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Original Article

Pharmacist Mediated Drug Dosage Adjustment in Patients with Renal Impairment: A Prospective Interventional Study

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ABSTRACT

Background: Chronic Kidney Disease (CKD) is an increasing global health challenge that significantly influences drug pharmacokinetics and pharmacodynamics. Impaired renal function reduces drug clearance, raising the likelihood of adverse drug reactions when dosages are not appropriately adjusted. **Objectives:** To assess the effectiveness of pharmacist-led interventions in detecting and correcting inappropriate drug dosages among patients with renal impairment in a tertiary care hospital. **Materials and Methods:** A prospective interventional study was carried out in the medicine, surgery, nephrology, and urology wards of a tertiary healthcare centre in Vijayapura, Karnataka. Data from 160 patients with renal impairment were collected. Estimated Glomerular Filtration Rate (eGFR) was calculated using the Cockcroft-Gault equation via Micromedex®", and dose appropriateness was evaluated using standard renal dose-adjustment guidelines. Pharmacist recommendations were communicated to physicians, and acceptance of interventions was documented. **Results:** Of the 160 patients, 115 were male and 45 female, with most aged 51-60 years. A total of 1460 medications were prescribed; 470 (32.2%) required renal dose adjustment. Of these, 171 (36.4%) were appropriately modified following pharmacist intervention, whereas 299 (63.6%) remained unadjusted. Antibiotics, diuretics, and cardiovascular drugs were the most frequently affected therapeutic classes. Commonly adjusted medications included meropenem, furosemide, cefotaxime, vancomycin, fluconazole, and atenolol. Hypertension and diabetes were the most prevalent comorbidities. **Conclusion:** Pharmacist-led review significantly improved recognition and correction of renal dosage errors. Nonetheless, the high proportion of unadjusted medications underscores the need for stronger pharmacist-physician collaboration and routine renal-dose monitoring to minimize toxicity and enhance clinical outcomes.

Keywords: Chronic kidney disease, Dose adjustment, Drug monitoring, Medication safety, Pharmacist intervention, Renal impairment.

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INTRODUCTION

The kidney plays a crucial role in maintaining homeostasis through excretion of drugs and metabolites, regulation of electrolytes, and fluid balance. Impaired renal function leads to drug accumulation, altered pharmacokinetics, and increased toxicity risk (Alahdal and Elberry, 2012). With the global increase in Chronic Kidney Disease (CKD), medication safety has become a major clinical concern, particularly among the elderly population and those with multiple comorbidities (Alhossan *et al*., 2020; Belletti *et al*., 2015).

Drug-induced nephrotoxicity accounts for approximately 15% of acute renal failure cases, largely due to hypersensitivity reactions and tubular inflammation (Bhatnagar *et al*., 2021). The Glomerular Filtration Rate (GFR) is considered the most reliable measure of renal function, and drug-dosing recommendations are typically based on estimated GFR or Creatinine Clearance (CrCl) (Bodenham *et al*., 1988). Although inulin clearance remains the gold standard, its clinical application is limited due to technical complexity; hence, serum creatinine-based equations such as Cockcroft-Gault or MDRD are commonly used (Craig, 1998).

Renal impairment alters both metabolism and elimination of drugs. Without appropriate dose adjustment, accumulation of

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parent compounds or active metabolites may lead to adverse effects, especially with agents such as aminoglycosides, vancomycin, and Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) (Decloedt and Maartens, 2010). For instance, opioid analgesics like codeine, morphine, and tramadol can accumulate and cause central nervous system or respiratory depression in advanced renal disease (Eppenga *et al*., 2016). Similarly, metformin must be used cautiously or avoided when serum creatinine exceeds 1.5 mg/dL in men or 1.4 mg/dL in women due to the risk of lactic acidosis (Fahimi *et al*., 2011).

Despite clear guidelines, inappropriate drug dosing in renal impairment remains frequent due to lack of awareness, time constraints, or absence of real-time renal function data (Garg *et al*., 2009; Gidey *et al*., 2015). Clinical pharmacists, through systematic drug review and renal function assessment, can play a critical role in identifying, recommending, and monitoring appropriate dosage regimens to optimize outcomes and minimize toxicity (Greenberg *et al*., 2009; Hammad *et al*., 2019).

