Editorial

The polypill: the solution for prevention of coronary heart disease?

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In Western countries, cardiovascular disease is the most common cause of death and it is expected that it will continue to be so in the near future.[1] If the resulting physical impairment and psychosocial disturbances are also taken into account, clearly this is a serious problem from the viewpoint of productivity, quality of life, as well as community health level. Therefore the institution of preventive measures is an important issue. Unfortunately, however, currently preventive measures that are effective, safe, and at the same time practical and economical, are almost nonexistent.

Changes in lifestyle and control of dietary patterns in themselves do not always produce the desired results. In addition, these measures can potentially reduce or eliminate only some of the risk factors, as changing personal lifestyle and dietary habits of an individual is not always easily accomplished. The lifestyle and dietary habits of an individual are commonly influenced by environmental and other factors, in addition to the individual himself or herself, particularly if the individual's motivation and willpower is not strong enough and his or her self-discipline is weak.

The addition of anti-platelet aggregation and anti-hyperlipidemic agents to changes in lifestyle and dietary pattern does not *per se* provide significant support. There are indeed reports suggesting that post-myocardial infarction patients who received four kinds of preventive drugs simultaneously, i.e. aspirin, beta-blockers, angiotensin-converting-enzyme (ACE) inhibitors, and statins, had a better survival rate in comparison with those who received no medication or only one or two drugs. Other studies have emphasized that patients with acute myocardial infarction to whom three preventive drugs were administered simultaneously, had a better one-year survival rate compared with those who received only one drug, either an anti-platelet aggregation, anti-hyperlipidemic, or anti-hypertensive agent.

The preliminary conclusion that may be drawn[2] is that by adding as many kinds of drugs as possible, in addition to changes in lifestyle and dietary pattern, a higher level of prevention may be attained. This is easily understandable since preventive measures that involve more risk factors should logically be more effective; however, this kind of approach is not without problems. Consuming too many drugs simultaneously may lower the effectiveness of the preventive measures, because of decreased compliance in taking the drugs and because of the high cost.

The concept of a "polypill", where a number of drugs for prevention of coronary heart disease, such as aspirin, beta-blockers, ACE inhibitors, and statins, are packaged as a single "pill", is neither a new idea nor an original one. With the polypill, prevention is expected to be more effective and efficient, due to better patient compliance.

On the basis of the results of a meta-analytical study by Wald and Law[3] published in 2003, a hypothetical polypill containing a beta-blocker, a thiazide antidiuretic, and an ACE inhibitor, all at half the standard dose, with the addition of folic acid, a statin and aspirin, if consumed daily by all individuals over 50 years of age, could be expected to reduce the incidence of coronary heart disease by more than 80%. Additionally, one third of the population would be free from heart attacks or stroke for the next 11-12 years of their life.[4] The objective of the hypothetical polypill was to improve four key risk factors of coronary heart disease simultaneously, namely hypertension, LDL cholesterol, serum homocysteine levels and platelet function. The adverse effects of the antihypertensive drugs contained in the polypill would presumably be reduced by using only half-doses. Wald and Law estimated the probability of discontinuation of the pill due to unwanted effects to be only around 1%-2%, whilst fatal side effects would occur in just less than 1:10,000 cases.

Sleight et al support the polypill concept, but are of the opinion that a sufficiently long period of time is needed for educating healthcare workers so that they would be prepared to accept this concept.

However, besides the promises of the polypill, there are still several doubts about its feasibility. Not every patient needs all of the drugs in the polypill with the same dosages. There may be individuals who have to avoid taking beta-blockers or aspirin, such as patients with asthma or peptic ulcer. Furthermore, not a few patients are unwilling to take such a large-sized pill, presumably leading to a high drop-out rate. It is also unclear if the total cost of taking polypills will be considerably lower than that of taking only the needed drugs individually. Discontinuation of treatment because of adverse effects is also much easier in the case of drugs that are administered separately.

Apart from the validity of the meta-analysis of Wald and Law, because the costs of production and promotion of the polypill has not yet been taken into consideration and its effectivity has still to be demonstrated in practice, compared to the currently accepted methods of preventing coronary heart disease, at present the polypill is still not more than a concept. It is to be hoped that research on the polypill be intensified, taking into consideration also the morbidity rates, epidemiological characteristics and risk factors prevalent in various communities with differing psychosocial and cultural conditions.

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