Pharmacological treatment of obesity: a public health perspective

During the past 30 years, prevalence of overweight (body mass index – BMI > 25kg/m^2) and obesity (BMI > 30kg/m^2) has dramatically risen worldwide. Since excess of weight contributes to the development and worsening of chronic illnesses such as type-2 diabetes, hypertension, cardiovascular diseases, stroke, depression, several types of cancer and other conditions, the prevention and effective treatment of obesity are expected to have a significant impact on morbidity, mortality, quality of life and cost of health care. The treatment of obesity is intended to prevent or attenuate morbidities associated with excess of weight, and not only to reduce weight or to achieve the patient's "ideal" body weight. Dieting and physical exercise are first-choice therapeutic options for obesity. It is generally agreed that pharmacological therapies, always alongside dieting and exercise, should be reserved for obese patients who had failed to respond to behavioral approaches alone. Nonetheless, pharmacological treatment of obesity has yielded disappointing results so far. A number of anti-obesity drugs (amphetamine-like agents, fenfluramine-derivatives, rimonabant, and others) were withdrawn from the market due to a clearly unfavorable risk to benefit ratio. Moreover, long-term effectiveness of appetite suppressants is at best questionable. Although causing weight loss during the first weeks of treatment, body weight reduction attributable to these medications (*i.e.*, the weight loss in excess of that achieved with diet and exercise alone) is in general modest, and a partial regain of weight occurs when anorexic drugs are used for periods longer than one year. In almost all cases, weight loss achieved with appetite suppressants is totally regained when drug therapy is discontinued. Since obesity is a chronic condition, and body weight is regained upon drug discontinuation, patients are expected to take these medicines for years, or even for the rest of their lives. It is believed that even modest weight losses (5-10%) achieved with diets and exercises ameliorate obesity co-morbidities. Modest weight losses obtained by means of appetite suppressants, however, do not necessarily translate into long-term health benefits, *i.e.*, into reduction of morbidity and mortality associated with overweight. The lack of long-term health benefits of an anorexic drug was recently revealed by a post-marketing 5-year clinical study (SCOUT – *Sibutramine Cardiovascular Outcomes Trial*) involving 10,744 obese patients with preexisting cardiovascular disease, type-2 diabetes or both. The SCOUT study showed that sibutramine increased risks of cardiovascular diseases (heart attack and strokes) instead of reducing them as expected. So far no controlled and randomized clinical study, with a sufficiently large number of patients, has demonstrated that other anorexic drugs produce long-term health benefits. After 13 years in the market, sibutramine was banned in the USA, Europe and most countries, where Orlistat, an inhibitor of pancreatic lipase that reduces fat absorption in the intestines, remains the only drug that has been approved for the long-term treatment of obesity. If large clinical trials on long-term safety and efficacy (*i.e.*, prevention and reduction of overweight co-morbidities) are not undertaken prior to marketing, new ineffective anti-obesity drugs are likely to enter and stay in the market for a long time.

Francisco J. R. Paumgartten
Escola Nacional de Saúde Pública Sergio Arouca, Fundação Oswaldo Cruz, Rio de Janeiro, Brasil.
paum@ensp.fiocruz.br