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Research Article

The impact of clinical pharmacists' intervention on the rational use of intravenous paracetamol vials in Baghdad Teaching Hospital: A case-control study

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Abstract

Paracetamol has been recognized worldwide as a safe and effective agent for relieving pain and reducing fever in many patients. This study aimed to investigate the role of clinical pharmacist interventions in the rational and appropriate use of intravenous paracetamol in surgical patients and the impact of this rational use on hospital costs. A case-control study was conducted on 794 patients (400 in the intervention group and 394 in the control group). The appropriate and rational use of the drug was compared between baseline and post-intervention in the intervention group and between the two groups. The result showed a significant reduction in dispensed IV paracetamol vials after the pharmaceutical intervention (4,151 vials recovered by the intervention), which led to a reduction in the cost (8,302 USD reduction in the total cost). There was a significant reduction in the dose of IV paracetamol, use with or without adjunctive opioid analgesics, frequency of administration, duration of intravenous paracetamol use, daily max exceeding 4 g, and concomitant use with oral paracetamol after applying the clinical pharmacist intervention. In conclusion, the clinical pharmacist plays a vital role in various aspects of healthcare; clinical pharmacist involvement positively impacts the patient's management plan by improving the optimal and rational use of intravenous paracetamol and decreasing hospital costs.

Keywords

clinical pharmacist intervention, cost, intravenous paracetamol

Introduction

Paracetamol is considered one of the most widely used analgesics in the world; this is attributed to its safety and effectiveness in reducing pain and fever; additionally, it can be used with relative safety in conditions like liver disease (Zacharia and Jacob 2023). In a more recent systemic review in 2021 that examined 2,356 scientific articles that covered 173,707 individuals during COVID-19, the authors concluded that paracetamol was highly safe (Romanov 2021). The intravenous (IV) formulation of paracetamol was approved in the United States in 2010 for managing mild-to-moderate and moderate-to-severe pain with adjunctive analgesics and reducing fever (Dart and Rumack 2012). Despite the availability of paracetamol in an IV form in the surgical wards, it should be dispensed to patients who cannot receive oral formulations or rectally due to nausea, vomiting, recovery from gastrointestinal surgery, or impaired drug absorption (Subramaniam et al. 2022).

The IV dosage form provides quicker and higher peak plasma and cerebrospinal fluid drug concentrations than oral or rectal dosing (Langford et al. 2016; Raffa et al. 2018); this resulted in increased prescribing of the IV formulation and increased its monthly dispensing in the surgical ward with an increase in its cost in the hospital (Fusco et al. 2014); at the same time, many concerns have been raised that intravenous paracetamol is not always appropriately prescribed, as its use is associated with many problems like consuming for nursing time, the potential for overdose with concomitant oral drugs containing intravenous paracetamol, failure to adjust the dose according to body weight or other patient factors, increased risk of infection with repetitive, prolonged administration due to the IV cannula remaining in situ, and in addition to increased relative costs comber with oral paracetamol (Jahr and Lee 2010).

As a global issue, rational medication use is a multifaceted subject; the role of governments, manufacturers, society, drug authorities, the educational system, the media, and other healthcare workers cannot be denied (Durga Prasad Reddy and Sharma 2020). The responsibility of healthcare professionals has assumed great significance (Olbrecht et al. 2018). Because hospitals are subject to more economic pressures than ever before, the work of drug consumption rationalization policy and cost reduction is paramount and important, particularly concerning costly branded pharmaceuticals (Salmon and Thompson 2021). In the hospital setting, appropriate medicine use is the responsibility of the drug and therapeutic committee (DTC), which consists of a multidisciplinary team responsible for developing policies and procedures to promote rational medication use (Yang et al. 2022). The clinical pharmacist is an important team member, normally consisting of physicians, pharmacists, nurses, microbiologists, and other health care professionals (Zachariah et al. 2018). All multidisciplinary team members have important roles in managing patients to achieve the goal of treatment with rational medication use (Zachariah et al. 2018). In recent decades, the pharmacist's role in therapy has expanded; many factors have an influence on prescribing and have expanded the pharmacist's role from a passive dispenser to an active participant in the therapeutic decision-making team and introduce many clinical pharmacists' activities as a selection of medications, consulting and advise about drug information, its formulation and preparation, drug use studies and research, clinical trials, pharmacokinetics/ therapeutic drug monitoring, pharmacoeconomic of drugs, dispensing, administration, teaching, and training to reach the main goal of clinical pharmacy in promoting the correct, appropriate, and rational use of medications products with reduce treatment cost (Mohiuddin 2020).

