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Original Research Article

Study of Prescription Patterns of Fixed Dose Combinations Prescribed by Medical Interns

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Abstract

Introduction: Illogical habits of prescribing irrational drug combinations have been deteriorating the health of the various communities. There are several benefits of fixed dose combinations (FDCs) but prescribing irrational combinations may be responsible for inadequate or incorrect treatment of patients even after correct diagnosis. The interns will constitute the major portion of the health care providers in our country in near future and irrational practices of prescribing FDCs among them will deteriorate the condition further in future. There is lack of research among these budding doctors will result in ineffective policy regarding teaching and training.
Objectives: 1. To study the prescription trends. 2. To study the various prescription patterns of FDCs.3. To find out the rationality of FDCs in a tertiary care hospital.
Methodology: Prescription audit study to study the trends, patterns and rationality of prescriptions made by a batch of 92 Interns posted in various departments in a tertiary care teaching hospital, Bareilly, UP, India. The prescriptions by the 52 interns during two months of their posting were analyzed using "R" Studio as per Policy guidelines-2013 for approval of fixed dose combinations in India.
Results: Out of total 994, 64.29% prescriptions contained any kind of fixed dose combinations. The maximum FDCs (27.34%) belonged to antimicrobial class. Only 13.31% FDCs were rational. Ninety five percent FDCs were prescribed by the brand names.
Conclusion: The prescription habits of one batch of interns of a teaching hospital are ringing alarm bell to develop effective training program to them and develop a national policy regarding FDCs.
Keywords: Prescription Patterns, Fixed Dose Combinations (FDCs), Interns.

1.Introduction

Health has been a prime importance in overall wellbeing in human history. Since the date of its birth the medical science has been trying to improve the health status of human beings with the help of promotive, preventive, curative and rehabilitative measures. Medicated drugs are being used as curative measures for long time. The drugs have been defined as "Any substance or product for human or veterinary use that are intended to modify or explore physiological states for the benefit of the recipient"[1]. Usually one or more drugs are needed as curative measure to treat the diseases. Administration of multiple drugs may be necessary many times to treat the disease; drugs are also combined with bad compliance to the treatment. Fixed dose combinations are answers of modern pharmaceutical science to these problems. World Health Organization (WHO) expert committee in its 49th report on specifications for pharmaceutical preparations defined a Fixed Dose Combination (FDC) as "A combination of two or more actives in a fixed ratio of doses. This term is used generically to mean a particular combination of actives irrespective of the formulation or brand. It may be administered as single entity products given concurrently or as a finished pharmaceutical product.[2]

Fixed dose combinations has several advantages like it improves compliance, it lowers costs of manufacturing compared to the costs of producing separate products, it reduces administration costs in terms of simplified packaging, fewer prescriptions, lesser

dispensing time and cost, synergistically improved efficacy of active pharmacological ingredients.

Scientific rationales for combined use of the components may be one or more among increased efficacy (additive or synergistic), reduced toxicity, and prevention of antimicrobial resistance and boosting of drug levels.[3]

Fixed dose combinations that do not follow these rationales can become irrational drug combinations. Though there are several benefits of Fixed dose combinations, prescribing irrational combinations may be responsible for inadequate or incorrect treatment of patients even after correct diagnosis. Lack of training, lack of clear cut guidelines and unethical practices by pharmaceutical companies are among main causes behind prescriptions containing the irrational drug combinations.

