

Episode 4 - Pharmacokinetics in obese patients

Considerations: i) attaining adequate peak plasma levels or adequate steady state levels, ii) side-effects, toxicity or prolonged duration of action.

Definition of obesity

Body mass index of $> 30 \text{ kg/m}^2$, or by another definition, their total body weight is greater than 120% of their ideal body weight. Dose adjustments need to be made only if the patient fits these criteria.

Body Composition

Total body weight > Adjusted body weight > Ideal body weight > Lean body mass

Lean body mass is about 80% of total body weight in healthy individuals. It determines initial drug distribution and correlates with cardiac output (perfusion of vessel rich tissues).

Both lean body mass and adipose tissue are increased in obese individuals. This increase is disproportionate however with only about 40% of the excess weight being lean body mass (see adjusted body weight).

Volume of distribution

Water soluble drugs	Larger volume of distribution. Dosing on adjusted body weight (bolus and infusions). Dosing on ideal body weight may theoretically result in ineffective peak plasma levels. This is rarely clinically significant however.
Lipid soluble drugs	Much larger volume of distribution. No significant effect on bolus dosing (initial drug distribution to vessel rich organs). Redistribution and accumulation with repeated doses or continuous infusion.

Metabolism

Cardiac output is increased as are hepatic and renal blood flow, increasing rates of drug metabolism and excretion (clearance).

Volatile agents

Decreased FRC but increased pulmonary blood flow, with little net difference in speed of onset. Accumulation with prolonged use. Desflurane has the lowest oil:gas partition coefficient = 19:1.

Drug dosing

In the operating theatre all drugs should be dosed according to ideal body weight or adjusted body weight (if available) - apart from Suxamethonium (dosed on total body weight).

On the intensive care unit drugs will be dosed according to adjusted body weight or body surface area, usually after consultation with the pharmacist.

Parameter	Notes
Body Surface Area (m ²)	Chemotherapy (including Prednisolone) = $\sqrt{(\text{cm} \times \text{kg} / 3600)}$
Total body weight	Suxamethonium (increased total plasma cholinesterase) Elefeld, Schider, Marsh and Minto TCI pumps
Adjusted body weight	Intensive care unit. Infusions and drugs with a narrow therapeutic index. = $\text{IBW} + [0.4 \times (\text{TBW} - \text{IBW})]$
Ideal body weight	Local anaesthetics, induction agents, neuromuscular blockers, reversal agents, Paracetamol, NSAIDs, opioids. Men = $50 + 0.91 \times (\text{cm} - 152.4)$ Women = $45.5 + 0.91 \times (\text{cm} - 152.4)$ Estimated IBW = height in cm - 100

Infusions

Problems include side-effects (bolus overdose) or prolonged duration of action (accumulation).

Fixed rate infusions (and loading doses) should be calculated according to ideal body weight or adjusted body weight. This applies to Propofol, and all opioid drugs irrespective of their lipid solubility and metabolism.

Target controlled infusions should be programmed with the total body weight (Elefeld, Schider, Marsh, Minto) as the pump will calculate a lean body mass and adjust dose accordingly.