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polypill

By Prerna Uppal

Stroke kills around 5.5 million people every year, worldwide. Two-thirds of these deaths take place in developing countries like India.

An estimate of cardiovascular disease (CVD) deaths in India suggests that 52 per cent of CVD deaths occur among people below 70 years as compared to 23 per cent in other countries.

Deaths from coronary heart diseases in India rose from 1.17 million in 1990 to 1.59 million in 2000. It is expected to rise to 2.03 million by 2010.

The prevalence of risk factors for coronary heart disease (CHD) and stroke in India is overwhelming.

It is estimated that 20-40 per cent urban Indians are hypertensive, 38 per cent are dyslipidemias (those with unhealthy amount of lipids in their blood) and 56 per cent of Indian men (12-60 years) are tobacco users. These numbers, combined with the rapid rate of urbanisation and unhealthy dietary habits, make them ticking bombs.

If the numbers have been rising constantly, the efforts to address the problem have also been equally sustained. Living up to the old saying that prevention is better than cure, researchers have been busy trying to find the perfect drug for preventing cardiovascular disease. "For long, researchers have been toying with the idea of combining several pertinent drugs to make a single pill that will take care of problems like hypertension, high cholesterol and other such risk factors that can give rise to cardiovascular diseases," explains a

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Polycap || One pill to prevent risk factors of cardiovascular diseases. But lifestyle changes remain the mainstay of treatment

senior scientist at Cadila Pharmaceuticals in Ahmedabad.

Says Dr Joy Thomas, cardiologist at Frontier Lifeline and K.M. Cherian Heart Foundation in Chennai: "Polypill was proposed to be a packaged solution for cardiovascular diseases and stroke. Its constituent drugs—statin, to prevent fat deposition leading to blockages in the arteries; aspirin, to ease the flow of blood by reducing platelet stickiness and ACE-inhibitors, to reduce the load on the heart and blood vessels by reducing blood pressure, and in some preparations anti-diabetic drugs to reduce blood sugar—act

together to prevent atherosclerosis by attacking the cardiometabolic syndrome which shows increasing prevalence in present urban society." Working on this premise, Cadila has developed a one-stop pill that will take care of many ills. They call it the Polycap. The pill is expected to reduce heart diseases by 80 per cent. According to official sources, the approval to market the pill is pending with the Drug Controller General of India.

Though many were flirting with the idea of a polypill since the early 1990s, it was in 2005 that two scientists gave the phantom a clear outline—N.J. Wald and M.R. Law

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This image is for illustrative purposes only.

of the Wolfson Institute of Preventive Medicine, London. Wald analysed the work that people had already done in the field and took the idea forward.

“He [Wald] gave meaning to a concept,” says I.A. Modi, chairman, Cadila Pharmaceuticals. At first there was an attempt to combine two or three drugs to make a polypill. Wald’s work showed the

way forward for the medical fraternity. The objective behind Wald’s experiment was to “determine the combination for drugs and vitamins and their doses for use in a single daily pill to achieve a large effect in preventing cardiovascular disease with minimal adverse effects”. The four cardiovascular risk factors that they were looking to address were low-density lipo-

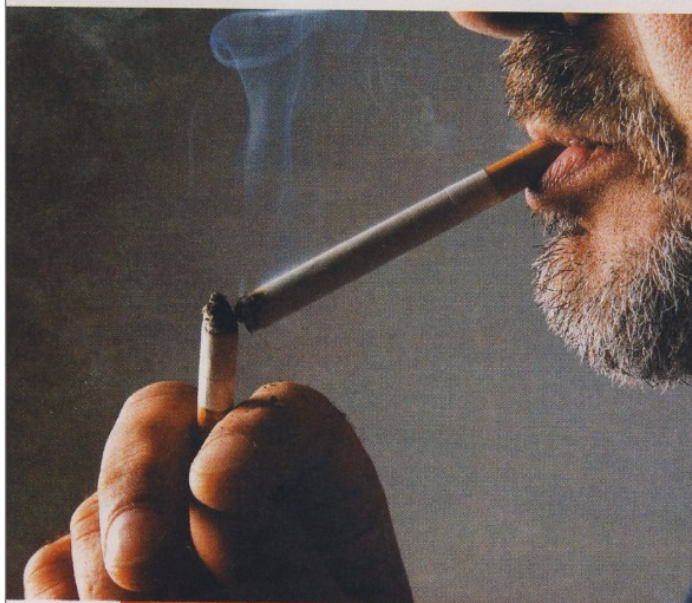
protein or LDL (better known as bad cholesterol), blood pressure, serum homocysteine and platelet function (for blood clotting). Thus began the race for a polypill. Virtually all big players in the pharma industry were involved in working out the formula for this proposed magic bullet that would revolutionise the treatment of cardiovascular diseases.

Keeping Wald’s template in mind, researchers at Cadila set out to find the right combination of drugs and so was born The Indian Polycap Study (TIPS). For five years researchers across 50 centres in India, under the leadership of Dr

Polycap contains three BP lowering drugs, a statin to reduce cholesterol and aspirin to prevent blood clotting.

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polypill

Anybody with risk factors such as hypertension, high cholesterol levels, diabetes, smoking and obesity, can pop this pill and reduce CVD risk.

result was a “combination of three widely used blood pressure lowering drugs, a statin to reduce cholesterol levels and aspirin to prevent blood clotting,” says Modi.

