



Pharmacology

A STUDY AIMED TO INCREASE THE KNOWLEDGE ABOUT THE FIXED DOSE COMBINATIONS (FDC'S) AND IRRATIONAL FDC'S AVIALABLE IN INDIA.

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KEYWORDS :

INTRODUCTION

Fixed dose combinations(FDC's) is a combination of 2 or more than 2 drugs in a single dosage formulations, it should not be confused with concomitant drug therapy which refers to taking 2 or more than 2 drugs separately. Fixed dose combinations may be rational or irrational. In India there are more FDC's than single drugs and majority of those FDC's are irrational. Many of these irrational FDC's are widely prescribed.²The WHO essential medicine list incorporates only 23 FDC's while as the National list of essential medicines(NLEM) of 2011 has only 12 FDC's.³

MATERIALS AND METHOD:

It was a questionnaire based study which was carried out in Government Medical College, Srinagar. A total of 95 students of second MBBS were enrolled in the study. A questionnaire was prepared after doing a literature survey, questions were based on fixed dose combination besides asking the students about various rational as well as irrational combinations. The questionnaire (Pre –lecture) was given to the students during their routine practical class, it was followed by two sessions of lecture's on FDC's focussing primarily on different irrational FDC's as well as rational FDC's. After 2 weeks of this intervention (lecture), the same questionnaire was given to the students and the data from pre and post-lectures was compiled and analysed using simple percentage method. Percentage increase in awareness in the post lecture compared to pre-lecture was calculated for each question.

RESULTS

The questionnaire given to the students is in table 1.

TABLE 1

1 HAVE U HEARD ABOUT THE TERM FDC

YES	NO	DONT KNOW
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2 FDC IS ALSO CALLED AS COMBINATION PRODUCT

YES	NO	DONT KNOW
-----	----	-----------

3 TAKING CONCOMITANT MEDICINE IS SAME AS FDC

YES	NO	DONT KNOW
-----	----	-----------

4 FDC's IMPROVE PATIENT COMPLIANCE

YES	NO	DONT KNOW
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5 FDC'S INCREASE THERAPEUTIC EFFICACY OF INDIVIDUAL DRUGS

YES	NO	DONT KNOW
-----	----	-----------

6 FDC'S DECREASE ADVERSE EFFECTS OF THE DRUG

YES	NO	DONT KNOW
-----	----	-----------

7 FDC'S INCREASE COST OF THE MEDICINE

YES	NO	DONT KNOW
-----	----	-----------

8 MAJORITY OF THE FDC'S ARE RATIONAL

YES	NO	DONT KNOW
-----	----	-----------

9 MAJORITY OF THE FDC'S ARE IRRATIONAL

YES	NO	DONT KNOW
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10 INDIVIDUAL DRUGS IN FDC'S SHOULD HAVE SAME HALF LIFE'S

YES	NO	DONT KNOW
TICK RATIONAL FDC BELOW		

DICLOFENAC- PARACETOMOL	
OFLOXACIN- ORNIDAZOLE	
DEXTROMETHORPHAN-GUAIFENESIN	
MULTIVITAMINS	
AMPICILLIN-CLOXACILLIN	
AMOXICILLIN-CLAVULANIC ACID	
PANTAPRAZOLE- DOMERIDONE	
L-DOPA – CARBIDOPA	
IMIPENEM-CILASTATIN	

Table 2

Question No.	Pre-test			Post-test			P-value
	Yes	No	Don't Know	Yes	No	Don't Know	
1	78 (82.1%)	10 (10.5%)	7 (7.4%)	95 (100%)	0 (0%)	0 (0%)	<0.001*
2	48 (50.5%)	5 (5.3%)	42 (44.2%)	88 (92.6%)	7 (7.4%)	0 (0%)	<0.001*
3	8 (8.4%)	30 (31.6%)	57 (60%)	6 (6.3%)	86 (90.5%)	3 (3.2%)	<0.001*
4	50 (52.6%)	3 (3.2%)	42 (44.2%)	91 (95.8%)	3 (3.2%)	1 (1.1%)	<0.001*
5	19 (20%)	36 (37.9%)	40 (42.1%)	56 (58.9%)	34 (35.8%)	5 (5.3%)	<0.001*
6	26 (27.4%)	25 (26.3%)	44 (46.3%)	73 (76.8%)	17 (17.9%)	5 (5.3%)	<0.001*
7	14 (14.7%)	43 (45.3%)	38 (40%)	90 (94.7%)	2 (2.1%)	3 (3.2%)	<0.001*
8	24 (25.3%)	28 (29.5%)	43 (45.3%)	5 (5.3%)	94 (94.7%)	0 (0%)	<0.001*
9	20 (21.1%)	19 (20%)	56 (58.9%)	90 (94.7%)	5 (5.3%)	0 (0%)	<0.001*
10	33 (34.7%)	18 (18.9%)	44 (46.3%)	93 (97.9%)	2 (2.1%)	0 (0%)	<0.001*

*Statistically Significant, P-value by McNemar Chi-square test

Table 2 compares knowledge of the students about basics of FDC, although some students were able to answer correctly but answers to majority of questions were incorrect, however 2 week's post lectures there was statistically significant improvement in giving correct answers for all the questions mentioned.