The Internship is a training program of one year duration and as per Medical council of India (MCI) it is compulsory after passing all academic medical examinations in multiple departments of a medical institution to provide budding doctors a practical training of medical sciences. This training is intended to develop habits of medical practice among Interns which is like permanent marks on long term memory of doctors of the country. In India, where Primary health care to everybody is still a distance dream, habits of prescribing irrational drug combinations further deteriorate the health of the community. Therefore, it is very important to train these budding doctors about fixed dose combinations. But there is lack of research regarding prescription patterns and habits of budding doctors therefore this research was done to study the prescription patterns and habits of Interns so that this piece of research can contribute to some extent in formulation of the national effective policy about fixed dose combinations and its prescriptions for the future Interns and subsequently the communities will be benefited with this change. Later on these changes in the policy can be extended to the Ayurvedic, Yoga, Unani, Siddha and Homeopathic (AYUSH) doctors that further will extend the benefits to the population for which the health care services are relatively inaccessible. And one more important reason which forced us to carry out this research work is that there was no such type of study conducted in this region. With these many views we carried out this study in a tertiary care level teaching hospital with the following objectives.

1. To study the prescription trends in a tertiary care hospital.
2. To study the various prescription patterns of FDCs.
3. To find out the rationality of FDCs.

2. Methodology

Clearance from Institutional Ethics Committee (IEC) was obtained before conducting the study. Following are the steps of methodologies which were used in the study. A prescription audit study was carried out in a tertiary care teaching hospital, Bareilly, UP, India, the study duration was two months from 1st January 2016 to 29th February 2016. The purposive sampling was used and sample size was 994 prescriptions and all these prescriptions were analyzed using R studio.

A total of 994 prescriptions made by 52 interns out of total 92 intern posted in various departments were taken and were audited in 2 months duration from 1st January 2016 to 29th February 2016. Data about prescribed fixed dose combinations was entered in a schedule for each prescription. These were entered in Microsoft excel sheets to evaluate directly. The only exclusion criterion was that the non-official prescriptions were excluded during the study.

The Fixed dose combinations were analyzed for rationality of use according to the Policy guidelines for approval of fixed dose combination in India (2013)[3].The following guidelines were adopted as criteria to analyze the rationality of Fixed Dose Combinations.

1. Active pharmacological ingredients (APIs) with complementary mechanism of action
2. There should be a medical rationale for combining the actives.
3. If the actives in an FDC are intended to relieve different symptoms of a disease state, it is a prerequisite that these symptoms commonly occur simultaneously at a clinically relevant intensity and for a period of time such that simultaneous treatment is appropriate. Occurrence of the individual symptom in isolation should not be indications for the FDC.
4. The FDC should have demonstrably one or more of the following features:
   a. Increased efficacy in comparison to the individual components given at the same dose.
   b. The incidence of adverse reactions in response to treatment with the combination is lower than in that in response to any of the component actives given alone, for example as a result of a lower dose of one component or a protective effect of one component.
   c. Dose reduction.
   d. Reduced cost.
   e. One drug acts as a booster for another (for example in the case of some antiviral drugs).
   f. Improved adherence, simplified therapy,
   g. For antimicrobials, the combination results in a reduced incidence of resistance.
   h. Minimize abuse of other actives
   i. Simplified logistics of procurement and distribution.
5. There should be an identifiable patient group for which this combination of actives and doses are indicated.

The larger the patient group in question, the more significant is this factor.

6. In general, the actives in a combination should have similar pharmacokinetics. If this is not the case, the applicant should explain and justify the combination.
7. In general, all of the actives in a combination should have a similar duration of action. If this is not the case, the applicant should explain and justify the combination.
8. Dose and proportion of each active ingredient present is appropriate for the intended use.

Drug combinations not satisfying above criteria were termed as irrational.

3. Results and Observations

All prescriptions over a period of 2 months in were analyzed. Fixed dose combinations prescribed were recorded and evaluated for rationality. A total of 994 prescriptions were scrutinized.

Out of total 994 prescriptions, 64.29% prescriptions contained any kind of fixed dose combinations [Table 1]. By excluding the intra-specialty repetitions, the total numbers of the fixed dose combinations prescribed to patients were 336. These 336 fixed dose combinations included inter-specialty repetitions, thus by excluding them; the total numbers of the fixed dose combinations were 278.

