Original article

Evaluation of Prescription Pattern and Rationality of Fixed-Dose Drug Combinations Among Patients Attending a Tertiary Care Hospital: A Cross-Sectional Study

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Abstract

Background: Fixed-dose drug combinations are widely used in clinical practice and may offer benefits such as improved compliance, reduced pill burden, synergistic therapeutic effect, and simplified treatment schedules. However, irrational fixed-dose combinations may increase the risk of adverse drug reactions, drug interactions, unnecessary cost, therapeutic duplication, and antimicrobial resistance. Evaluation of fixed-dose combination prescribing is important for promoting rational pharmacotherapy.

Aim: To assess the prescription pattern and rationality of fixed-dose drug combinations among patients attending a tertiary care hospital.

Materials and Methods: A cross-sectional observational study was conducted in the Department of Pharmacology. A total of 286 prescriptions containing at least one fixed-dose drug combination were analyzed. Data regarding demographic profile, clinical diagnosis, number of drugs per prescription, type of fixed-dose combination, therapeutic category, number of active ingredients, route of administration, generic or brand-name prescribing, and rationality of combinations were recorded. Rationality was assessed based on pharmacological justification, therapeutic need, dose appropriateness, safety, and inclusion in standard treatment references or essential medicine principles. Data were analyzed using descriptive statistics.

Results: Among 286 prescriptions, males constituted 162 (56.6%) and females 124 (43.4%). The most common fixed-dose combinations prescribed were analgesic combinations, antimicrobial combinations, cough and cold preparations, vitamin and mineral combinations, gastrointestinal combinations, and antihypertensive combinations. Most fixed-dose combinations were prescribed by brand name. Two-drug combinations were most common, followed by three-drug and multiple-ingredient combinations. Rational combinations accounted for 154 (53.8%) prescriptions, while 92 (32.2%) were considered irrational and 40 (14.0%) were difficult to classify due to inadequate clinical details. Common reasons for irrationality included therapeutic duplication, unnecessary multiple ingredients, inappropriate antimicrobial combinations, absence of clear pharmacological advantage, and increased risk of adverse effects.

Conclusion: Fixed-dose combinations were frequently prescribed in routine clinical practice. Although some combinations were rational and clinically useful, a considerable proportion lacked clear therapeutic justification. Periodic prescription audit, prescriber education, essential medicine-based prescribing, and regulatory control are necessary to promote rational use of fixed-dose combinations.

Keywords- Drug Utilization, Fixed-Dose Combination, Pharmacology

Introduction

Fixed-dose drug combinations are pharmaceutical formulations containing two or more active ingredients in a fixed ratio in a single dosage form. These combinations are commonly used in several therapeutic areas, including infectious diseases, hypertension, diabetes mellitus, pain management, respiratory disorders, gastrointestinal conditions, and nutritional supplementation. When scientifically justified, fixed-dose combinations may improve therapeutic efficacy, reduce pill burden, enhance adherence, simplify prescribing, and improve patient convenience.[1]

The rationality of a fixed-dose combination depends on several factors. Each component should have a clear therapeutic role in the condition being treated. The pharmacokinetic profile of the combined drugs should be compatible, the dose ratio should be appropriate for most patients, and the combination should offer an advantage over separate administration of individual drugs. The safety profile should be acceptable, and the combination should not increase unnecessary exposure to drugs.[2]

Rational fixed-dose combinations are particularly useful in chronic diseases where long-term adherence is important. Examples include certain antihypertensive combinations, antitubercular combinations, antiretroviral combinations, and selected antidiabetic combinations. In these situations, combinations may reduce pill burden and improve treatment continuation.[3]

However, irrational fixed-dose combinations are a major concern in pharmacotherapy. Irrational combinations may contain drugs with overlapping actions, mismatched pharmacokinetics, antagonistic effects, unnecessary ingredients, inappropriate dose ratios, or increased toxicity. Such combinations may increase cost without improving efficacy and may expose patients to avoidable harm.[4]

Analgesic combinations are commonly prescribed in clinical practice. Some combinations may offer benefit when drugs act through different mechanisms. However, combining multiple non-steroidal anti-inflammatory drugs or adding unnecessary ingredients may increase gastrointestinal, renal, hepatic, and hypersensitivity risks. Irrational analgesic combinations are especially concerning when used repeatedly or without supervision.[5]

Antimicrobial fixed-dose combinations require careful evaluation. Some antimicrobial combinations are rational when they broaden coverage, prevent resistance, or produce synergistic effect for specific indications. However, irrational antimicrobial combinations may promote resistance, increase adverse effects, and complicate culture-guided therapy.[6]

Cough and cold combinations are frequently used for symptomatic relief but often contain multiple ingredients such as antihistamines, decongestants, antitussives, expectorants, analgesics, and caffeine. Such multi-ingredient preparations may not be suitable for every patient and can cause sedation, palpitations, hypertension, dryness of mouth, and drug interactions.[7]

Drug utilization studies provide useful information regarding prescribing behavior and rationality of medicine use. Evaluation of fixed-dose combination prescribing helps identify irrational patterns and supports educational and regulatory interventions. The present study was conducted to assess prescription pattern and rationality of fixed-dose drug combinations among patients attending a tertiary care hospital.