Table 3

Drugs	Pretest		Posttest		P-value
	No.	%age	No.	%age	
Ibuprofen-Paracetamol	42	44.2	31	32.6	0.001*
Ofloxacin-Ornidazole	29	30.5	13	13.7	<0.001*
Dextromethorphan-Guaifenesin	16	16.8	13	13.7	0.251
Multi Vitamin	61	64.2	11	11.6	0.002*
Ampicillin-Cloxacillin	15	15.8	8	8.4	0.016*
Amoxicillin-Clavulanic Acid	43	45.3	85	89.5	<0.001*
Pantoprazole-Domperidone	55	57.9	16	16.8	<0.001*
Levo Dopa-Carbidopa	63	66.3	90	94.7	<0.001*
Imipenem-Cilastatin	11	11.6	60	63.2	<0.001*

TABLE 3 tests the knowledge of the students about the common FDC's available in the market, it includes both rational as well as irrational FDC's. The students were asked to tick the rational FDC's. Percentage of students marking a FDC's as rational was compared before and after the lecture session; there was statistically significant improvement in the knowledge of rational FDC's post lecture for majority of questions.

DISCUSSION

FDC are also called as combination product,⁴ it means combinations of two or more than two active drugs in a single dosage form, it is not same as concomitant therapy which means administering drugs separately.¹

Rational FDC's ideally should have drugs having same half life, Amoxicillin and clavulanic acid have a half life of 1-1.5 hours while trimethoprim and sulfamethoxazole have around 10 and 11 hours half life respectively. Besides half life ratio of drugs in a FDC depends on volume of distribution and peak plasma level of the drugs. FDC's have many advantages mainly improved therapeutic efficacy and decreased incidence of side effects. With regard to therapeutic efficacy we discussed few FDCs with the students. Trimethoprim and sulfamethoxazole are individually bacteriostatic drugs but when combined in form of an FDC (Clotrimoxazole) this combination becomes bactericidal besides increasing the spectrum and decreasing the resistance.¹ Similarly combining amoxicillin with clavulanic acid (beta lactamase inhibitor) prevents action of beta lactamase producing bacteria on amoxicillin. Imipenam is inactivated by the enzyme dehydropeptidase in kidney by once combined with cilastatin which inhibits the enzyme dehydropeptidase this inactivation is prevented.⁵

FDCs also decrease the incidence of many individual drugs .e.g Antacids like Aluminium hydroxide causes constipation while as magnesium hydroxide causes diarrhoea but once both these drugs are combined in form of an FDC these side effects are nullified.⁴

Similarly L -Dopa if used as a monotherapy for the treatment of parkinsons disease is converted into dopamine peripherally by enzyme decarboxylase which causes nausea and vomiting, so when it is given in combination of carbidopa which inhibits the enzyme decarboxylase these side effects are nullified.¹

However there are some disadvantages associated with use of FDCs like inability to change the dose of individual drugs, increased cost of FDCs, and inability to find out which drug is causing adverse drug reaction in a FDC.²

There are only 25 rational FDCs while majority of the FDCs are irrational in Indian market.³

Some of the irrational combinations which were explained the students in details were

- 1 anti bacterial drugs with anti amoebic drugs like FDCs of ciprofloxacin/norfloxacin/ofloxacin with tinidazole/ornidazole.⁷
- 2 ampicillin with cloxacillin.⁵
- 3 Proton pump inhibitors with domperidone.⁶
- 4 Antacids with Anti-anxiety.⁸
- 5 Mucolytics with antibacterial. Ambroxol with ciprofloxacin.⁹
- 6 Anti-tussives with expectorant. dextromethorphan with Guaphenesin, Bromhexine.⁸
- 7 FDCs of analgesic acting by same mechanism of actions..Ibuprofen with paracetamol.¹⁰
- 8 FDCs with one drug having no proven efficacy..Diclofenac with seratio-peptidase.¹¹
- 9 Multi-vitamins.⁸
- 10 sulphonyl-ureas with Metformin.⁸

CONCLUSION

Increasing awareness about FDC's in general and irrational FDC's in particular among the medical students who are the future doctors is necessary as it will promote use of rational FDC's only which will decrease the incidence of adverse drug reactions as well as put less financial burden on the patient due to widespread use of irrational FDC's .Medical Colleges and associated hospital should include CME's on this topic to constantly update the health professionals about the irrational FDC's prevalent in the market besides pharmacovigilance centres can also provide data regarding incidence of high ADR's due to these combinations. The government on her part should strictly regulate the laws regarding the approval of new drugs besides taking steps to identify and ban any irrational FDC's already in the market.

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