Pharmacotherapy in critical care medicine

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DOI: https://doi.org/10.52340/9789941519109.07

Keywords: Critically ill patient, rational pharmacotherapy, dosing regimen, clearance, Good Prescribing.

Abstract

It is critically important to conduct daily review and monitoring of the medication list and dosing regimens prescribed for hospitalized critical care patients, based on consultation with a clinical pharmacologist in intensive care departments. In critically ill patients, rapid fluctuations in key physiological parameters often lead to changes in drug pharmacokinetics and pharmacodynamics. These variations complicate both the dosing of medications and the prediction of clinical outcomes. Determining appropriate dosing regimens is particularly challenging and potentially hazardous in patients with renal or hepatic insufficiency.

In cases of renal pathology or reduced cardiac output, drug clearance—primarily dependent on renal function—is often diminished. Hepatic impairment can also reduce clearance, usually due to decreased hepatic blood flow. This reduction in hepatic clearance may occur in conditions such as chronic heart failure, liver cirrhosis, or hepatic failure of other origins. When adjusting dosages for renally eliminated drugs, it is essential to consider the glomerular filtration rate (GFR). If urine output is less than 0.5 mL/kg/hour, the GFR is effectively zero.

Dosage adjustment is even more complex in the setting of hepatic dysfunction due to the absence of an in vivo surrogate marker (like serum creatinine for renal dysfunction) for predicting hepatic drug clearance. Nevertheless, certain liver function tests are crucial for estimating the degree of hepatic impairment. These include:

- Serum bilirubin (>4–5 mg/dL),
- Prothrombin time (>1.5× control),
- Serum albumin (<2.0 g/dL),
- Elevated liver enzymes — ALT and AST (typically more than three times the upper limit of normal).

Drugs primarily eliminated via the kidneys may exhibit prolonged half-lives in patients with renal dysfunction (e.g., active metabolites of midazolam, carbapenems). Similarly, drugs metabolized hepatically (e.g., propofol, argatroban) may have prolonged effects in patients with liver dysfunction due to reduced elimination.

Patients in intensive care units (ICUs) are often prescribed 10 or more medications simultaneously. As disease severity and patient age increase, so too does the risk of drug-related adverse effects or toxicities due to polypharmacy. ICU physicians must exercise particular caution when prescribing medications with a narrow therapeutic index or those associated with potentially serious side effects.

Appropriate drug dosing requires consideration of five key pharmacokinetic principles:

1. Absorption
2. Distribution and protein binding
3. Metabolism

4. Elimination
5. Half-life

The goal of pharmacotherapy is to rapidly achieve and maintain an effective, non-toxic drug concentration in the target tissue or organ. In critically ill patients, this is often accomplished through tailored loading and maintenance dosing regimens.

The main principles of rational prescribing, especially in critical care, include:

- Accurate diagnosis
- Consideration of the pathophysiological consequences of the diagnosis
- Selection of a specific therapeutic strategy
- Choice of the most appropriate drug or drug combination
- Determination of the optimal dosing regimen
- Development of a plan to monitor drug efficacy and safety
- Defining the course of therapy

The core elements of **"Good Prescribing"** include:

- Selecting the most effective and safest drug or combination of drugs
- Justifying the choice based on individual patient characteristics and the severity of illness

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