This study was therefore undertaken to evaluate the impact of pharmacist-mediated assessment of drug monitoring and dosage adjustment among patients with renal impairment in a tertiary care hospital in southern India.

MATERIALS AND METHODS

Study Design and Setting

A prospective interventional study was conducted in a tertiary care clinical setting in Vijayapura, Karnataka. The study included inpatients from the departments of nephrology, urology, medicine, and surgery who exhibited abnormal renal function tests and required pharmacotherapy review (Figure 1).

Ethical Considerations

The study was approved by the institutional ethics committee. Written informed consent was obtained from all participants or their legal guardians before inclusion.

Study Population and Inclusion Criteria

Patients aged >18 years with documented renal impairment (based on decreased eGFR<60 mL/min/1.73 m^2) were included. Patients with incomplete laboratory data or those on temporary renal replacement therapy without stable renal parameters were excluded.

Data Collection and Assessment

Patient demographic details, clinical diagnosis, comorbidities, laboratory values, and prescribed medications were extracted from medical case files and verified with treating physicians. eGFR was computed using the Micromedex calculator employing the Cockcroft-Gault equation. Male:

$$CrCl = (140 - age) \times weight / (72 \times serum\ creatinine)$$

Female: $CrCl = (140 - age) \times weight \times 0.85 / (72 \times serum\ creatinine)$

Renal impairment was classified as follows: Stage 1 (>90 mL/min), Stage 2 (60-89 mL/min), Stage 3 (30-59 mL/min), Stage 4 (15-29 mL/min), and Stage 5 (<15 mL/min).

Pharmacist Intervention

Each prescription was reviewed by a clinical pharmacist to identify drugs requiring dosage modification based on renal function. Dosage recommendations were derived from primary, secondary, and tertiary sources including Micromedex®, AHFS Drug Information, and the KDIGO 2012 renal dosing guidelines (Hammad *et al*., 2019). Identified interventions were discussed with the treating physician, and the outcome was categorized as: Intervention Accepted - dose adjusted; Intervention Not accepted - no modification; Intervention Not applicable - drug discontinued or replaced.

Data Analysis

All data were compiled in Microsoft Excel 2019. Descriptive statistics were used to summarize demographic details, drug categories, and intervention outcomes. Continuous variables were expressed as Mean±SD, while categorical variables were presented as frequencies and percentage.

RESULTS

Patient Demographics and Clinical Characteristics

A total of 160 patients with renal impairment were included in the study. The study population was predominantly male (71.9%), with a mean age of 49.6±17.6 years. The largest proportion of patients belonged to the 51-60-year age group (19.4%) (Table 1).

Regarding clinical diagnosis, 31.9% of patients had Acute Kidney Injury (AKI), 23.1% had Chronic Kidney Disease (CKD), and 45% were diagnosed with other renal disorders. Dialysis support was required in 69.4% of patients, whereas 30.6% were managed without dialysis (Table 1). Renal impairment, defined by serum creatinine levels >1.4 mg/dL, was observed in 86.3% of the study population, with stage 5 renal disease being the most prevalent (48.8%). Most patients were admitted to the medicine and nephrology wards. Hypertension (24.38%) and diabetes mellitus (14.38%) were the most commonly reported comorbid conditions (Table 1).

Drug Utilization, Polypharmacy and Drug - Drug Interaction

A total of 1,460 medications were prescribed to the study population, with a mean of 5.6±2.4 drugs per patient, indicating a high prevalence of polypharmacy. Among these, 470 drugs

(32.2%) required dose adjustment based on renal function, while 990 drugs (67.8%) did not require modification (Table 2).

The drugs most frequently requiring dose adjustment included *meropenem, furosemide, cefotaxime, vancomycin, fluconazole, atenolol, and cefixime*; other commonly involved medications were *diclofenac, linezolid, acetaminophen, tramadol*, and *metformin* (Table 3). Major drug-drug interactions (26.3%) were predominantly observed with combinations involving loop diuretics, antibiotics, and other high-risk medications (Table 4).

