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RESEARCH ARTICLE

Assessment of knowledge, attitude, and practices about prescribing fixed dose combinations among doctors - An observational study

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ABSTRACT

Background: A fixed dose combination (FDC) comprises of two or more active drugs in a single dosage. The trend of prescribing FDCs is increasing in clinical practice. However, irrational prescribing of FDCs is a major health concern. The knowledge about FDCs is important for doctors as a large number of FDCs are being manufactured and marketed every year. **Aims and Objective:** The aim of this study is to evaluate knowledge, attitude, and practice (KAP) regarding the use of FDCs by doctors at a tertiary care teaching hospital. **Materials and Methods:** A cross-sectional study was carried out using a pretested questionnaire in a tertiary care teaching hospital of Jammu (Jammu and Kashmir). The questionnaire was designed to assess the KAP about FDCs. The doctors working in this institution during the study period from the Departments of Medicine, obstetrics and gynecology, surgery, pediatrics, skin and psychiatry, who gave their informed consent, were included in the study. Data were analyzed with suitable statistical tests. **Results:** In the present study, it was observed that the doctors were not aware about all of the advantages and disadvantages of FDCs. Out of the 74 doctors, the knowledge regarding the WHO essential medicine list (EML) was 82.4%. However, knowledge about the rationality of given FDCs was lacking in 53% of the doctors. The common sources of information were textbooks and journals. A majority of residents (73%) agreed that FDCs should be allowed to be marketed. The doctors opined that most commonly prescribed FDCs were of antimicrobial drugs, among which amoxicillin + clavulanic acid was the most frequent. **Conclusion:** There is a need to improve knowledge about rationality, EML, usage, and banned FDCs among doctors to promote the rational use of drugs.

KEY WORDS: Essential Medicine List; Fixed Dose Combinations; Knowledge; Attitude and Practice; Doctors

INTRODUCTION

A fixed dose combination (FDC) comprises of two or more active drugs in a single dosage form.[1] A new FDC is considered as "new drug" according to Drugs and Cosmetics Act, 1940; hence, it should undergo clinical trials before entering the market.[2] FDC products are acceptable when the combination has a proven advantage over single compounds administered separately in therapeutic effect, safety, or compliance. More than one-third of all the new drug products introduced worldwide during the past decade were FDCs preparations.[3] The FDCs are also highly popular in the Indian pharmaceutical market. FDCs are seen to enhance the efficacy of individual drugs, decrease the chances of drug resistance (e.g., antimicrobial drugs), improve patient compliance, and also decrease the pill burden on the patients. However, there are some disadvantages associated with the use of FDCs such as irrational prescription of FDCs, ineffective and unsafe

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treatment, exacerbation or prolongation of illness, and higher treatment cost.[4]

At present, there is a lot of debate over rationality and irrationality of FDCs. It is up to the stakeholder to misuse it or use it judiciously by maintaining the balance. The rationality of FDCs should be based on certain aspects such as: The drugs in combination should act by different mechanisms, the pharmacokinetics must not be widely different, and the combination should not have the supra-additive toxicity of the ingredients.[5] The trend of prescribing FDCs is increasing in clinical practice. The reasons for misuse are as follows: Most commercial approach of industry and casual approach of all the stakeholders of health care regarding the rational drug therapy. Furthermore, there is a lack of awareness and orientation among patients and the doctors.[5-7] Irrational prescribing of FDCs leads to increased risk of adverse drug reactions, higher treatment cost, emergence of resistant organisms, and sometimes treatment failure.[8]

The seventeenth WHO model list of essential medicines (March 2011) contains only 25 approved FDCs, while in India, irrational drug combinations are easily available and many of them available as over the counter drugs.[9] FDCs are available for the treatment of various disorders, for example, cardiovascular diseases, diabetes, infectious diseases (bacterial infections), gastrointestinal (GI) infections, orthopedic conditions, cough and cold, HIV infection, tuberculosis, psychiatric disorders, and respiratory diseases.[10]

A large number of FDCs are manufactured every year, and hence, the knowledge about prescribing FDCs is becoming increasingly important for better health outcomes. As prescription of medicine in India solely lays in the hands of the doctor, their basic knowledge about the drugs and their proper rational prescription lays the foundation for effective treatment. Thus, the present study was undertaken to evaluate the knowledge, attitude, and practices about prescribing FDCs among doctors at a tertiary care teaching hospital of North India.