This study aimed to investigate the role of specialist clinical pharmacist interventions in the rational and appropriate use of intravenous paracetamol post-surgical patients, the impact of this rational use with restriction and lowering the prescribing post-operative dose for the correct indication at the correct dose, the correct duration, and finally the cost in the hospital.

Patients and method

Study design and settings

A case-control study began from 01 February 2023 to 31 July 2023, in the surgical wards at the Bagdad Teaching Hospitals of the Baghdad Medical City Complex. The study was carried out on 794. Patients were admitted to the hospital for various surgical indications, and they were prescribed an IV paracetamol vial (1000 mg/100 ml).

During the period of study, 820 patients were initially recruited, 26 patients were excluded (10 patients from group A with insufficient and incomplete data reported and 16 patients from group B with missing data), and the final number of patients was 794 (400 in group A and 394 patients in group B), as illustrated in Fig. 1.

Patients were divided into two groups: Group A (the interventional group) consisted of 400 patients (197 females and 203 males) followed up by a specialist clinical pharmacist during their admission till their discharge; these patients underwent extensive pharmaceutical intervention regarding the appropriate use of IV paracetamol, and group B (the control group) consisted of 394 patients (185 females and males 209); these patients received the regular pharmaceutical followed up and did not receive additional intervention by a specialist clinical pharmacist.

Pharmaceutical intervention

The pharmaceutical intervention by the specialist clinical pharmacist that was introduced to group A consisted of a follow-up of the patient treatment, dose calculation (which depended on the paracetamol doses used in the treatment of post-operative fever with monitoring of body temperature), dose adjustment (all dose adjustment was based on the official dosing of the drug), improvement