With multiple drugs isn't there a fear of side-effects and problems of drug interaction? One of the key findings of The Indian Polycap Study was the tolerability of Polycap.

The study also found that patients who had no history of cardiovascular disease but had only one risk factor (for instance, they were either hypertensive, diabetic, obese or were smokers) tolerated the treatment well.

But doctors do put in a word of caution. “Since individual doses of the combined drugs can't be altered, constant monitoring would be required to see what kind of dosage will suit the patient, whether he requires one pill or more,” says Dr Praveen Chandra, director, interventional cardiology, Max Devki Devi Heart and Vascular Institute, Delhi.

Salim Yusuf, professor of medicine at Michael G. DeGroote School of Medicine, McMaster University in Ontario, Canada, toiled to find the right balance of drugs to make the right formulation. “The experience was like bringing up a child; a number of people influence his upbringing, they give their best to bring up the perfect child.... Similarly, various groups of scientists worked on a single problem, combining various drugs, trying to hit upon the right formula,” explains a senior scientist at Cadila, who, too, was part of the team that developed Polycap.

More than 2,000 individuals,

who had only one risk factor for developing CVD, took part in the double-blind study (a portion of the subjects are given the drug and the others a placebo; evaluators as well as the subjects aren't aware which group received which medicine, so as to make the study foolproof). The trial assessed the effects of nine different pills containing either single agents or combinations of up to five drugs to measure their effect on risk factors such as blood pressure and cholesterol concentration. The trial also assessed whether patients can tolerate the single pill. The team tasted success a few months ago. The

How is this different from a plethora of combination drugs for CVDs available in the market? “For one, no drug has five components such as the ones used in Polycap. Also, this pill is aimed at reducing the risk of developing a cardiovascular disease,” explains Modi. So, anybody with risk factors such as hypertension, high cholesterol levels, diabetes, smoking and obesity can pop this pill to reduce the risk of becoming a heart patient. As Chandra points out, it will be an easier regimen to follow, especially for those patients who are now consuming two or more pills for their condition.

According to WHO, non-commu-

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One pill fits all

Polycap, a polypill containing five elements, developed by Cadila Pharmaceuticals, is meant for primary prevention of cardiovascular diseases and stroke. It is a combination of atenolol (50mg), thiazide (12.5mg), ramipril (5mg), simvastatin (20mg) and aspirin (100mg).

The drug and what it does

- Thiazides are diuretics. They remove excess fluids from the body and reduce heart strain**
- Statins are cholesterol-lowering drugs. They decrease plaques, prevent narrowing of arteries and reduce chances of clots**
- Aspirin is an anti-clotting medicine effective for stroke and heart attack prevention. It also reduces incidence of colon cancer**
- Beta-blockers inhibit or decrease transmissions or commands to the heart to speed up and pump more; heart rate slows, pressure drops**
- ACE-inhibitors inhibit the activity of BP-increasing enzyme ACE (angiotensin converting enzyme)**

How it works

The participants in The Indian Polycap Study (TIPS) had only one of the risk factors such as hypertension, diabetes, obesity and smoking, but no cardiovascular disease. The results from TIPS show that each of the components of the polypill did what was intended: the statin reduced cholesterol, the three antihypertensives reduced BP and aspirin reduced blood-clotting. Patients on this combination drug will be under constant monitoring to evaluate the effects of each drug on the respective disease. The dosage is determined after this.

nicable diseases, including cardiovascular disease, are reaching alarming proportions in southeast Asia, busting the myth that the problem is mainly a western headache or something that the affluent need to deal with. The success of this pill may reduce the huge disease burden CVDs threaten to impose on India. The problem becomes more peculiar because Indians are genetically predisposed to heart problems. They succumb to diabetes and heart attacks 5-10 years earlier than their western counterparts, who develop complications of the heart around 60-65 years. This means that most Indians fall prey to heart attacks, strokes and diabetes in their most productive years, when they are at the peak of their careers and most of the family responsibility is on them. This translates into a huge economic burden on the country. Highlighting the crisis, Dr Swati Piramal of Nicholas Piramal

Group, says: "Cardiovascular disease, now the leading cause of death, strikes Indians early and kills many in their productive mid-life years. Unless an innovative and effective intervention is discovered, India will continue to be plagued with these life-threatening disorders." The polypill may be the answer.

"People with a family history of premature heart attacks (occurring before 55 years in males), stroke and

who fear that it will lead to letting up on healthy lifestyle practices. "There is a chance that complacency can set in," says Thomas. This complacency means that those with risk factors may assume that once on the pill they need not watch their diet or exercise. Chandra cautions: "A healthy lifestyle is the foremost way to keep your condition under control. Nothing, absolutely nothing, can substitute it."

Educating the public so that polypill users follow good lifestyle practices is a preliminary to polypill use. The makers of Polycap have put safeguards in place. "Polycap is a scheduled drug and will be available on doctor's prescription only. Moreover, through patient education programme, people will be motivated to adopt healthy lifestyle changes for optimum risk reduction," adds Modi. So, a polypill is an addition rather than a replacement for lifestyle interventions. Eating healthy, exercising and quitting smoking are proven ways of lowering BP and ensuring overall good health. No pill can be a substitute for a healthy lifestyle. ●

those with cardiometabolic syndrome which includes obesity, high BP, smoking and high insulin levels in blood, and high stress jobs are likely to benefit from Polycap," says Thomas.

But there are those

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