Materials and Methods

This cross-sectional observational study was conducted in the Department of Pharmacology. A total of 286 prescriptions containing at least one fixed-dose drug combination were collected from outpatient and inpatient departments.

Prescriptions of patients of all adult age groups and both sexes were included. Prescriptions containing at least one fixed-dose drug combination in oral, injectable, topical, or inhalational form were considered. Incomplete prescriptions where the drug name or active ingredients could not be identified were excluded.

Data were collected using a structured proforma. The following details were recorded: patient age, gender, department, clinical diagnosis, total number of drugs prescribed, number of fixed-dose combinations, name of fixed-dose combination, active ingredients, therapeutic category, route of administration, brand or generic prescribing, and duration of therapy where mentioned.

Fixed-dose combinations were categorized into analgesic combinations, antimicrobial combinations, cough and cold preparations, gastrointestinal combinations, vitamin and mineral combinations, antihypertensive combinations, antidiabetic combinations, dermatological combinations, and others.The number of active ingredients in each fixed-dose combination was recorded. Combinations were categorized as two-drug, three-drug, or more than three-drug combinations.

Rationality assessment was performed using pharmacological criteria. A combination was considered rational if the drugs had complementary mechanisms of action, compatible pharmacokinetics, appropriate dose ratio, improved therapeutic benefit, reduced resistance, improved adherence, or accepted clinical indication. A combination was considered irrational if it showed therapeutic duplication, unnecessary multiple ingredients, increased toxicity without benefit, inappropriate dose ratio, doubtful indication, or avoidable cost burden.

Where adequate clinical details were not available to judge rationality, the combination was classified as difficult to assess. The assessment was descriptive and based on available prescription information.Data were entered in Microsoft Excel and analyzed using descriptive statistics. Results were expressed as frequencies and percentages.Institutional permission was obtained before conducting the study. Patient identity and prescription details were kept confidential.

Results

A total of 286 prescriptions containing fixed-dose drug combinations were analyzed.

Table 1: Demographic Characteristics of Patients

Variable	Frequency (%)
Male	162 (56.6)
Female	124 (43.4)
Age 18–30 years	58 (20.3)
Age 31–50 years	126 (44.1)
Age 51–65 years	72 (25.2)
Age >65 years	30 (10.5)

Males constituted 56.6% of the study population. The majority of patients belonged to the 31–50 years age group.

Table 2: Therapeutic Categories of Fixed-Dose Combinations

Therapeutic Category	Frequency (%)
Analgesic combinations	68 (23.8)
Antimicrobial combinations	54 (18.9)
Cough and cold preparations	42 (14.7)

Vitamin/mineral combinations	38 (13.3)
Gastrointestinal combinations	34 (11.9)
Antihypertensive combinations	24 (8.4)
Antidiabetic combinations	12 (4.2)
Dermatological combinations	8 (2.8)
Others	6 (2.1)

Analgesic combinations were the most commonly prescribed fixed-dose combinations, followed by antimicrobial combinations and cough and cold preparations.

Table 3: Number of Active Ingredients in FDCs

Number of Active Ingredients	Frequency (%)
Two-drug combinations	164 (57.3)
Three-drug combinations	72 (25.2)
More than three ingredients	50 (17.5)

Two-drug combinations were most common. Multi-ingredient combinations with more than three active components were mainly seen among cough and cold preparations and vitamin-mineral combinations.

Table 4: Route of Administration

Route	Frequency (%)
Oral	232 (81.1)
Topical	28 (9.8)
Injectable	18 (6.3)
Inhalational/others	8 (2.8)

Most fixed-dose combinations were prescribed by the oral route. Topical and injectable combinations were less common.

Table 5: Prescribing Pattern

Parameter	Frequency (%)
Prescribed by brand name	252 (88.1)
Prescribed by generic name	34 (11.9)
Single FDC in prescription	214 (74.8)
Two or more FDCs in prescription	72 (25.2)
Duration clearly mentioned	198 (69.2)
Duration not mentioned	88 (30.8)

Most fixed-dose combinations were prescribed by brand name. Duration of treatment was not clearly mentioned in 30.8% prescriptions.

Table 6: Rationality Assessment of FDCs

Rationality Category	Frequency (%)
Rational	154 (53.8)
Irrational	92 (32.2)
Difficult to assess	40 (14.0)

Rational fixed-dose combinations accounted for 53.8% prescriptions. Irrational combinations were observed in 32.2% prescriptions. In 14.0% prescriptions, rationality was difficult to assess due to inadequate clinical information.

Table 7: Reasons for Irrationality

Reason	Frequency (%)
Therapeutic duplication	28 (30.4)
Unnecessary multiple ingredients	24 (26.1)
Inappropriate antimicrobial combination	16 (17.4)
No clear pharmacological advantage	14 (15.2)
Increased risk of adverse effects	10 (10.9)

Therapeutic duplication and unnecessary multiple ingredients were the most common reasons for irrationality.