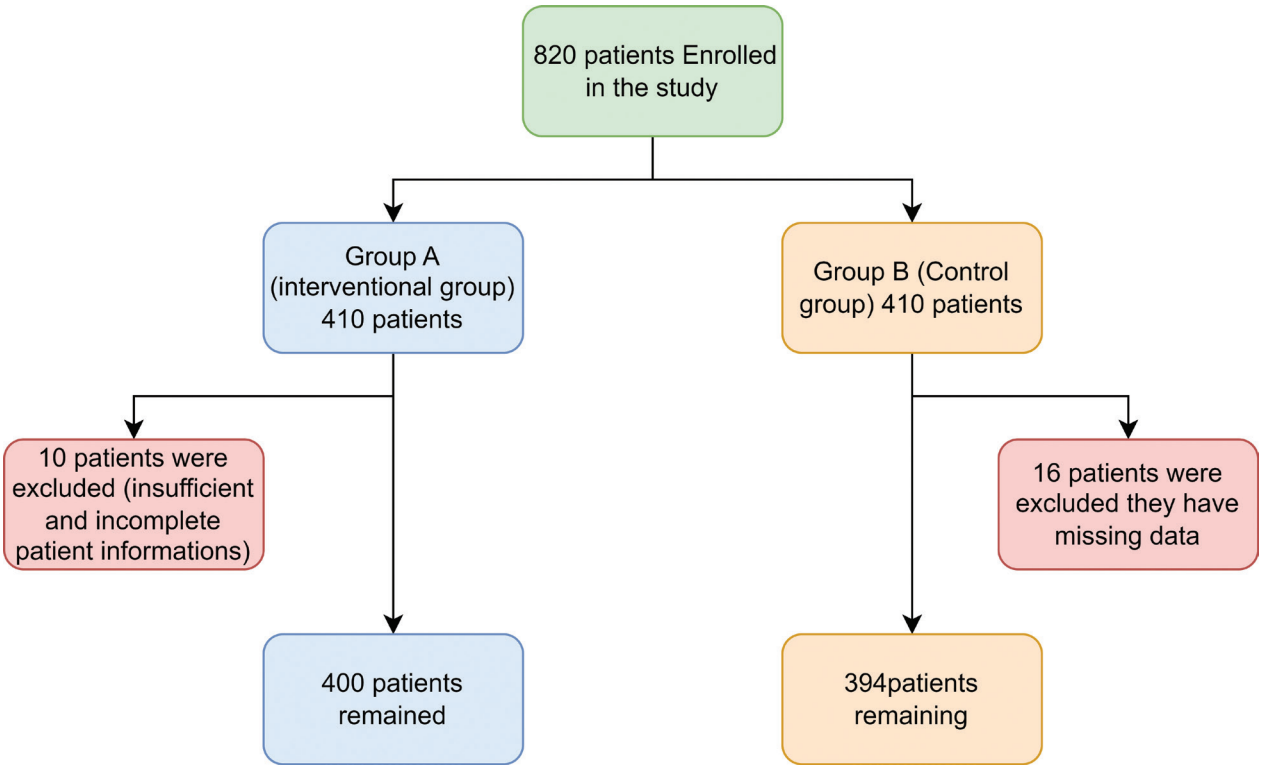

Figure 1. Flow chart of the study.

in the duration that IV paracetamol was prescribed (this was selected based on the indication of the paracetamol in the case by case scenario), correction in the frequency of administration, converting to oral paracetamol, converting to another analgesic, giving instructions about patient adherence with treatment, record related adverse events, identify drug-drug interaction, drug-food interaction, and resolve any medication-related problems.

All the clinical examinations, patient past medical and surgical history, and medication prescriptions in this study would be done under the supervision and consultation of a consultant surgeon.

Eligibility criteria

All adult patients that were admitted to the surgical wards were included in the study; the exclusion criteria from this study include patient refusal to participate, known allergy to or intolerance of paracetamol, patients with hepatic dysfunction (defined as three times the reference value of alkaline phosphatase (ALP), alanine aminotransferase (ALT), and aspartate aminotransferase (AST), patients with renal insufficiency (defined as RIFLE (Risk, Injury, Failure, Loss, End Stage Renal Disease) category, and acute kidney injury defined as estimated creatinine clearance reduced by 50% and urine output of less than 0.5 mL/kg per h for 16 h.

Data collection

The details about IV paracetamol, like the type of manufacture, vial strength, the daily dose (grams received/24 hours), indication, the need for prescribing additional adjunctive analgesics, frequency of administration, duration of administration, and concomitant use of oral paracetamol, were recorded in both groups, as was the difference in the total number of vials and their costs of dispensing to patients in both groups.

All patients were observed clinically throughout their stay in the surgery ward, and vital signs, hemodynamic data, and organ dysfunction were monitored daily.

Laboratory investigations

Hematological and biochemical tests were conducted to investigate the complete blood count and white blood cells with differential liver and kidney function tests.

Ethical consideration

The scientific committee in the Baghdad Teaching Hospital approved the study (number: 907, date: 19 June 2022), and the Research Ethical Committee in Al-Mustafa University College (code: AP002, date: 13 January 2023). Written informed consent was obtained before participating in the study. The study was prepared following STROBE guidelines (Cuschieri 2019).

Sample size

It was determined using the G*Power version (3.1.9.7) (Faul et al. 2007; Faul et al. 2009); the effect size was 0.25, α-level 0.05, β-level 0.05 (95% power), t-test family (two-tailed), and the total sample size was 834 (417 in each group).

Statistical analysis

The SPSS 20 (Chicago, IL, USA) software package was used for statistical analysis. Values were considered significant when P-values were equal to or less than 0.05. Student's Independent t-test was used to assess the difference in mean between the two groups, while the significance of differences between the mean values of the same group before and after treatment was calculated using a paired student's t-test. Numbers and percentages express the categorical variables, and the chi-square test is used for the statistical analysis.

