

## STUDY TO EVALUATE USE OF IRRATIONAL FIXED DRUG COMBINATIONS

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### ABSTRACT

**Objective:** To identify fixed drug combinations causing the adverse drug reactions both rational and irrational.

**Methods:** A prospective observational study was carried out over a period of 6 mo (between June 2016 to December 2016) to evaluate adverse drug reactions related to fixed drug combinations in a tertiary care teaching hospital using suspected adverse drug reaction reporting form.

**Results:** A total number of 64 adverse drug reactions were reported during this period. Of the total adverse drug reactions reported, 27 (42%) were due to fixed drug combinations. 6 (28.5%) were serious and 21(71.5%) were non-serious. Causality was certain in 4 (14.8%) cases and probably in remaining 23 (85.2%) cases. 19(70%) irrational fixed drug combinations were reported.

**Conclusion:** The above results show that irrational fixed drug combinations contribute major extent to adverse drug reactions. Hence, awareness programs should be conducted for all the health care workers to improve the rationality of prescription and to decrease adverse drug reactions.

**Keywords:** Fixed Drug Combinations (FDC), Adverse Drug Reactions, Rationality, Pharmacovigilance, National list of essential medicines (NLEM)

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### INTRODUCTION

The World Health Organization (WHO) defines fixed Dose Combinations (FDCs) as combination of two or more active ingredients in a fixed ratio of doses [1]. Polypharmacy is the commonest mode of prescription for single or multiple ailments. Irrational FDC are a part of polypharmacy, which need to be curbed. It is need of the hour to adopt essential medical list and preferred drugs to improve rational therapeutics. The estimated number of FDCs in India is over 6000 and financial turnover associated with it is Rs 7000 crores. Whereas only 24 FDCs out of 376 entities in the National List of Essential Medicines of India (NLEM) 2015 [2] are considered to be rational. Recently health ministry banned 344 fixed-dose combination drugs [3] in March due to questionable efficacy, safety, and rationality. But pharma companies obtained a judicial stay on the order. So the present study was conducted to evaluate irrational fixed dose combinations.

### MATERIALS AND METHODS

The present study is carried out at Bhaskar General Hospital Adverse drug reactions monitoring centre after obtaining permission from Pharmacovigilance committee members and ethics committee. No financial implications are seen. The study is done for a period of 6 mo, it is a prospective observational study wherein adverse drug reactions were collected through notification form (yellow form) and CDSCO form (red form), and further evaluated for irrational prescriptions. Hartwig and Seigelscale do severity assessment of the adverse drug reaction. Causality assessment is done by WHO-UMC causality assessment scale. Rationality was assessed using National List of Essential Medicines of India (NLEM) 2015[2].

Inclusion criteria: Suspected adverse drug reaction reported in Bhaskar Medical College and General Hospital, for 6 mo.

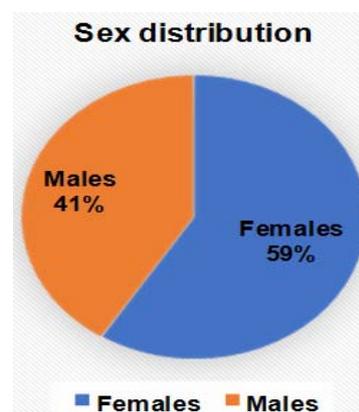
Exclusion criteria: ADR due medication error, over dosage, non-compliance, natural products, alternate medicines and unidentified drugs were excluded.

### Statistical methods

Data entry and analysis was done using Microsoft Excel 2010 version. Data was presented in percentages and proportions. Bars diagrams and pie charts were used to depict percentages.

### RESULTS

A total of 64 adverse drug reactions were reported during this period out of which 27 were due to fixed dose combinations.



Pie Chart 1: Sex distribution

Table 1: ADR s due to fixed dose combination and single drugs

Fixed dose combinations	Single drugs
27 (42%)	37 (58%)

Table 2: Age distribution table

Age group	No of patients
Paediatric (0-19yrs)	1
Adult (22-64yrs)	22
Geriatric (>65yrs)	4

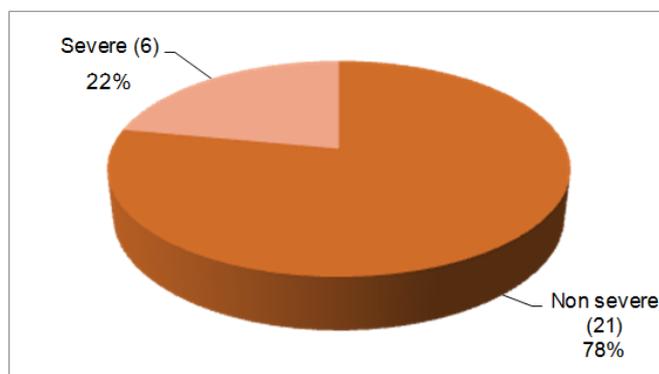
Most of the patients were in adult age group and mean age of patients is 43.2 y.