Discussion

The present study evaluated the prescription pattern and rationality of fixed-dose drug combinations among 286 prescriptions in a tertiary care hospital. Fixed-dose combinations were commonly prescribed across several therapeutic categories. Analgesic combinations were the most frequent, followed by antimicrobial combinations, cough and cold preparations, vitamin-mineral combinations, gastrointestinal combinations, and antihypertensive combinations.

World Health Organization emphasized that rational drug use requires appropriate medicine, dose, duration, and cost according to patient needs.[8] Fixed-dose combinations should therefore be prescribed only when they provide clear therapeutic advantage over separate drug administration.

Pillans discussed the rational use of fixed-dose combinations and emphasized that such products are justified only when the combination improves efficacy, safety, adherence, or resistance prevention.[9] In the present study, only 53.8% combinations were considered rational based on available prescription information.Chaudhury discussed essential medicines and rational drug use, highlighting that irrational combinations increase cost and expose patients to unnecessary medicines.[10] The present study found that 32.2% fixed-dose combinations were irrational, indicating the need for prescription review.

Study of Gautam and Saha reported concerns regarding irrational fixed-dose combinations and the need for critical evaluation of marketed combinations.[11] The present study similarly found unnecessary multiple ingredients and therapeutic duplication in a significant proportion.Joshi reviewed fixed-dose combinations and noted that irrational combinations may create prescribing confusion and increase adverse effects.[12] In the present study, multi-ingredient cough and cold preparations and analgesic combinations contributed to irrational prescribing.

Patel et al. evaluated fixed-dose combinations and observed that many combinations lack rational pharmacological basis.[13] The present study supports this observation, especially for combinations with overlapping analgesic or antimicrobial components.Desai studied drug utilization patterns and emphasized that prescription audits are important tools for identifying irrational prescribing practices.[14] The present study demonstrates the usefulness of prescription audit in identifying irrational fixed-dose combination use.

Bapna et al. discussed rationality of drug combinations and emphasized the need for prescriber awareness.[15] The present findings highlight that prescriber education is essential for reducing irrational fixed-dose combination prescribing.Analgesic combinations were the most commonly prescribed category. Some analgesic

combinations may be useful when drugs have different mechanisms and safety is acceptable. However, combinations of multiple NSAIDs or analgesics without clear indication may increase gastrointestinal, renal, and hepatic toxicity.

Antimicrobial combinations were the second most common category. Some combinations, such as beta-lactam with beta-lactamase inhibitor, are rational for specific indications. However, combinations of unrelated antimicrobials without microbiological or clinical justification may promote resistance and increase adverse effects.

Cough and cold preparations often contained multiple ingredients. These may provide symptomatic relief, but unnecessary inclusion of sedating antihistamines, decongestants, caffeine, analgesics, and expectorants may not be suitable for all patients. Such combinations should be used cautiously.

Vitamin and mineral combinations were commonly prescribed. While useful in documented deficiency or specific physiological states, routine use without indication may increase cost and encourage unnecessary medication use.

Gastrointestinal combinations included antacid, antiflatulent, antispasmodic, antiemetic, and acid-suppressing combinations. Some may be symptomatically useful, but multi-ingredient products should be selected according to specific patient symptoms rather than routine use.

Antihypertensive fixed-dose combinations were relatively rational when they included drugs with complementary mechanisms, such as diuretic with ACE inhibitor or ARB, or calcium channel blocker with ARB. Such combinations may improve adherence in chronic therapy.

Generic prescribing was low in the present study. Most fixed-dose combinations were prescribed by brand name. Brand-based prescribing may increase cost and reduce transparency regarding active ingredients. Prescribers should be encouraged to identify the components before prescribing.

Duration of treatment was not clearly mentioned in nearly one-third of prescriptions. This is important because unclear duration may lead to prolonged use, increased adverse effects, and treatment confusion.

Therapeutic duplication was the most common reason for irrationality. This occurred when two drugs with similar action were combined without clear benefit. Such duplication increases toxicity without improving efficacy.

Unnecessary multiple ingredients were also common. The more ingredients a product contains, the greater the risk of adverse effects, drug interactions, contraindications, and difficulty in identifying the cause of adverse reactions.

Conclusion

Fixed-dose combinations were frequently prescribed in routine clinical practice. Analgesic combinations, antimicrobial combinations, cough and cold preparations, vitamin-mineral combinations, and gastrointestinal combinations were commonly used. While some combinations were rational and clinically justified, a considerable proportion was irrational due to therapeutic duplication, unnecessary multiple ingredients, inappropriate antimicrobial combinations, lack of clear pharmacological advantage, and increased risk of adverse effects. Rational prescribing of fixed-dose combinations requires pharmacological justification, appropriate dose ratio, safety assessment, patient-specific need, and cost consideration. Prescription audit, essential medicine-based prescribing, prescriber education, and regulatory control are necessary to reduce irrational fixed-dose combination use.

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