MATERIALS AND METHODS

The present questionnaire-based study was carried out with doctors working in medicine, surgery, pediatrics, obstetrics and gynecology, skin and venereal diseases as well as the psychiatry departments of Acharya Shri Chander College Of Medical Sciences and Hospital, Sidhra, Jammu (Jammu and Kashmir), from February 2017 to April 2017. A total of 83 doctors were given the questionnaire, of which 74 returned the completed questionnaires, giving a response rate of 89.1%. Before this survey, the Institutional Ethics Committee approval and written informed consent from doctors of various departments of the tertiary care teaching hospital were obtained. Participants were informed about the objectives of the study and were assured that their response shall be anonymous. The participation was voluntary and without compensation. A prevalidated questionnaire, with both open- and closed-ended questions regarding knowledge, attitude, and prescribing practice of FDCs, was used as a tool to collect the data from the participants.[8] Analysis was carried out using descriptive statistics. Results were expressed in frequencies and percentages.

RESULTS

The present study was carried out on doctors of various departments of tertiary care teaching hospital, Jammu (Jammu and Kashmir). A total of 74 doctors from medicine, surgery, pediatrics, obstetrics and gynecology, skin and venereal diseases as well as the psychiatry departments were involved. An analysis of their knowledge about advantages and disadvantages of FDCs revealed that improved patient compliance (64%) and less cost (40%) were the major advantages, while difficulty in dosage adjustments (63%) was the common disadvantage of prescribing FDCs mentioned by the study population as summarized in Table 1.

The knowledge about the WHO essential medicine list (EML) showed that 82.4% of the doctors knew about its availability and 17.5% did not know about the availability of the WHO EML. However, among the doctors who knew about the WHO EML, 42.6% did not know even a single FDC included in the WHO EML as shown in Figure 1. In the present study, about 47% of the doctors were able to mention the rationality of given FDCs as shown in Figure 2.

Antimicrobials were the most commonly prescribed FDCs (52.7%). Out of these, amoxicillin + clavulanic acid was

Table 1: Knowledge of advantages and disadvantages about FDCs (*n*=74)

Parameters	Number of doctors *n* (%)
Advantages	
Improve patient compliance	47 (64)
Decrease chances of adverse drug reactions	13 (18)
Enhances drug efficacy	16 (21)
Patient demand	9 (12)
Less cost	30 (40)
Convenience	24 (33)
Disadvantages	
Multiple formulations (polypharmacy)	22 (30)
Increased cost	17 (23)
Difficulty in dose adjustments	47 (63)
More chances of adverse drug reactions	8 (11)

FDCs: Fixed dose combinations

the most commonly prescribed antimicrobial FDC. It was prescribed by 37.8% of the doctors as summarized in Table 2. Other most commonly prescribed FDCs are also mentioned in Table 2. Amoxicillin + clavulanic acid was the most commonly prescribed FDCs by doctors of skin and venereal diseases (71.4%), pediatrics (53.8%), medicine (42.1%), surgery (33.3%), and obstetrics and gynecology (16.7%) except psychiatry where olanzapine + fluoxetine (80%) was prescribed more frequently as shown in Table 3.

According to the participants, the most common conditions for prescribing FDCs were infections in pediatrics (69.2%), surgery (50%), obstetrics and gynecology (50%), skin and venereal diseases (42.9%), and medicine (31.6%) except psychiatry where depression (60%) was the most common condition reported for prescribing FDCs. The detailed results about the conditions for which the FDCs were prescribed frequently in various departments are mentioned in Table 4.

