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Physical activity and dietary intervention for chronic diseases: a quick fix after all?

Ever since the general acceptance of the established links between lipids and atherosclerosis, study after study has shown the tangible clinical benefits of reducing the risk factors for both dyslipidemia and atherosclerosis on overall mortality. However, most of these studies have included interventions that have shown benefits only after many months to years of such treatments. For example, the landmark Finnish Diabetes Prevention Study (7) and the US Diabetes Prevention Program Trial (3) were the first clinical trials to show that engaging in an active lifestyle regimen reduces the incidence of new-onset diabetes by 58% in both trials in subjects with impaired glucose tolerance at the start of the study, but these results were obtained after 2.8–3.2 years. High-fiber diets were shown to protect against obesity and cardiovascular disease by lowering insulin levels, with a follow-up of over 10 years (5). The American culture of “one size fits all” and a “quick fix” to the multitude of problems associated with chronic health conditions have made the most potent treatments, physical activity and dietary interventions, hard to translate into efficacious clinical practice, in contrast to that obtained by pharmaceuticals.

The provocative report by Roberts et al. (6) in this issue of the Journal may help to overcome the above barriers of time and effect. Their study of just 3 wk of treatment showed a phenomenal clinical response of ~50% decrease in metabolic syndrome (defined using the WHO criteria) and Type 2 diabetes. At the start of the study, 48 and 42% of the 31 subjects had metabolic syndrome and Type 2 diabetes, respectively. This number decreased to 19 and 23%, respectively, after the 3-wk intervention and was associated with enhanced insulin sensitivity. So what was the miracle treatment? The treatment was intense lifestyle modification consisting of diet and physical activity. To our knowledge, no current pharmaceutical product has made a claim in a peer-reviewed publication for an approximate halving the metabolic syndrome and Type 2 diabetes in 3 wk.

It is thus important to emphasize the details of the treatment that produced the remarkable changes. The diet was light on fat (12–15% of calories) with a polyunsaturated-to-saturated fatty acid ratio of 2.4:1), medium on protein (15–20% of calories), and high in unrefined carbohydrates (65–70% of calories) and fiber (>40 g), in contrast to the more widely publicized low-carbohydrate diets. Interestingly, food was provided ad libitum and subjects were not calorically matched or restricted. The physical activity regimen consisted of 45–60 min/day walking on treadmill at a heart rate of 70–85% of maximum, which was individualized to each subject on the basis of a graded treadmill stress test according to a modified Bruce protocol. All exercise and dietary sessions were supervised in this 21-day residential program at the Pritikin Longevity Center, with adherence to the diet and activities being essentially 100%.

This short-term combined intervention consisting of a high-fiber, low-fat diet and regular physical activity reduced stress indicators, inflammation, and dyslipidemia associated with metabolic syndrome and Type 2 diabetes in obese men. The

3-wk lifestyle intervention 1) beneficially modified the dyslipidemic profile by decreasing low-density lipoprotein cholesterol by 26%, total cholesterol by 21%, and triglycerides by 28%; 2) enhanced insulin sensitivity and decreased fasting serum insulin by 6 and 30%, respectively; 3) reduced serum oxidative stress, myeloperoxidase and 8-iso-PGF_{2α}, by 20 and 35%, respectively; 4) decreased the inflammatory marker CRP by 39% in serum; 5) decreased vascular endothelial cell and platelet activation mediators, ICAM-1 and sP selectin, by 20 and 8%, respectively; 6) decreased monocyte adhesion by 31% and monocyte chemotactic activity by 29%; 7) decreased a marker of plaque stability and progression, MMP-9 by 25%; and 8) decreased in vitro production of MCP-1, VCAM-1, and reactive oxygen species (hydrogen peroxide or superoxide) by 8, 15, and 8%, respectively and increased nitric oxide production by 9%. Thus an intensive 3-wk lifestyle intervention resulted in significantly modifying factors associated with metabolic syndrome and Type 2 diabetes.

Remarkably, the above changes occurred despite a mere 3.6 and 2.8% decrease in body weight and body mass index (BMI), respectively, and both the pre- and postintervention groups remained obese. Therefore, the prevalence of disease and many of its associated risk factors decreased largely independent of BMI with intense changes in diet and exercise. Although this study by Roberts et al. (3) did not provide actual quantification of fitness levels in their patients pre- and postintervention, these findings are nevertheless consistent with others, in that being at least moderately fit seems to confer protection against premature mortality across a range of BMI categories to such an extent that obese fit men have been reported to have a lower risk of mortality than unfit lean men (4). Lee et al. (4) recommended that for long-term health benefits the focus should be on improving fitness by increasing physical activity rather than relying only on diet for weight control. These comments are important because the role of physical activity in health seems to be emphasized less than diet and obesity by the popular media.

It should be noted that although several indexes of vascular function, inflammation, and oxidative stress were measured in this study, diabetes-related microvascular complications were not determined and likely unchanged after 3 wk. Therefore, reducing diabetes prevalence by 45% does not likely extend to cell damage already done by diabetes. Also, the precise relevance to each of these markers to clinical outcomes is unknown. Another limitation to the study was that the separate effects of the diet and exercise alone were not determined so the relative contributions of these lifestyle modifications are not known. Such knowledge would be helpful. The percentage reduction in metabolic syndrome was likely underestimated because blood pressure was not determined, making the diagnosis conservative. Measurement of waist circumference, which was not done, would also have been useful. Lastly, this study was limited by the small number of subjects. However, their earlier 1991 publication (1) had 4,587 subjects with determinations limited to blood lipids that showed almost identical percentage decreases in total cholesterol, low-density

lipoprotein cholesterol, and triacylglycerides as the present study.

Despite the above caveats, and given that many believe weight loss is difficult to achieve and maintaining the weight loss is an even greater challenge (2), the report of Roberts et al. (6) encouragingly shows that a 3-wk, intense lifestyle modification can in fact result in a marked improvement in health parameters without a major change in body mass.

Their findings raise many questions for future research. If these subjects continued the intense lifestyle modification, would they have seen more substantial decreases in body fat? Because the subjects were tested in 2001, what is the long-term follow-up of these 31 male subjects? Would female subjects have similar benefits? Did they continue with the intense lifestyle modification outside of the controlled environment of the study? Did the beneficial anti-inflammatory effects of the 3-wk intensive lifestyle intervention persist long term, and what are the underlying molecular triggers of these anti-inflammatory effects? Perhaps most importantly, does a short-term intensive intervention such as this have an impact on overall mortality?

Thus much work is needed to answer these and other questions arising from this exciting research. Though not the panacea, the results from Roberts et al. (3) provide a clear “proof of principle” to the notion that tangible health benefits can indeed be obtained by engaging in one type of lifestyle intervention, even as short as 3 wk. The weaving together of the independent strands of epidemiological information and novel interventional studies of these epidemic lifestyle diseases can provide a new fabric for designing more efficacious therapeutic strategies.

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