

Anti-Obesity Drugs Safety

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EDITORIAL NOTE

Obesity is a major health problem worldwide. Although diet and physical activity are crucial within the management of obesity, the long-term success rate is low. Therefore anti-obesity drugs are of great interest, especially when lifestyle modification has failed. As obesity isn't an instantaneous life-threatening disease, these drugs are required to be safe. Anti-obesity drugs that are developed thus far have limited efficacies and considerable adverse effects affecting tolerability and safety. Therefore, most anti-obesity drugs have been withdrawn. Fenfluramine and dexfenfluramine were withdrawn due to the potential damage to heart valves.

Sibutramine was related to a rise in major adverse cardiovascular events within the Sibutramine Cardiovascular Outcomes (SCOUT) trial and it had been withdrawn from the market in 2010. Rimonabant was withdrawn due to significant psychiatric adverse effects. Orlistat was approved in Europe and therefore the use for long-term treatment of obesity, but many patients cannot tolerate its gastrointestinal side effects. Phentermine and diethylpropion can only be used for fewer than 12 weeks because the long-term safety of those drugs is unknown.

Ephedrine and caffeine are natural substances but the consequences on weight reduction are modest. As a result there's an enormous unmet need for effective and safe anti-obesity drugs. Recently lorcaserin and topiramate plus phentermine are approved for the treatment of obesity but long-term safety data are lacking.

Obesity is a major public health problem worldwide. It is related to increased risks of hypertension, dyslipidemia, type 2 diabetes, cardiovascular diseases, obstructive apnea, osteoarthritis, and certain cancers. Reduced anticipation has also been linked to obesity thanks to increase cardiovascular and cancer risks. Treatment of obesity is therefore important, but it must be efficacious, well tolerated, sustainable, and in particular, safe.

While it is documented that obesity is caused by overeating and physical inactivity, the pathophysiology of obesity is complex and incompletely understood. Genetic predisposition has been extensively evaluated.

Studies of twins have shown that obesity may be a highly heritable trait. In addition, genome-wide association studies also as studies of candidate genes have identified many of the associated genes, suggesting that multiple mechanisms are involved in obesity. Besides, there's increasing evidence in support of obesity being an inflammatory disorder.

It is believed that adiposity is due to an imbalance between the levels of pro-inflammatory cytokines, such as interleukins and tumor necrosis factors, and the levels of anti-inflammatory cytokines. Therefore, one drug is unlikely to be effective.

The current anti-obesity drugs mainly act on the appetite, but there are many other systems that control weight, including absorption, metabolism, and thermogenesis. When these pathways are targeted, it's likely to cause undesirable effects.

The safety of medicine for the treatment of obesity is undermined by poor understanding of the pathophysiology of obesity, lack of excellent therapy, poor uptake and usage of therapy, and poor compliance. There are also regulatory and societal issues.

The history of anti-obesity drugs is littered with instances of early promises but late failure. We do not understand the genetic, biochemical, physiological, psychological, behavioral, and social mechanisms that cause obesity tolerably to stop or reverse it effectively. Many drugs treat just one a part of this complex interaction and produce unacceptable side effects.

Thus, in spite of favorable results in terms of body weight reduction, most anti-obesity drugs developed so far have not been approved or have been withdrawn from the market due to significant adverse effects. There is an urgent need for brand spanking new anti-obesity drugs. Newly approved drugs including lorcaserin and phentermine plus topiramate were proven effective in weight reduction but their long-term safety and tolerability should be carefully evaluated within the future.

It should even be remembered that, in clinical trials, anti-obesity drugs were utilized in combination with a reducing diet. The key to successful weight reduction remains good adherence to a reducing diet and adequate regular physical activity.

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