The attitude of the physicians toward FDCs was mixed-neutral response (29%), 54% of the study population felt that FDCs are superior to the individual drugs, and 17% of the participants disagreed that the FDCs are superior (Figure 3). Nearly 53% of the participants supported that FDC could be cost-effective for the patients. About 63% of participants opined that FDCs should be allowed to be marketed.

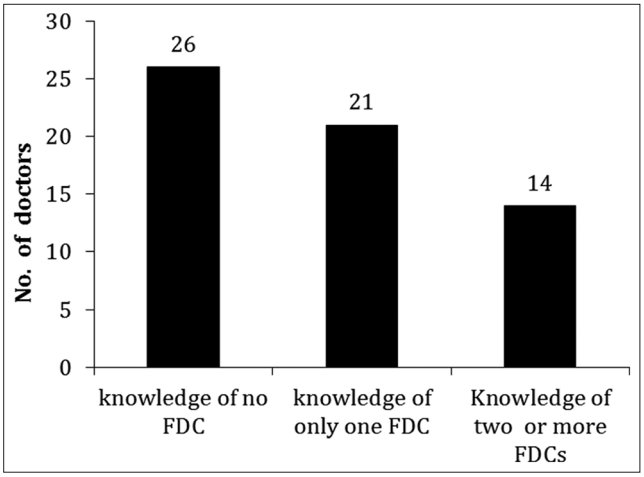

Figure 1: Assessment of knowledge about fixed dose combinations included in the WHO essential medicine list

Table 2: Commonly prescribed FDCs by doctors

FDCs	Number of doctors (*n*=74)
Amoxicillin+clavulanic acid	28
Paracetamol+diclofenac sodium	8
Olanzapine+fluoxetine	4
Amlodipine+atenolol	4
Aspirin+clopidogrel+atorvastatin	1
Paracetamol+chlorpheniramine maleate +Phenylpropanolamine	2
Norfloxacin+tinidazole	5
Trimethoprim+sulfamethoxazole	3
Aspirin+clopidogrel	2
Escitalopram+clonazepam	1
Losartan+hydrochlorothiazide	1
Paracetamol+diclofenac sodium +Serratiopeptidase	2
Paracetamol+ibuprofen	3
Paracetamol+domperidone	2
Ofloxacin+ornidazole	2
Multivitamins	1
Others	5

FDCs: Fixed dose combinations

Table 3: Commonly prescribed FDCs in various departments (*n*=74)

Department	Most commonly prescribed FDCs (%)
Medicine	Amlodipine+atenolol (21.1)
	Amoxicillin+clavulanic acid (42.1)
	Aspirin+clopidogrel (10.5)
	Losartan+hydrochlorothiazide (5.3)
	Pentoprazole+domperidone (10.5)
	Paracetamol+chlorpheniraminemaleate+ phenylpropanolamine (5.3)
	Aspirin+clopidogrel+rosuvastatin (5.3)
Surgery	Amoxicillin+clavulanic acid (33.3)
	Paracetamol+diclofenac sodium (22.2)
	Norfloxacin+tinidazole (16.7)
	Paracetamol+ibufrofen (11.1)
	Ofloxacin+ornidazole (11.1)
	Diclofenac+chlorzoxazole (5.6)
Obstetrics and gynecology	Amoxicillin+clavulanic acid (16.7)
	Paracetamol+diclofenac sodium+ serratiopeptidase (16.7)
	Paracetamol+diclofenac sodium (33.3)
	Paracetamol+ibuprofen (8.3)
	Clindamycin+clotrimazole (16.7)
	Paracetamol+chlorpheniraminemaleate+ phenylpropanolamine (8.3)
Pediatrics	Amoxicillin+clavulanic acid (53.8)
	Norfloxacin+tinidazole (15.4)
	Cefotaxime+sulbactum (7.7)
	Trimethoprim+sulfamethoxazole (7.7)
	Piperacillin+tazobactum (7.7)
	Multivitamins (7.7)
Skin and venereal diseases	Amoxicillin+clavulanic acid (71.4)
	Trimethoprim+sulfamethoxazole (28.6)
Psychiatry	Olanzapine+fluoxetine (80)
	Escitalopram+clonazepam (20)

FDCs: Fixed dose combinations

Textbooks (66%), Journals (58%), medical representatives (MRs) (53%), colleagues/peers (51%), monthly index of medical specialities (MIMS) (43%), and continuous medical education (CMEs) (39%) were the most common sources of information of FDCs, followed by others which included internet (27%), EML (14%), and newspapers (7%) as shown in Figure 4.