Table 2 shows the percentage of FDCs prescribed to patients of different specialty. Maximum FDCs were prescribed to patients attending medicine OPD (25.59%), followed by surgery (15.47%), and ENT (13.69%). Minimum FDCs were prescribed to patients attending obstetrics and gynecology (6.54%).

Table no 3 shows distribution of prescribed FDCs according to various pharmacology classes. Out of total 278 FDCs, maximum 27.34% belonged to antimicrobial class followed by anti-inflammatory agents (25.54%).

Table no 4 shows categorization of the FDCs according to WHO guidelines for rationality. Out of 278 FDCs, only 13.31% were rational and 86.69 % were irrational.

Among the various pharmacological classes, all the FDCs prescribed in digestive enzymes and hypo-lipidemic drugs classes were irrational followed by cough & cold agents (94.87%), Anti-ulcer (92.31%) and Anti-microbial (92.1%) [Table 5].

Table no 6 shows mode of prescription for FDCs. The majority of the FDCs (95%) were prescribed by the brand names in comparison with generic names which were used only for 5% FDCs.

Table 1: Distribution of prescription as per presence of Fixed dose combinations (n = 994)

Presence of Fixed dose combinations	No of prescriptions	Percentage
Yes	639	64.29
No	355	30.71
Total	**994**	**100.00**

Table 2: Total numbers of fixed dose combinations prescribed to patients including inter-specialty repetitions (n=336)

Departments	No of FDCs prescribed	Percentage
Medicine	86	25.59
Surgery	52	15.47
Obstetrics & Gynecology	22	6.54
Pediatrics	35	10.41
Ophthalmology	38	11.31
ENT	46	13.69
Skin	30	8.93
Orthopedics	27	8.36
Total	**336**	**100.00**

Table 3: Distribution of prescribed FDCs according to Pharmacological classes (n = 278)

Class of FDC	No of FDCs prescribed	Percentage
Antimicrobials	76	27.34
Anti-inflammatory agents	71	25.54
Nutritional supplements	54	19.42
Cough and Cold agents	39	14.03
Anti-ulcers	13	4.68
Anti-hypertensives	11	3.96
Hypo-lipidemics	7	2.52
Anti-diabetics	3	1.08
Digestive enzymes	4	1.44
Total	**278**	**100.00**

Table 4: Categorization of the FDCs based on WHO criteria for rationality (n = 278)

WHO category	No of FDCs prescribed	Percentage
Rational	37	13.31
Irrational	241	86.69
Total	**278**	**100.00**

Table 5: Pharmacological classes of FDCs prescribed with categorization as per WHO guidelines (n = 278)

Class of FDC	Rational	Irrational	Total
Antimicrobials	6 (7.90%)	70 (92.1%)	**76 (100.00%)**
Anti-inflammatory agents	10 (14.09%)	61(85.91%)	**71 (100.00%)**
Nutritional supplements	15 (27.78%)	39 (72.22%)	**54 (100.00%)**
Cough and Cold agents	2 (5.13%)	37(94.87%)	**39 (100.00%)**
Anti-ulcers	1 (7.69%)	12 (92.31%)	**13 (100.00%)**
Anti-hypertensives	1 (9.09%)	10 (90.91%)	**11 (100.00%)**
Hypolipidemics	0 (0.00%)	7 (100%)	**7 (100.00%)**
Anti-diabetics	2 (66.67%)	1 (33.33%)	**3 (100.00%)**
Digestive enzymes	0 (%)	4 (100%)	**4 (100.00%)**
Total	37(13.31%)	241(86.69%)	**278 (100.00%)**

Table 6: Comparison of FDCs prescribed as brand name & generic names (n = 278)

Mode of prescription of FDCs	No of FDCs prescribed	Percentage
Brand name	264	95
Generic name	14	5
Total	**278**	**100.00**

4. Discussion

The present study was designed to know the prescribing patterns of FDCs by Medical graduate interns. There is scarce as well as scary data about prescription of FDCs by budding doctors.

