Practical Tips for Prescribing Anti-obesity Drugs

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The prevalence of obesity is increasing rapidly in Asia. It is estimated that one in three people are obese in Hong Kong. Developing effective strategies in combating the obesity epidemics has become a healthcare priority in many Asian countries.

Importance of life-style modification

Diet and exercise remain the best way forward for weight reduction. Pharmacological intervention of obesity plays a supportive role in weight management and is never effective in the long-term without life-style modification. The pharmacokinetics and pharmacodynamics of the two anti-obesity drugs approved by Food Drug Administration (FDA), orlistat (Xenical) and sibutramine (Reductil) are well-known to many general practitioners. However, effective usage of these drugs requires careful history taking, counselling, in combination with life-style modification.

Initial assessment

Obtaining detailed medical and dietary history will not only enable the practitioner to have a better understanding of the patient's current health status which determines to some extent the need for anti-obesity therapy, but also serves as a good first step towards building trusty rapport with the patient. A careful dietary history will help to decide which therapy is most appropriate, taking into account the patient's background, culture, belief, occupation and dietary pattern. There are no fixed guidelines as to when anti-obesity drugs should be started. They should, however, be generally reserved for those with BMI > 25, and especially those with weight-related co-morbidities.

Orlistat

Orlistat has been shown to be effective for weight reduction in many studies, the largest one being XENDOS[1], in which orlistat also reduced the progression of impaired glucose tolerance to overt type 2 diabetes. Insulin resistance and cardiovascular risk factors have also been shown to be improved by orlistat in Hong Kong Chinese[2]. Orlistat is suitable for subjects taking high-fat diet, and those who eat out frequently. It is important to explain to the subject that a maximum of 30% of dietary fat will be excreted with the use of orlistat. It is crucial to stress that they need to be compliant with their dietary content and they should not feel that they can eat fatty food with the false belief that no fat will be absorbed. Many people may wrongly underestimate the fat content in the food and orlistat may serve to remind them the actual fat content in their meals. Steatorrhoea is a well-recognised side-effect feared by many dietary non-compliant patients. Simply by avoiding fatty food will improve this side-effect. A useful way to tell patients not to rely on orlistat is to tell them that for every one drop of oil excreted, two will be absorbed. Patients should be explained about the frequency and duration of therapy. Orlistat has recently been approved by FDA for treating obese children age between 12-16 years. Malabsorption of fat-soluble vitamins is only a theoretical concern and is of no clinical relevance provided that it is not taken long-term (over 1 year). Hence patients should be reassured about this and the lack of drug interactions with commonly used drugs.

Sibutramine

For those with a large appetite and high in carbohydrate intake, sibutramine may be a better therapeutic option[3]. Similarly, sibutramine has been shown in numerous clinical trials to be effective in weight reduction and the most well-known being the STORM trial[4]. The dual mode of action of sibutramine (satiety effect and thermogenesis in adipose tissue) should be carefully explained. Unlike orlistat which can be taken regularly or when required, sibutramine should only be taken regularly. One should start with low dose and increase after at least 2-3 weeks and titrate against side-effects. The main side-effects are dry mouth and constipation. These can be ameliorated by increasing fluid intake. Occasionally constipation is severe enough to warrant drug withdrawal. Sleep disturbance seldom occurs and cardiovascular effects such as tachycardia and uncontrolled hypertension are very rare. One should avoid prescribing to patients with psychiatric illness or depression since they may be prescribed monoamine oxidase inhibitors which could lead to drug interaction with sibutramine.

Combination therapy

No one should require combination anti-obesity drug therapy if they are dietary compliant. Occasionally, sibutramine-treated patients may take orlistat when they eat out. Overall, combination therapy is not specifically recommended and the main emphasis should be on life-style modification (diet and exercise).

Anti-obesity drugs and diabetes

Type 2 diabetes is one of the commonest co-morbid conditions associated with obesity. Diabetic patients should be warned that their anti-diabetic medication such as sulphonylurea and insulin may hinder the speed of their

weight reduction. This will help to adjust their expectations and help them to set realistic goals. Both orlistat and sibutramine monotherapy has been shown to be effective in improving glycaemic control via weight reduction in diabetic patients. It is important to be aware that anti-diabetic drugs such as metformin and acarbose have gastrointestinal side-effects such as diarrhea (common with metformin), bloating and fluctuance (acarbose). Hence, orlistat-related stearrhoea may aggravate their gastrointestinal upset and therefore dose reduction of metformin or acarbose may be necessary. In summary, diet and exercise remain the main stay of therapy for weight reduction. Anti-obesity drugs improve the speed of weight reduction. Careful assessment and history taking are required to determine the need for anti-obesity drug and the choice of drug as well as its duration. Detailed counselling and explanation is the key to drug compliance.

References

1. Torgerson JS, Hauptman J, Boldrin MN, Sjostrom L. XENical in the prevention of diabetes in obese subjects (XENDOS) study: a randomized study of orlistat as an adjunct to life-style changes for the prevention of type 2 diabetes in obese patients. *Diabetes Care* 2004; **27**(1):155-61.
2. Tong PC, Lee ZS, Sea MM, Chow CC, Ko GT, Chan WB, So WY, Ma RC, Ozaki R, Woo J, Cockram CS, Chan JC.The effect of orlistat-induced weight loss, without concomitant hypocaloric diet, on cardiovascular risk factors and insulin sensitivity in young obese Chinese subjects with or without type 2 diabetes. *Arch Intern Med* 2002;**162**(21):2428-35.
3. Astrup A, Toubro S. When, for whom and how to use sibutramine? *Int J Obes Relat Metab Disord* 2001;25 **Suppl 4**:S2-7.
4. James WP, Astrup A, Finer N, Hilsted J, Kopelman P, Rossner S, Saris WH, Van Gaal LF. Effect of sibutramine on weight maintenance after weight loss: a randomised trial. STORM Study Group. Sibutramine Trial of Obesity Reduction and Maintenance. *Lancet* 2000;**356** (9248):2119-25.