

Critical Care

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Pharmacokinetic Considerations in Obese Intensive Care Unit Patients

Patients in the intensive care unit (ICU) represent some of the most complicated and vulnerable patients seen in practice. Unfortunately, there is a lack of strong evidence for dosing obese ICU patients. Reasons for this include a high variance among the types of patients and disease states commonly seen in the ICU, difficulty in performing clinical pharmacokinetic (PK) studies in this population, or simple exclusion from clinical trials. Prevalence of these disease states depends on the type of ICU setting: medical, surgical, cardiac, trauma, burn, neurological, or combined units. This chapter will focus on reviewing the available evidence for dosing of medications in the obese critically ill patient.

PK parameters can be altered (or not altered) in any of these patients. Absorption can be affected by surgical procedures involving resection or manipulation of the gastrointestinal (GI) tract, decreased perfusion due to splanchnic constriction, inflammation, or simply a patient who is made nothing per oral for an extended period of time.¹ The volume of distribution (V_d) can be altered by changes in protein binding, patients aggressively volume resuscitated in septic shock, or in patients that are fluid overloaded.¹ The primary mechanisms of clearance (Cl) and elimination for the majority of medications rely on renal and hepatic function. Patients with septic shock

can develop multiorgan failure in the form of acute or acute-on-chronic kidney injury as well as hepatic injury. These changes in end-organ function result in a decline in the ability to metabolize and eliminate medications. Given the state of chronic inflammation in obese patients with excess interleukins, tumor necrosis factor alpha, and other cytokines released by adipose tissue, alterations in the inflammatory response during sepsis are also thought to occur.²

Considerations for Obese ICU Patients

Risk of Complications

All patients in the ICU are at risk for infections, thromboembolism, or medication errors that could lead to iatrogenic injury. Outcomes specific to obese patients are not widely available. A review of seven studies showed mixed results for the impact of obesity on sepsis mortality.² The differences in the methods and statistical analysis of the seven trials did not allow the authors to make true comparisons. Three studies showed no difference in mortality; one study showed an increase in mortality; and three studies found reduced mortality.² Obesity has been shown to increase the risk of nosocomial infections, antibiotic treatment failure, pressure ulcers, and risk for acute respiratory distress syndrome development.²⁻⁴

Challenges from an Informatics Perspective

Technology is becoming more and more complex in the healthcare industry. Many institutions are moving or have moved toward electronic health records, computer physician order-entry (CPOE) software, and smart infusion pumps. With this increasing complexity, there is a risk for input errors regarding weight-based drugs. Patients' height and weight are stored in the CPOE system, which can be used to prepopulate medication doses for electronic orders to make calculations easier for prescribers. This may lead prescribers to dose off of total body weight (TBW) when an adjusted body weight or ideal body weight (IBW) would be more appropriate. Another example is in smart pumps where the "brain" is programmed for a weight for the channel that infuses the medication. If another infusion is added, which requires an additional channel, the brain will automatically use the already programmed weight. If one medication is based on TBW dosing and the other is based on IBW, then medication errors could potentially occur. It is important to realize the complexity of the technology to prevent medication errors from occurring in the obese ICU patient by implementing training and guardrails.

Vasopressors and Inotropes

Few published data exist on vasopressors and inotropes used in obese patients. All of these agents, except for vasopressin, are weight-based infusions, have short half-lives, and are titrated to goal blood pressure (BP) targets. It is unclear at this point which weight would have the best correlation with therapeutic success, and thus no formal recommendation can be made.⁵ Careful monitoring of hemodynamics based on the patient's clinical response should be implemented, similarly to normal-weight individuals.

Helpful Tips

- Make sure to always remind healthcare professionals to assess for extravasation.