In our study, 64.29% prescriptions by interns contained one or more fixed dose combinations. Different results were obtained in various studies in past. Angelika Batta *et al* in Mahatma Gandhi Medical Hospital, Jaipur in 2014 found that 60.4% prescriptions by specialist doctors contained fixed dose combinations [4]. Londhe *et al* found that 33% case sheets of indoor patients contained fixed dose combinations [5]. Balat *et al* found that 80.3% prescriptions by all practitioners (general + specialist) contained fixed dose combinations [6].

In our study, antimicrobial (27.34%) were most frequently prescribed fixed dose combinations followed by anti-inflammatory-anti-pyretic combinations (25.54%). Similar finding were obtained by Raut *et al*, Londhe SP *et al* and Eesha *et al* who found antimicrobials as most frequently used fixed dose combination i.e. 26%, 23% & 17.5% respectively [5-8]. On the other hand, Goswami *et al* found very high proportion of antimicrobial combinations among all prescriptions i.e. 45% and Balat found nutritional supplements as most prescribed Fixed dose combination [6,9].

Study conducted by Hindoliya *et al* in Ujjain District showed that only 8% of the FDCs were rational as they fulfilled all the WHO criteria [10]. Our study had similar findings with previous observations that there was scientific justification for combining ingredients in only 13.31% FDCs and 86.69% fixed dose combinations did not have any rational justification. Similar finding was observed by Balat *et al* who found 81.5% fixed dose combinations as irrational prescribed [6]. Goswami *et al* and Londhe *et al* found 54%, 33% fixed dose combinations as irrational for use whereas Sagar Raut *et al* found 22% of prescriptions found irrationally given fixed dose combinations [5,7,9].

Patel V in a prescription survey in Goa found that Ninety five percent of the FDCs were prescribed by the brand names and only 5% of the FDCs were prescribed by generic names [11]. Our study had similar findings which indicate that 95% fixed dose combinations were prescribed using brand names.

More than one third of new drugs added to the therapeutic armamentarium are FDCs.[10] Some are very popular and flourishing and experts worldwide express serious concerns about these as most of them are irrational. Such FDCs do not find mention in standard text books, journals etc., but manufacturers rip the benefit of huge sale and hence promote them vigorously by influencing prescribers unethically.[12] Large numbers of FDCs are of little importance in terms of essential health care.

Clear objective should be to prescribe generic FDCs with correct dose and duration, considering appropriate information to the patient. Unethical promotional activities by the manufacturers not only influence the prescribers, but also the retailers, homeopaths, ayurvedic practitioners to prescribe or sell FDCs. There is no formal training for undergraduates, post graduates or CMEs for practitioners, no proper drug information centres for the physician or patient use. Health care professionals should keep themselves updated about irrational drugs and banned drugs by the Drug Controller General of India (DCGI).

5. Conclusions

In India the patients are neither well informed nor the doctors are prescribing rational FDCs to them. At the same time, many doctors may also be ignorant about the essential drugs. Physicians and regulators should *get al*erted in time and regulatory actions or government laws should be made mandatory time to time according to the need of the common population of the country. Manufacturers are in business of profit but they should self-regulate themselves and should follow the moral code of conduct thinking in larger perspective of community health and health of nation as use of irrational FDCs result in non-eradication of diseases, spread of resistance, chronic persistence of unhealthy, unproductive population, wastage of precious government resources, under development of nation and economic down growth. All the health care providing institutions especially teaching hospitals should focus on the teaching of FDCs to all the budding doctors starting from inception i.e. graduation level training with the following suggestions:

1. There should be due emphasis on FDCs during teaching Pharmacology.
2. All clinical departments should adopt rational practice of prescribing FDCs
3. Emphasis on developing rational and ethical thinking among undergraduates during training about clinical practice to prescribe FDCs.

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