Pharmacist-Led Interventions and Outcomes

Pharmacist-led interventions were recommended for all 470 drugs identified as requiring renal dose adjustment. Of these recommendations, 171 (36.4%) were accepted and implemented, resulting in appropriate dose modifications. However, 299 recommendations (63.6%) were not accepted and the prescribed doses remained unchanged, primarily due to physician clinical judgment or patient-specific considerations (Figure 2).

DISCUSSION

This study highlights the critical role of clinical pharmacists in optimizing drug therapy among patients with renal impairment. The finding that nearly one-third of prescribed medications required renal dose adjustment underscores the substantial burden of potential drug-related problems in this vulnerable population.

The study included 160 patients with a mean age of 49.6±17.6 years and a predominance of males (71.9%), which is consistent with previously reported demographic patterns in patients with renal dysfunction (Hammad and Ahmed, 2016; Heintz *et al.*, 2009). With respect to diagnosis, acute kidney injury (31.9%) and chronic kidney disease (23.1%) constituted a significant proportion of cases, while 45% of patients were categorized under other renal disorders. This distribution aligns with observations from comparable nephrology cohorts where mixed etiologies of renal impairment are frequently encountered in hospitalized patients (Heintz *et al.*, 2009; Khan *et al.*, 2021). The high prevalence of advanced renal dysfunction, with stage 5 disease accounting for 48.7% of patients, reflects the severity of illness typically observed in tertiary care settings (Craig, 1998; Decloedt and Maartens, 2010). Additionally, more than two-thirds of patients required dialysis support, further emphasizing the complexity of pharmacotherapy management in this population.

Hypertension and diabetes mellitus were the most commonly observed comorbid conditions, reinforcing their well-established role in the development and progression of renal disease (Klaassen *et al.*, 2013; Matzke *et al.*, 2011). The presence of multiple comorbidities contributed to polypharmacy, with an average of 5.6±2.4 drugs prescribed per patient. This level of polypharmacy is comparable to findings from previous studies and highlights the increased risk of medication-related complications in patients with renal impairment (Mudge *et al.*, 2014; Tuttle and Short, 2010).

Table 1: Distribution of demographic and clinical characteristics of the study population (*n*=160).

Characteristics	Frequency	Percentage %
Department wise distribution of cases		
Nephrology	89	55.6
Medicine	37	23.1
Urology	26	16.3
Surgery	8	5.0
Gender		
Male	115	71.9
Female	45	28.12
Age group		
>20	7	4.3
21-30	25	15.6
31-40	24	15
41-50	27	16.9
51-60	31	19.4
61-70	30	18.8
>70	16	10
Diagnosis		
Acute kidney injury	51	31.9
Chronic kidney disease	37	23.1
Other renal disorders	72	45.0
Renal Characteristics (GFR mL/min)		
Stage I (>90)	8	5
Stage II (60-89)	15	9.3
Stage III (30-59)	22	13.8
Stage IV (15-29)	37	23.1
Stage V (<15)	78	48.8
Dialysis status		
On Dialysis	111	69.4
Dialysis not required	49	30.6
Co-Morbidities		
Hypertension	39	24.38
Diabetes Mellitus	23	14.38
Anaemia	20	12.50
Sepsis	15	9.38
COPD	13	8.12
Urinary Tract Infection	07	4.37
Others	43	26.87

COPD: Chronic Obstructive Pulmonary Disease

In the present study, 32.2% of prescribed drugs required dose adjustment based on renal function, which is consistent with prior reports indicating adjustment requirements ranging from 25% to 45% (Varun *et al.*, 2016; Vishwas *et al.*, 2017). Despite pharmacist-led recommendations, only 36.4% of drugs requiring adjustment were modified, while 63.6% remained unadjusted. Similar acceptance rates have been reported in other studies, suggesting that physician clinical judgment, patient-specific factors, and the acute severity of illness often influence decision-making regarding dose modification (Winter, 1994; Wright *et al.*, 2011).

Major drug-drug interactions were identified in 26.3% of cases, primarily involving combinations of antibiotics, diuretics, and other high-risk medications. These findings underscore the importance of vigilant medication review and therapeutic monitoring in renally impaired patients, particularly when multiple nephrotoxic or pharmacodynamically interacting agents are prescribed concurrently (Hammad and Ahmed, 2016).

