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The Perioperative Implications of New Weight Loss Drugs

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Key points

- Obesity can affect pharmacokinetics, and, to a lesser extent, pharmacodynamics of administered medications.
- New weight loss drugs approved by the US Food and Drug Administration (FDA) include lorcaserin, phentermine/topiramate, and bupropion-naltrexone, each with potential implications for perioperative care.
- Lorcaserin is a serotonin 2C receptor agonist with modest weight loss efficacy and no statistically significant increase in valvulopathy. Patients on lorcaserin are at risk of serotonin syndrome. Coadministration of seritonergic agents and monoamine oxidase inhibitors should be avoided.
- Phentermine/topiramate has been correlated with the greatest sustained weight loss. Phentermine is a sympathomimetic amine and thus does have abuse potential.
- Naltrexone/bupropion is well tolerated and nonaddicting. Naltrexone is a pure opioid antagonist normally used for alcohol and opioid dependence, suppressing β-endorphin negative feedback. Bupropion may cause an increased heart rate, and blood pressure may not be reduced to the degree expected with weight loss.

INTRODUCTION: NATURE OF THE PROBLEM

According to the US Centers for Disease Control and Prevention (CDC), over one-third of US adults, or 78.6 million people, are obese, defined as a body mass index (BMI) of at least 30 kg/m^2 [1]. The Behavioral Risk Factor

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Surveillance System delineates the self-reported prevalence of obesity on a state-by-state basis. In 2014, every state had a prevalence of obesity of at least 20%; 22 states exceeded 30% or greater, and 3 states (Arkansas, Mississippi, and West Virginia) reported over 35% [2]. In 2006, the annual per capita medical spending for an obese adult was estimated to be $1429 higher than a normal weight individual, a 41.5% difference [3]. This is largely because of associated comorbidities, ranging from osteoarthritis and gall bladder disease to hypertension, coronary artery disease, obstructive sleep apnea, diabetes, stroke, and certain cancers [4].

The continuing rise in obesity prevalence can be expected to translate into a greater number of patients affected by severe obesity appearing in operating rooms and procedural suites. There has only recently been an increase in drug studies specific to or including obese patients. The US Food and Drug Administration (FDA) encourages, but does not require, inclusion of patients with obesity in most pharmaceutical trials unrelated to weight loss. Frequently, this results in insufficient numbers of higher BMI patients having been included to enable creation of specific dosing recommendations.

Obesity will influence the pharmacokinetics (PK) of a drug–what the body does to a particular medication. PK alterations may occur at several points in the system: absorption, distribution, metabolism, and/or excretion. Limited studies exist investigating obesity's effects on oral and subcutaneous drug administration. Insulin, as 1 reassuring example, shows no changes in absorption rate at equal doses in obese patients versus those of normal BMI [5].

Obesity is associated with a number of factors that can potentially affect the volume of distribution (Vd), defined as the amount of drug in the body divided by the blood concentration [6]:

- Decreased tissue perfusion
- Increased lean tissue mass
- Increased adipose tissue mass
- Increased cardiac output
- Increased splanchnic blood flow
- Changes in plasma proteins

In theory, a lipid-soluble drug has a high Vd; lipid-insoluble, low Vd. Thus, a lipid-soluble drug (as are many anesthetic medications) would require a larger bolus dose and would demonstrate a longer elimination phase. However, the nonlinear relationship between increasing adipose and increasing lean body weight at higher BMI levels [7] and the relatively poor perfusion of adipose tissue make this generalization less useful in clinical practice.

One might expect altered drug metabolism to be a significant concern, given that liver function tests are elevated in 20% to 30% of patients with obesity. However, no consistent correlation has been shown between these laboratory findings and decreased metabolism of anesthetic drugs. Conversely, phase 2

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