Results

There was no significant difference in the patient's age, sex, body weight, type of surgery, duration of hospitalization, or liver and kidney functions, as illustrated by Table 1.

Table 1. Demographic characteristics and patient characteristics.

Variables		Group A	Group B	p-value
Total number		400	394	
Age (years) mean±SD		41.54±15.43	39.78±16.2	0.118
Body weight (Kg) Mean±SD		83.01±7.69	84.02±8.26	0.098
Sex N (%)	Female	197(49.25%)	185(46.95%)	0.518
	Male	203(50.75%)	209(53.04%)	0.686
Types of surgery N (%)	Emergency	80 (20%)	83(21.06%)	0.710
	urgent	88(22%)	92(23.35%)	0.650
	elective	73(18.25%)	67(17%)	0.646
	Scheduled	159(39.75%)	152(57.32%)	0.681
Duration of hospitalization (days) Mean±SD		4.53±1.28	4.67±1.94	0.265
Liver function test Mean±SD	AST (U/L)	26.56±12.09	25.64±11.29	0.271
	ALT (U/L)	29.48±12.15	28.82±11.85	0.441
	ALP (U/L)	83.25±26.55	81.24±25.46	0.278
	Bilirubin mg/dl	0.63±0.29	0.62±0.25	0.646
Renal function test mean±SD	Sr.cr mg/dl	0.79±0.17	0.78±0.16	0.107
	Urea mg/dl	19.18±7.25	18.29±6.09	0.064

SD: standard deviation; Sr: serum; Cr: creatinine; ALP: alkaline phosphatase; ALT: alanine transaminase; AST: Aspartate transaminase.

There was no significant difference between the two groups in the indication of intravenous paracetamol vial, the indication of IV paracetamol, use of adjuvant analgesics, frequency of administering paracetamol, duration of IV paracetamol administration, patients that exceeded the maximum recommended dose of 4 gm per day, and concomitant use of oral paracetamol.

The most common reason for prescribing intravenous paracetamol vials in two groups has been reported for pyrexia, followed by analgesia, then pyrexia and analgesia, and then not documented, as illustrated in Table 2.

There was a significant difference in all details of IV paracetamol prescribed to the patients in group A before and after intervention, including the dose of IV paracetamol (grams received/24 hours), use with or without adjunctive opioid analgesics, frequency of administration (q4h, q6h, q8h), duration of intravenous paracetamol use, daily max exceeded (4 g/24 hours), and concomitant use with oral paracetamol, as illustrated in Table 3.

Table 2. Comparison of the details of intravenous paracetamol prescribed to the patients at baseline.

Variables		Group A	Group B	p-value
Numbers		400	394	
Dose of intravenous paracetamol (grams received /v24 h), mean±SD		3.65±0.83	3.70±0.75	0.44
Indication of intravenous paracetamol, n (%)	Pyrexia	135(33.75%)	128(32.48%)	0.706
	Analgesia	108(27%)	116(29.44%)	0.445
	Analgesia and pyrexia	97(24.25%)	101(25.63%)	0.653
	Not documented	60(15%)	49(12.43%)	0.295
Without any other adjunctive analgesics, n (%)		193(48.25%)	181(45.93%)	0.515
With adjunctive opioid analgesics, n (%)		207(51.75%)	214(54.31%)	0.514
Frequency of administration:	q4h (4-hourly)	56(14%)	50(12.69%)	0.588
	q6h (6-hourly)	141(35.25%)	159(40.35%)	0.138
	q8h (8-hourly)	202(50.5%)	186(47.20%)	0.354
Duration of intravenous paracetamol use (d)		4.50±1.37	4.52±1.79	0.854
Daily max exceeded (4 g/24 hours), n (%)		53 (13.25%)	49 (12.43%)	0.732
Concomitant use with oral paracetamol, n (%)		67 (16.75%)	70 (17.76%)	0.854

Table 3. Comparison of the details of intravenous paracetamol prescribed to the patients in Group A before and after intervention.