Non-acceptance of pharmacist recommendations may be attributed to several factors, including prescribers' reliance on individualized dosing decisions, concerns regarding therapeutic efficacy in critically ill patients, and the absence of standardized renal dosing protocols or integrated clinical decision-support systems. In emergency and intensive care settings, immediate clinical priorities may supersede guideline-based dose optimization. Strengthening interdisciplinary collaboration through early pharmacist involvement, shared treatment protocols, and continuous education on renal pharmacotherapy may improve acceptance of pharmacist interventions and enhance patient safety outcomes.

Table 2: Distribution of various drugs in the study population (*n*=1460).

Drug Class	Frequency	%
Antibiotic	268	18.35
Anti-peptic ulcer	202	13.83
Antihypertensive	181	12.4
Sodium supplements	169	11.57
Calcium supplements	152	10.41
Diuretics	139	9.52
Analgesics and Antipyretics	109	7.5
Antiemetic	76	5.2
Anticoagulants	47	3.2
Bronchodilators	44	3.01
Anti-diarrheal	29	1.99
Vitamin supplements	16	1.1
Corticosteroids	14	0.96
Antifungal	14	0.96

Clinical Implications of Pharmacist Intervention

Of the 470 drugs identified as requiring renal dose adjustment, pharmacist intervention resulted in appropriate dose modification in 171 cases (36.4%), thereby reducing the risk of drug accumulation and toxicity. Antibiotics such as *β-lactams, aminoglycosides,* and *vancomycin* were among the most frequently implicated drug classes and require careful dose individualization due to predominant renal elimination and narrow therapeutic indices (Hammad and Ahmed, 2016; Heintz *et al.*, 2009). Other medications, including fluconazole, atenolol, and furosemide, also necessitate individualized dosing strategies, consistent with published evidence emphasizing cautious titration in patients with renal dysfunction (Hammad and Ahmed, 2016; Heintz *et al.*, 2009).

Pharmacokinetic alterations in renal impairment extend beyond reduced drug excretion and may involve changes in protein binding, hepatic metabolism, and volume of distribution, all of which influence dosing requirements. Therapeutic drug monitoring, particularly for aminoglycosides and other narrow-therapeutic-index drugs, remains a well-established

Table 3: Distribution of drugs their dosage were adjusted (*n*=171).

Drugs	Frequency	%
Furosemide	19	11.1
Meropenem	16	9.36
Diclofenac	17	9.94
Ondansetron	16	9.36
Cefotaxime	11	6.4
Fluconazole	10	5.85
Prednisolone	9	5.3
Piperacillin and Tazobactam	8	4.7
Vancomycin	8	4.7
Orinidazole and Ofloxacin	7	4.1
Tramadol	7	4.1
Heparin	6	3.5
Metronidazole	5	2.92
Metformin	5	2.92
Deriphylline	5	2.92
Amikacin	5	2.92
Cefixime	3	1.75
Levofloxacin	3	1.75
Aspirin	3	1.75
Tolvaptan	3	1.75
Gentamicin	3	1.75
Metoclopropamide	1	0.58
Atenolol	1	0.58

Table 4: Drug-Drug Interactions Reported.

Drug-Drug Interactions	Frequency	Severity	Outcome
Furosemide<>Tolvaptan	07	Major	Increase risk of plasma concentration
Ondansetron<>Tramadol Hcl	08	Major	Increase risk of serotonin syndrome
Metronidazole<>Ondansetron	07	Major	May cause arrhythmias
Furosemide<>Metolazone	05	Major	Increase risk of fluid and electrolytes balance
Metoclopropamide<>Tramadol	05	Major	Concurrent use may increase risk of CNS depression
Amitriptyline<>Fluconazole	03	Major	Increase risk of cardio toxicity.
Clonidine<>Metoprolol	03	Major	May results increase the risk of bradycardia
Levofloxacin<>Ondansetron	03	Major	Increase the risk of QT interval prolongation
Budesonide<>Levofloxacin	02	Major	Increase risk of tendon rupture.
Dexamethasone<>Nimesulide	02	Major	Increase the risk of QT interval prolongation

