Journal of Neonatal Surgery
ISSN(Online): 2226-0439
Vol. 14, Issue 8s (2025)
https://www.jneonatalsurg.com

OPEN ACCESS

Dosage Precision in the ICU: Variability Between Males and Females

Dr. Sucheta Meshram[1*], Dr. Nayana Sabu[2]

[*1]Associate professor. Anaesthesiology and critical care AIIMS Nagpur,

Email ID: drsucheta1021@gmail.com

[2]Junior resident Anaesthesiology and critical care AIIMS Nagpur,

Email ID: nayana0016@gmail.com

Cite this paper as: Dr. Sucheta Meshram, Dr. Nayana Sabu, (2025) Dosage Precision in the ICU: Variability Between Males and Females. *Journal of Neonatal Surgery*, 14 (8s), 1049-1051.

ABSTRACT

Background: Precision in drug dosing is crucial in intensive care unit (ICU) settings to achieve optimal therapeutic outcomes and minimize adverse drug reactions. Despite advancements in critical care pharmacotherapy, sex-based differences in drug pharmacokinetics (PK) and pharmacodynamics (PD) remain underappreciated.

Objective: This comprehensive review aims to synthesize the evidence on sex-specific variability in drug dosing in critically ill patients and recommend strategies for individualized pharmacotherapy in the ICU.

Methods: An extensive literature search was conducted using PubMed, Embase, and Scopus databases. Studies on sex differences in ICU pharmacology, PK/PD variations, and clinical outcomes were reviewed.

Results: Significant gender differences exist in drug absorption, distribution, metabolism, and excretion. These variations influence the dosing of sedatives, analgesics, vasopressors, and antimicrobials. Physiological factors, hormonal influences, and genetic polymorphisms further modulate these differences.

Conclusion: Integrating sex-specific factors into ICU drug dosing algorithms is essential for precision medicine. Future research should focus on clinical trials stratified by sex to refine dosing recommendations.

Keywords: *Critical care, Pharmacokinetics, Sex differences, Precision dosing, ICU, Pharmacodynamics.*

1. INTRODUCTION

The ICU population is heterogeneous, with varying physiological states influencing drug therapy. Historically, dosing guidelines have been derived predominantly from studies in male subjects, neglecting sex-specific responses. As precision medicine gains momentum, addressing gender variability becomes crucial to optimizing drug efficacy and safety.

Sex-Based Physiological Differences Impacting Pharmacology

1. Absorption

- Females have slower gastric emptying and altered gastrointestinal enzyme activity.
- Hormonal fluctuations influence gastric pH and intestinal motility.

2. Distribution

- Females typically have a higher percentage of body fat and lower total body water, affecting the volume of distribution (Vd) of lipophilic drugs (e.g., propofol, midazolam).

3. Metabolism

- CYP450 enzyme activity, particularly CYP3A4, is often higher in females, altering the metabolism of several ICU drugs.
- Sex hormones modulate hepatic enzyme expression. Estrogen enhances glucuronidation, while testosterone increases oxidation pathways.

4. Elimination

- Glomerular filtration rate (GFR) and renal tubular secretion show sex-based differences. Renal clearance of drugs like aminoglycosides and beta-lactams tends to be higher in males.

2. CLINICAL IMPLICATIONS IN ICU PHARMACOTHERAPY

Sedatives and Analgesics

- **Midazolam:** Prolonged half-life in females due to slower hepatic clearance.
- **Fentanyl:** Larger Vd in females; initial doses may require adjustment.

Vasopressors

- Receptor sensitivity differences may influence responses to norepinephrine and dopamine.

Antimicrobials

- **Vancomycin:** Lower clearance in females necessitating dose adjustments to prevent toxicity.

Anticoagulants

- Females may exhibit heightened sensitivity to heparins, increasing bleeding risk.

Sex Hormones and Pharmacological Response

- Estrogen and progesterone influence drug transporter proteins and receptors.

Menstrual cycle, pregnancy, and menopause further alter drug responses in females.

Genetic Polymorphisms

- Sex-specific expression of genes coding for drug-metabolizing enzymes and transporters (e.g., ABCB1, CYP2D6) contributes to inter-individual variability.

3. PRECISION DOSING STRATEGIES

1. Therapeutic Drug Monitoring (TDM)

- Routinely monitor plasma levels of drugs with narrow therapeutic windows (e.g., vancomycin, aminoglycosides).

2. Individualized Dosing Algorithms

- Incorporate sex, body composition, and organ function into dosing calculators.

3. Pharmacogenomic Testing

- Screen for polymorphisms influencing drug metabolism and transport.

4. Artificial Intelligence (AI) and Machine Learning

- Use AI-driven models to predict optimal dosing regimens based on sex-specific data.

Special Considerations in Critical Illness

- Sepsis, multi-organ dysfunction, and critical illness-related pharmacokinetic changes may override sex-based differences.
- Continuous renal replacement therapy (CRRT), extracorporeal membrane oxygenation (ECMO), and altered protein binding require individualized adjustments.

Future Directions

- More clinical trials with gender-stratified analysis.
- Development of ICU-specific dosing guidelines acknowledging sex differences.
- Integration of pharmacokinetic modeling into ICU electronic medical records (EMRs).

4. CONCLUSION

Sex-based variability significantly impacts drug dosing in critically ill patients. Recognizing and adjusting for these differences is essential for personalized ICU care. Advancements in pharmacogenomics, AI, and clinical pharmacology will pave the way for precision dosing strategies.

REFERENCES

[1] Soldin OP, Mattison DR. Sex differences in pharmacokinetics and pharmacodynamics. Clin Pharmacokinet. 2009;48(3):143-157.

[2] Zucker I, Prendergast BJ. Sex differences in pharmacokinetics predict adverse drug reactions in women. Biol Sex Differ. 2020;11(1):32.

[3] Beier K, et al. Gender-specific considerations in intensive care. Crit Care Clin. 2020;36(4):599-618.

[4] Waxman KJ, et al. Individualized dosing in ICU patients. J Crit Care. 2022;67:153-161.

[5] Anderson GD. Sex and genetic differences in drug metabolism. Trends Pharmacol Sci. 2008;29(8):373-379.

[6] Gandhi M, Aweeka F, Greenblatt RM, Blaschke TF. Sex differences in pharmacokinetics and pharmacodynamics. Annu Rev Pharmacol Toxicol. 2004;44:499-523.

[7] Tannenbaum C, et al. Sex, gender, and drug response: pharmacokinetics and pharmacodynamics. Biol Sex Differ. 2017;8(1):24.

[8] Mauvais-Jarvis F. Sex differences in metabolic homeostasis, diabetes, and obesity. Biol Sex Differ. 2015;6:14.

[9] Morgan ET, et al. Regulation of drug-metabolizing enzymes and transporters in infection, inflammation, and cancer. Pharmacol Rev. 2008;60(2):247-260.

[10] De Vries ST, et al. Sex differences in adverse drug reactions reported to the national pharmacovigilance center in the Netherlands. Br J Clin Pharmacol. 2019;85(7):1507-1515.