DISCUSSION

Drugs are the main sword of modern medicine in the treatment of ailments. As a principle, single medicines are to be preferred. FDCs should only be used if there is clear therapeutic objective justifying its use, when a patient needs all components of a FDC and when combination is proven to be better than single drug for that combination. There are a number of advantages associated with the use of FDCs, but inappropriate and indiscriminate use of FDCs due to poor knowledge may lead to irrational prescription.[11,12] There are a number of studies to find the rationality of FDCs, but studies to determine the awareness of doctors about FDCs are very much limited, and hence in view of that, the present study was planned.

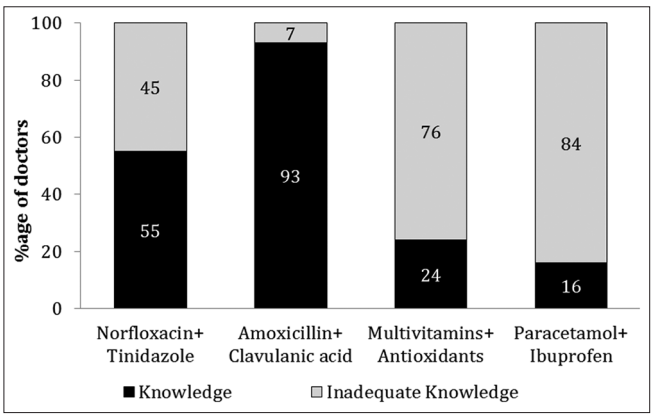

Figure 2: Knowledge regarding rationality of fixed dose combinations

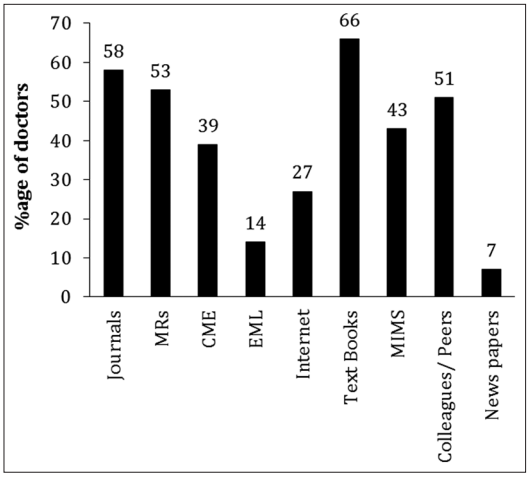

Figure 3: Sources of information about fixed dose combinations

It was observed from the present study that the improved patient compliance and less cost were the most common advantages while difficulty in dosage adjustment was the most common disadvantage of FDCs mentioned by the doctors. These results are similar to the results of a study done by Goswami et al.[8]

Table 4: Common conditions for prescribing FDCs in various departments (*n*=74)

Department	Most common conditions for prescribing FDCs (%)
Medicine	Hypertension (26.3)
	Infections (31.6)
	Myocardial infarction (15.8)
	Diabetes mellitus (10.5)
	Common cold (5.3)
	Parkinsonism (5.3)
	Tuberculosis (5.3)
Surgery	Wound infections (50)
	Pain relief (27.8)
	Abscess (11.1)
	Fever (11.1)
Obstetrics and gynecology	Infections (50)
	Pain relief (33.3)
	Contraceptive pills (8.3)
	Fever (8.3)
Pediatrics	Infections (69.2)
	Common cold (30.8)
Skin and VD	Acne vulgaris (28.6)
	Infections (42.9)
	Pemphigus (14.3)
	Pyoderma (14.3)
Psychiatry	Depression (60)
	Schizophrenia (40)

