by looking at a new pathway which both prevents and reverses calcification," says Dr. Pibarot, a professor at Laval University and Canada Research Chair in Valvular Heart Diseases, Québec Heart & Lung Institute. "It broadens how we can approach therapies, opening up new avenues of research, and has tremendous potential to lead to a major discovery."

From a health economics point of view, drug treatment is also far less expensive than replacing a valve through surgery, which Dr. Pibarot says costs at least $30,000.

Every year, AS is responsible for 10,000 to 15,000 deaths in North America, and upwards of 80,000 heart surgeries. Now, this promising research suggests the first possible drug therapy to treat AS.

"AS is one of the most common types of heart disease, yet the only option to save lives has been open heart surgery. And valve replacement

surgery is the second most frequent heart surgery after coronary artery bypass," says Dr. Pibarot. "We may be able to slow the progress of AS to the point that most people won't need surgery."

Picture a normal heart valve as soft and thin, like a slice of tomato, Dr. Pibarot says. Compare that to a valve that has hardened and narrowed – more like a cauliflower. That's calcific AS, the most common type of AS, where deposits of calcium form in the valve, which prevents it from opening properly and creates a dangerous 'pressure overload' within the heart.

For years, he notes, the assumption was that AS was a degenerative disease related to aging and the cumulative wear and tear on a heart valve. But more recent studies have indicated that AS development also has some genetic and lifestyle factors (such as obesity).

As a result, several trials have looked at whether statins (a class of drugs used to lower cholesterol levels) could also be effective against AS. Those results have not been promising. Dr. Pibarot and colleagues took another approach, examining medication that is typically used to treat high blood pressure (hypertension).

The renin-angiotensin system (RAS), specifically a molecule called angiotensin II, is a major target for drugs that lower blood pressure. Some hypertension drugs block the production of angiotensin II itself – they are known as angiotensin-converting enzyme inhibitors (ACE inhibitors). Other drugs focus on the receptors of angiotensin II – angiotensin-receptor blockers (ARBs).

Over three-and-a-half years, Dr. Pibarot's study followed 340 patients who had AS, 73 per cent of whom also had some degree of hypertension. Among the patients, 34 per cent were on ACE inhibitors, 16 per cent were on ARBs, and 50 per cent were on no RAS medication.

The follow-up involved measuring the velocity of the blood across the affected valve. As Dr. Pibarot explains, just as water flows faster when a river narrows, creating rapids, a narrowing valve raises pressure too. "A quicker blood velocity means the stenosis is progressing faster," he says.

Compared to the individuals who were on no medication, those who were on ACE inhibitors had less rapid narrowing of their valve. But the biggest difference was seen in patients on ARBs, where the receptors of angiotensin II are blocked. In those patients, the progress of the disease was slowed considerably – three times slower than in the individuals who weren't taking any medication, reports Dr. Pibarot.

In effect, he says that with ARBs the current is slower, like on a calmer river.

In the absence of a drug treatment for AS, Dr. Pibarot's findings are potentially very significant, says Heart and Stroke Foundation spokesperson Dr. Beth Abramson.

"Open heart surgery can be effective, but is risky for many patients because of their age," says Dr. Abramson. "ARBs have the potential of slowing aortic stenosis significantly, so that we can prolong life without surgery."

She says that the need to find a medication solution is even more urgent when you consider that with the aging population the prevalence of valvular heart disease is expected to double within 15 years.

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