Table 3: Drug classes used in FDCs contributing to adverse effects

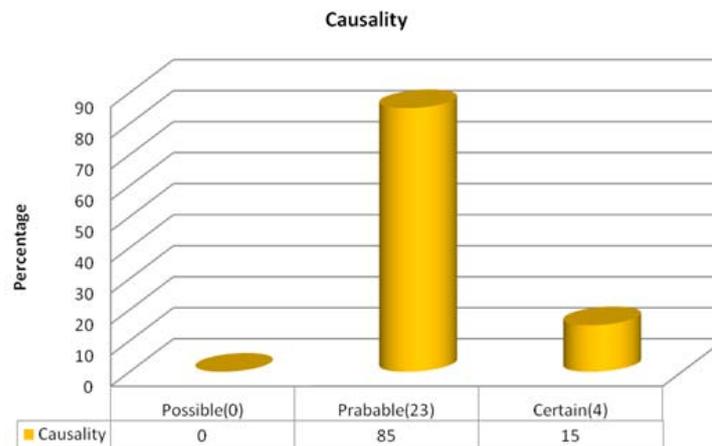
Drug class	Rational	%	Irrational	%
Antimicrobials	10	37	6	22.2
NSAID	0	0	3	11.1
Oral Hypoglycemics	0	0	2	7.4
Proton Pump Inhibitor With Prokinetic	0	0	2	7.4
Antihistamine With NSAID	0	0	2	7.4
Multivitamin	1	3.7	1	3.7

Table 4: Pattern of ADRs reported with the use of irrational FDCs

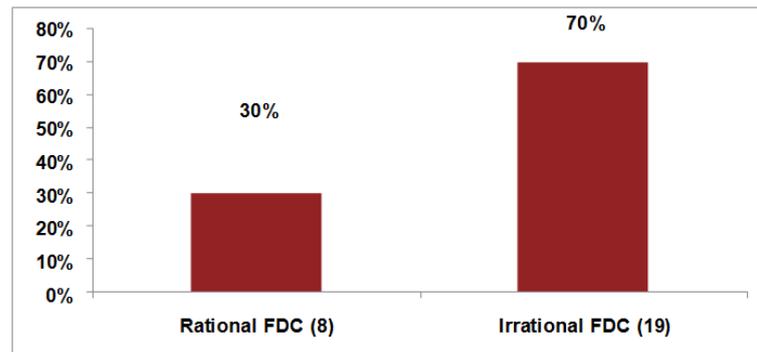
ADR reported with FDC	Irrational
Edema	5
Nausea And Vomiting	5
Rash	2
Itching	2
Syncope	1
Gastric Irritation	2
Tightness Of Chest	1
Fixed Drug Eruption	1
Angioedema	1
Eruption	1



Pie Chart 2: Percent of severe cases reported due to FDC according to hartwig and siegel scale



Bar Diagram 1: Percent of cases reported to be possible, probable, certain



Bar Diagram 2: Rational Vs irrational FDC

## DISCUSSION

Spontaneously reported adverse drug reactions were evaluated for a period of 6 mo in this study. Of the total adverse drug reactions reported, 27 (42%) were due to fixed drug combinations. This shows that FDCs contribute significantly to adverse drug reactions, which is supported by a study conducted by Vijay Khjauria *et al.* [4], who reported that FDC was responsible for 26.67% of the total adverse drug reactions reported. Adverse drug reaction reported by irrational and rational FDC were 19(70%) and 8 (30%) respectively. Balat JD *et al.* [5] in relation to study conduct this where irrational FDC contributed to 90%. Antimicrobial class has the highest incidence (59.2%) of adverse drug reactions, which is consistent with a study done by Radhika MS *et al.*, [6] who reported that antimicrobials cause 65.52% Adverse drug reactions. Manu Gangadhar *et al.*[7]evaluated knowledge, attitude and practices about prescribing fixed dose combinations among postgraduate's and suggested in accordance with our study that concepts of rational drug use should be implemented in undergraduate curriculum vigorously.

## CONCLUSION

The above results show that irrational fixed drug combinations contribute major extent to adverse drug reactions. Hence, awareness programs should be conducted for all the health care workers to improve the rationality of prescription and decrease the adverse drug reactions. Improvisation can be done by -

1. Conducting training sessions at every step of healthcare by higher authorities.
2. Educating Health Care professional from undergraduate level regarding fixed dose combination.
3. Promoting prescription audit every six months to see that strict adherence to rationality is followed.

Further studies are needed to delineate the cause for irrational FDC prescriptions.

## CONFLICT OF INTERESTS

Declare none

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