variables		Group A Before intervention	Group A After intervention	p-value
Numbers		400	400	
Dose of intravenous paracetamol (grams received /24 h) Mean±SD		3.65±0.83	2.99±0.47	<0.001
Without any other adjunctive analgesics		193(48.25%)	294(73.5%)	<0.001
With adjunctive opioid analgesics		207(51.75%)	106(26.5%)	<0.001
Frequency of administration:	q4h (4-hourly)	56(14%)	0.0(0%)	<0.001
	q6h (6-hourly)	141(35.25%)	104(26%)	0.005
	q8h (8-hourly)	202(50.5%)	295(73.75%)	<0.001
Duration of intravenous paracetamol use		4.40±1. 38	2.35±0.47	<0.001
Daily max exceeded (4 g/24 hours)		53 (13.25%)	0.0(0%)	<0.001
Concomitant use with oral paracetamol		67 (16.75%)	0.0(0%)	<0.001

In intervention group A, dose adjustment was the most common intervention (48.5%), followed by conversion to oral paracetamol (32%). The rest of the interventions are illustrated in Table 4.

There was a significant reduction in the number of dispensed IV paracetamol vials after the pharmaceutical intervention (4,151 vials recovered by the intervention), which led to a reduction in the cost (8,302 USD reduction in the total cost), as illustrated in Table 5.

Table 6 illustrates the causes for the recovery of the IV paracetamol vial during the patient administration in group A; the most common cause was stopping the medication, followed by dose reduction.

If we calculated the prices of the medical supplies used for the patient, including those retrieved along with the returned paracetamol, the total cost would be 1256.369 USD, as illustrated in Table 7. The final cost of retrieving vials and medical supplies has been (8612 USD plus 1256.369 USD)= 9868.369 USD.

Table 4. Pharmacist intervention outcomes during the follow-up of the patient in group A.

Pharmacist intervention	Number	Percentage
Dose adjustment	194	48.5%
Converting to oral paracetamol	128	32%
Identify and resolve medication-related problems	118	29.5%
Converting to another analgesic	112	28%
Change in the duration that IV paracetamol was prescribed	110	27.5%
Giving instructions about patient adherence to treatment	106	26.5%
Correct the frequency of administration	102	25.5%
Recorded drug-drug interaction and food-drug interaction	98	24.5%
Identify related adverse events	50	12.5%

Table 5. Cost analysis regarding the intravenous paracetamol administered to patients in Group A.

Parameters	Before intervention	After intervention	The differences (the vial recovered from the patient)	p-value
Total number of vials dispensed to patients in group A	6452	2301	4151	<0.001
Cost of total number of vials dispensed to patients in group A	12904 USD	4602 USD	8302 USD	<0.001

Table 6. The cause of the vial recovered from the patient.

Parameters	Numbers	Percentage %
The total number of vials recovered from the patient	4151	-
Stop the medication (optimum temperature the patient does not need for it)	938	22.59%
Converting to oral paracetamol	796	19.17%
Replace it with another treatment or analgesia	388	9.34%
Patient discharge	465	11.20%
Decrease the duration of treatment	670	16.14%
Decrease in the dose	894	21.40%

Table 7. Number and costs of medical supplies that are used with the retrieved paracetamol vial from the patients in group A after intervention.

Medical Supplies	Number	Costs of pcs (USD)	Total costs (USD)
Disposable syringe 5cc	4151	0.333	138.367
Intravenous cannula	4151	0.116	481.516
Intravenous administration set	4151	0.1533	636.486
Total			1256.369

Discussion

Hospitals are subject to more economic pressure than ever, and cost reduction is critical, especially concerning expensive brand-name medicines. On the other hand, quality measures and value-based compensation are detrimental to patients' health care, especially concerning expensive brand-name medicines (Bouayad et al. 2020). Therefore, the DTC worked to develop plans to provide the best health services without waste in dispensing medications (Dalton and Byrne 2017).