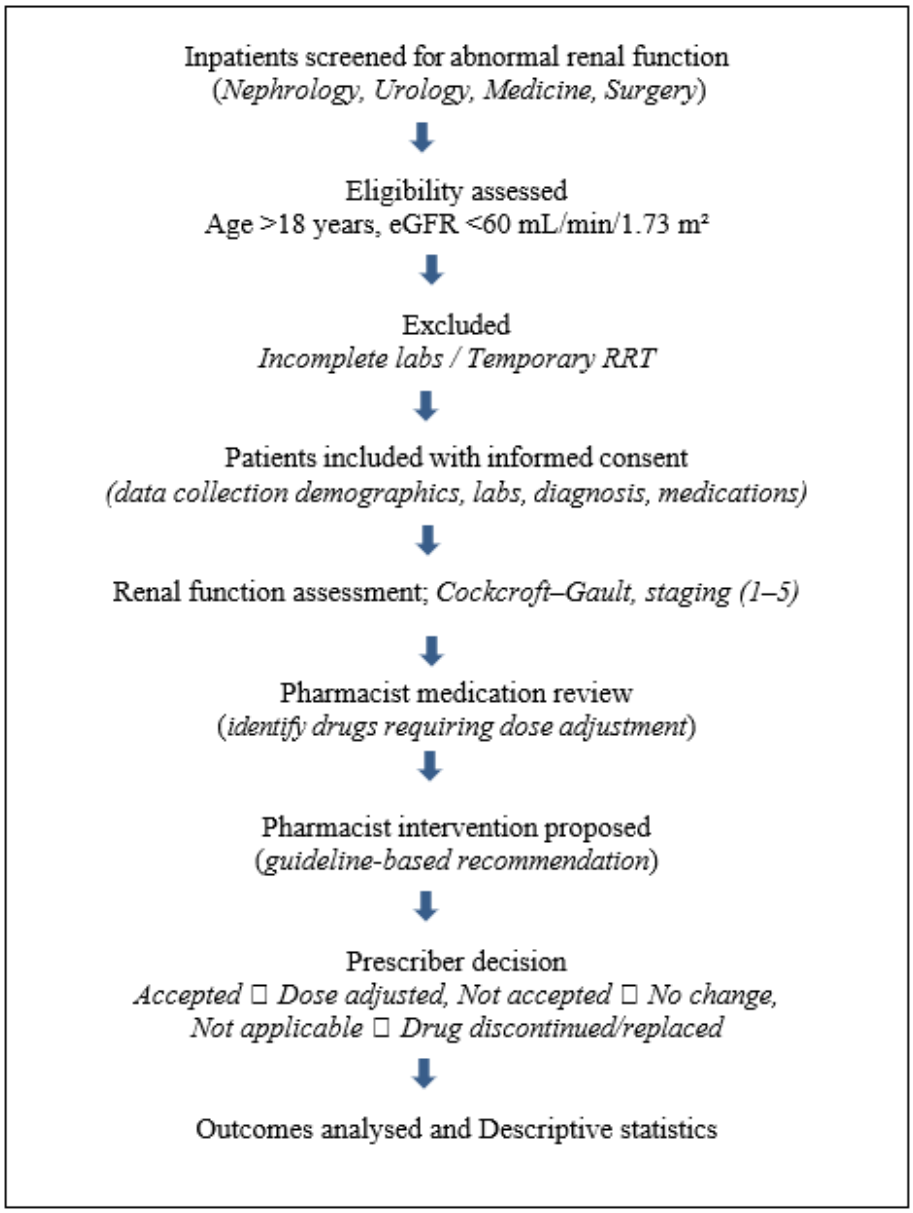

Figure 1: Study flow Chart.

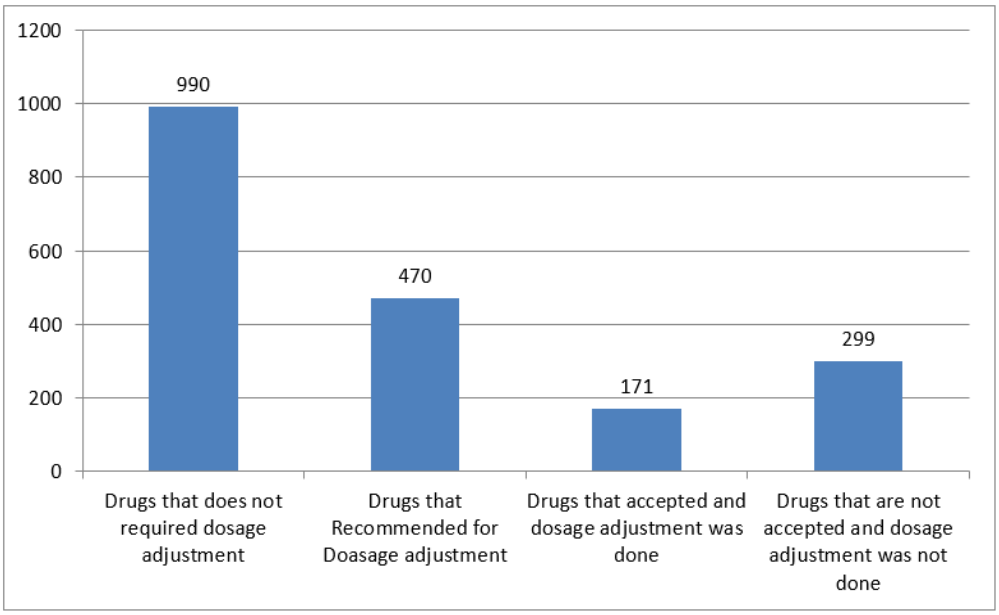

Figure 2: Dosage Adjustments and Intervention Outcomes in Renal Impairment.

strategy to optimize efficacy while minimizing toxicity (Khan *et al.*, 2021).

The high prevalence of polypharmacy observed in this study reinforces the essential role of clinical pharmacists in managing complex drug regimens, identifying potential interactions, and preventing adverse drug events (Klaassen *et al.*, 2013; Matzke *et al.*, 2011). Barriers to physician acceptance of pharmacist recommendations highlight the need for institutional support, clearly defined clinical roles, and collaborative practice models (Mudge *et al.*, 2014; Tuttle and Short, 2010).

The integration of automatic eGFR reporting and renal dosing alerts within electronic prescribing systems has been shown to reduce dosing errors and improve clinical outcomes (Varun *et al.*, 2016; Vishwas *et al.*, 2017). Pharmacist-led interventions in renal dose adjustment have demonstrated positive impacts, particularly in resource-limited settings where medication error rates remain high (Bhatnagar *et al.*, 2021; Heintz *et al.*, 2009; Winter, 1994). Expanding the role of pharmacists to include real-time monitoring, patient counseling, and active participation in ward rounds can further enhance medication safety and continuity of care (Matzke *et al.*, 2011; Mudge *et al.*, 2014). Establishing structured pharmacy-physician collaboration and implementing mandatory renal dose verification protocols are essential to minimizing adverse drug events and reducing associated healthcare costs (Vishwas *et al.*, 2017; Wright *et al.*, 2011).

CONCLUSION

This study demonstrates that pharmacist-mediated drug monitoring significantly improves the detection and correction of inappropriate dosing among renal impaired patients. Although nearly one-third of medications required dosage modification, only about one-third of those were adjusted after pharmacist recommendation, indicating room for improvement in interdisciplinary cooperation.

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ABBREVIATIONS

CKD: Chronic Kidney Disease; **GFR:** Glomerular Filtration Rate; **CrCl:** Creatinine Clearance; **MDRD:** Modification of Diet in Renal Disease (Study Equation); **eGFR:** Estimated Glomerular Filtration Rate; **NSAIDs:** Non-Steroidal Anti-Inflammatory Drugs; **KDIGO:** Kidney Disease: Improving Global Outcomes.

CONFLICT OF INTEREST

The author declares that there is no conflict of interest.

SUMMARY

A prospective study in a tertiary hospital evaluated pharmacist-led interventions for renal dose adjustment in 160 patients with impaired kidney function. Of 1460 prescribed drugs, 470 required adjustment, yet only 36.4% were corrected after pharmacist recommendations. Antibiotics, diuretics, and cardiovascular drugs were most frequently involved. Pharmacist involvement improved detection and correction of dosing errors, but a large proportion of unadjusted medications highlight the need for stronger pharmacist-clinician collaboration and routine renal-dose monitoring to enhance patient safety.

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