FDCs: Fixed dose combinations

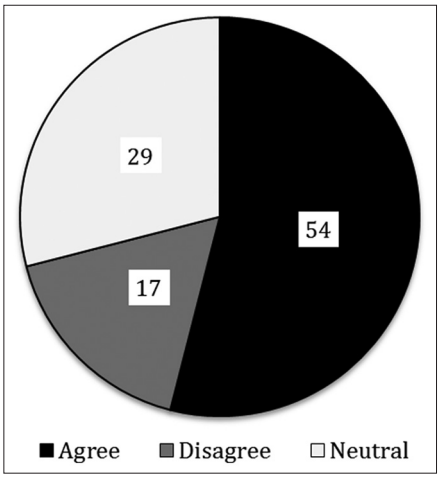

Figure 4: Attitude toward superiority of fixed dose combinations to individual drugs

In the present study, it was observed that majority of the doctors were aware of the WHO EML (82.4%), but only 40.2% had the knowledge of FDCs included in it. The lack of basic awareness about FDC in the essential list of medicines is 60%. Ravichandran et al. also yielded similar results.[13] In India, a variety of combinations of drugs are available that are irrational and not included in the WHO EML.[14] There is a need to sensitize the health-care professionals about the drugs included in EML so that they can prescribe the drugs rationally that require that patients receive medicines appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and the community.[15]

In the present study, about 47% of the doctors were able to mention the rationality of the given FDCs. This is consistent with the results of the study done by Ravichandran et al.[13] The rationality of a FDC is the one of the most burning issues in today's clinical practice. The Indian laws, till recently, were not properly defined to grant marketing approvals for the FDCs by state or central drug controlling authorities. Therefore, the state drug controlling authorities have continuously been approving various FDCs, lacking pharmacodynamics or pharmacokinetic advantages, and acceptable rationale.[16]

Antimicrobials were the most commonly prescribed FDCs (52.7%) in the present study. Pillay et al. and Rayasam et al. also yielded similar results in their study.[17,18] Quinolones + nitroimidazoles (norfloxacin + tinidazole) are commonly used in the treatment of diarrhea and GI infections. Although these combinations have no proven clinical synergism, they are currently prescribed for the diagnostic imprecision. These combinations are not only harmful to the patient but also are also major contributors for the development of resistance, which is a serious concern nowadays.[5]

It was observed that the most common source of information regarding FDCs among doctors was textbooks, followed by journals, both of which are authentic sources. Other less common sources were internet, MRs, MIMS, and colleagues. These results are consistent with the study done by Goswami et al.[8] Doctors should rely on authentic sources of information to prevent the irrational use of the drugs.

From the present study, it can be regarded that the hit and trial method of combining drugs should be replaced by a rational and logical basis for bringing out a fixed dose formulation.

It is high time that some serious action is taken either by strict monitoring of drugs or to prescribe FDCs only in a justifiable case for which a better rationality and knowledge of FDCs are necessary. Thus, there is a need to strengthen the mechanism for continuing professional development of medical practitioners to ensure that they have the necessary knowledge and skills to prescribe FDCs rationally.[19]

However, the present study suffers from few limitations of having less sample size and including only medical practitioners in the study. Moreover, no attempt was made to assess the awareness of postgraduate students about FDCs.

CONCLUSION

It was observed from the present study that the doctors were aware about the advantages and disadvantages of FDCs. However, knowledge regarding rational/irrational FDCs and availability of FDCs included in the WHO EML were lacking. Poor knowledge about FDCs leads to irrational prescriptions. Lack of utilization of authentic sources of drug information could be the most common cause of poor knowledge. Other factors which may be responsible for the present status could be increased patient load, lack of education sessions about FDCs during post-graduation training, and sparse number of CMEs stressing on the rational use of medicines. Sensitization toward authentic sources of information such as EML, education programs about FDCs as well as day-to-day updates regarding banned FDCs is quite necessary to promote the rational use of drugs.[19,20]

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