



## Assessment of Use of Fixed Dose Combinations in Indoor Patients of Medicine Department of A Tertiary Care Hospital in India

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### ABSTRACT

**Background:** Use of FDCs is associated with increased efficacy, reduced pill burden and cost of therapy and hence better patient compliance but they have certain disadvantages too. Some FDCs are used despite having no advantage. This study aimed to assess use of FDC in indoor patients of Medicine department of a government hospital.

**Methods:** Total 615 patients bed head tickets were analyzed and total number of FDC out of all prescription drugs were analyzed, expressed in the percentage. Number of FDC present in WHO and National essential medicine list of India were calculated.

**Results:** Overall 4547 drugs were prescribed among all patients, out of which 484 were FDCs (10.64% of all drugs). number of FDCs prescribed per patient was 0.79. Out of 484 FDC, 71 combination drugs are included in National list of essential medicine 2015 and 52 are from WHO essential medicine list. 17 FDC (3.51%) were from the list which are irrational or banned combination as per recent notification by DCGI in 2016.

**Conclusion:** Continuous medical education is necessary to make Physicians aware of this and they should be encouraged to write more combination drugs from the essential medicine list and avoiding writing irrational combinations.

**KEYWORDS :** Fixed dose combinations, Essential medicine List, In-patient, Banned combinations

### Introduction

A 'Fixed Dose Combination (FDC) is a combination of two or more active ingredients in a fixed ratio of doses. This term is used generically to mean a particular combination of active ingredients irrespective of the formulation or brand.<sup>1</sup> Use of FDCs is associated with many advantages like synergistic action and increased efficacy (e.g. cotrimoxazole), reduced adverse effects (e.g. thiazides with potassium sparing diuretics), reduced pill burden and cost of therapy and hence better patient compliance (e.g. anti-tubercular drug combinations). However, certain disadvantages like incompatible pharmacokinetics, inflexible dose ratio, increased toxicity and cost, decreased their utility. