MI Q&A

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# Important dosing considerations in overweight and obese patients: what matters?

*The physiological changes in obesity significantly alter the pharmacokinetics and pharmacodynamics of many medications. This Q&A will briefly cover the pharmacokinetic and pharmacodynamic changes that occur in obesity and their relevance to general medication management. Specific medication classes and their use in overweight and obese patients will be described in future Q&As.*

Obesity is defined as "abnormal or excessive fat accumulation that presents a risk to health", and is commonly accepted as a Body Mass Index (BMI) of greater than 30 kg/m$^2$ (WHO). It is a major risk factor for cardiovascular disease and type 2 diabetes. In 2017–18, 25% of Australian children and adolescents and 67% of adults, were obese or overweight. Over 8% of the disease burden in Australia in 2015 was attributable to obesity (AIHW).

Recommendations for the dosing of medications in obesity can vary significantly, depending on whether ideal body weight (IBW), adjusted body weight (AdjBW), lean body weight (LBW), body mass index (BMI), body surface area (BSA) or actual body weight (ABW) dosing is used[1]. Each method has limitations, and certain medications may be dosed using a specific measure of patient size (e.g. chemotherapeutic agents are often dosed using BSA; thromboprophylaxis with enoxaparin can be based on ABW).

**Pharmacokinetics**

Obesity affects all four aspects of pharmacokinetics: absorption, distribution, metabolism and elimination (LITFL). There is limited data for appropriate dosing of many agents, as clinical trials often exclude this population of patients. Clinical judgement, therapeutic drug monitoring and careful consideration of pharmacokinetics and pharmacodynamics in obesity is often required.

Differences in absorption and bioavailability of medications between obese and non-obese patients is inconsistent. Obese patients have increased gut perfusion and accelerated gastric emptying, which theoretically may enhance absorption and hence drug bioavailability.

However, studies have shown that some oral medications (including ciclosporin, midazolam, and propranolol) display no difference in bioavailability between obese and normal body-weight patients.

Absorption following subcutaneous enoxaparin was delayed by up to an hour in obese patients, though the aetiology is poorly understood. Adipose tissue receives a much lower proportion of cardiac output than viscera and lean tissues (5% v 73% and 22% respectively) and altered perfusion may play some part in this delay.

The increase in adipose tissue in obese patients results in altered distribution of medications. Due to the tissue composition of obese patients, it is necessary to use different measures of body weight to ensure more accurate drug dosing. The use of LBW and IBW has been shown to correlate well with hydrophilic medications that are generally confined to the vascular compartment (and have low volumes of distribution). Total body weight has been shown to be a better guide for dosing of lipophilic drugs.

[1] Refer to Barras & Legg (2017) for further information

**Pharmacodynamics**

There is limited evidence regarding the pharmacodynamic effects of various agents in obesity. However, the pharmacodynamic profile of certain agents can be affected in obese patients; for example, obesity is associated with obstructive sleep apnoea (OSA). OSA-related symptoms can be worsened with sedatives and opioids by reducing effective breathing, resulting in pronounced respiratory depression.

**The Challenge**

Implementing dosage recommendations in overweight and obese patients in clinical practice is challenging. Whilst evidence is evolving, it is not always clear what dosage or weight parameter to use, as dosage recommendations can be lacking or unclear. Where this is the case, ensure your references are up-to-date and individualised to the patient. Consult your Medicines Information service for assistance.

**Refer to the SHPA Medicines Information Procedure Manual and the Electronic Medicines Information Training (EMIT) for up-to-date, curated education on seeking information you can trust and that is clinically relevant to our Australian practice when providing expert advice about medicines.**

**Join the SHPA Specialty Practice: Medicines Information Interest Group forum for additional references related to MI.**

## Further Reading and resources


- Zaidi & Roberts. Demystifying Drug Dosing in Obesity. Drug Dosing in Obesity Vol 1: Antimicrobials Springer (2016) https://www.springer.com/gp/book/9783319440323#aboutBook
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- Matson et al. Medication Dosage in Overweight and Obese Children. J Pediatr Pharmacol Ther 2017;22(1):81–83
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- Erstad, B.L., Barletta, J.F. Drug dosing in the critically ill obese patient—a focus on sedation, analgesia, and delirium. Crit Care 2020;24,315 https://doi.org/10.1186/s13054-020-03040-z



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MI Q&A aims to present concise, factual information on issues of current interest in therapeutics, drug safety and cost-effective use of medications. The topics presented are based on frequently encountered medicines information requests made to Medicines Information centres and/or matters of current clinical importance. Note that any treatment decisions should be made with careful consideration of the individual clinical circumstances of each patient. Comments, contributions or suggestions are welcome. Please join the SHPA Medicines Information stream at: https://onlinecpd.shpa.org.au/course/view.php?id=235 or email specialtypractice@shpa.org.au