The findings of the current study showed pharmaceutical interventions had led to a reduction in the number of IV paracetamol vial prescriptions, which is associated with a reduction in hospital expenditure by 9868.369 USD (8612 USD came from a reduction of vial prescriptions and 1256.369 USD came from a reduction of other medical supplies). This indicates that there was a positive impact of pharmacist involvement in the patient's management plan on improving the optimal and rational use of medication and decreasing the cost in the hospital. The result of this study confirms a previous study (Zeinab et al. 2020). Another study that evaluated pharmacist- based interventions to optimize the utilization of IV paracetamol has demonstrated a reduction in the mean monthly number of vials following the pharmacist intervention by educational and protocol interventions (59% reductions) (Laali et al. 2020).

In the current setting of rising healthcare expenditures, it is increasingly important to deliver safe healthcare (Dalton and Byrne 2017). Rational drug use is well recognized as an important part of health policy, especially with widely used medications like intravenous paracetamol (Ofori-Asenso and Agyeman 2016). Therefore, the hospital directors and health workers interested in developing the health system in the hospital adopted several strategies and established policies to control the dispensing of medications (Rowe et al. 2018). The most important of these strategies is the involvement of the clinical pharmacist in the management plan of the patients in the hospital, which provides the pharmacist with a greater role to activate his responsibilities from passive dispensing medicines to being an important member of the DTC team to develop the treatment process for the patient (Mohiuddin 2019). In past decades, the activities of the pharmacist primarily focused on the dispensing and supply of medications; recently, the role of the pharmacist has evolved substantially by increasing the interaction with other healthcare professionals, ensuring the rational and cost-effective use of medicines, promoting healthy living, and improving clinical outcomes by actively engaging in direct patient care and collaborating with many healthcare disciplines (Mohiuddin 2019).

With this expanding scope of practice, pharmacists are recognized as key components in providing individualized patient care as part of multidisciplinary healthcare teams (Mohiuddin 2019). Pharmacists can play a large and important role when involved in the patient management plan; they can improve patients' outcomes by identifying and reconciling medication discrepancies, introducing patients to education, giving instructions about patient compliance with treatment, and providing consultation on medications to reduce adverse outcomes with the identification of related adverse events, dose adjustment, change in the duration of medications that are prescribed, and correcting the frequency of administration (Bronkhorst et al. 2020). All these activities of follow-up and treatment of the patient can improve the patient's treatment process, prevent irrational use of the drug, reduce the patient's treatment cost in the hospital, and prevent medication waste (Religioni and Pakulska 2020).

There are many reasons for the increase in the irrational use of IV paracetamol in hospitals; one of the most important reasons is that IV paracetamol is not used appropriately; sometimes, its use is not according to the therapeutic protocol, and its dosage is not adjusted according to the age, weight, and medical condition of the patient (Procter et al. 2018). At other times, prescriptions for intravenous paracetamol and all medicines are written using the trade name and not the generic name; this will confuse the medical staff (Manias et al. 2019). Oral paracetamol is sometimes mistakenly dispensed simultaneously with its IV formulation, leading to exceeding the maximum daily dose of paracetamol (Trebach et al. 2023).

Study limitations

This study was presented in a single ward in one hospital, and for the results to be more useful, it is better to generalize the study to the rest of the hospital wards or other hospitals across the country.

Conclusion

The clinical pharmacist intervention plan was associated with a reduction in the overall cost caused by the inappropriate use of IV paracetamol. Clinical pharmacist interventions are associated with improved prescribing patterns and the efficiency of using intravenous paracetamol; thus, clinical pharmacist services are recommended.

We recommend increasing awareness about the role of clinical pharmacist interventions in reducing the improved use of drugs in hospitals, which will be associated with better health care outcomes and a reduction in the overall cost of the healthcare system.

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Competing interests

The authors have declared that no competing interests exist.

Author contributions

Conceptualization (KFN, AH, HAF, AS), Methodology (KFN, AH, HAF, AS), Software (KFN, HAF), Validation (AS, OZS, ZRJ, AAO), Formal analysis (KFN, AH, HAF), Investigation (AS, OZS, ZRJ, AAO, AAO), Resources (AS, OZS, ZRJ, AAO, AAO), Data Curation(KFN, AH, HAF, AS), Writing - Original draft, Writing - Review and Editing (KFN, HAF), Visualization (KFN, HAF), Supervision (HAF), Project administration (KFN).

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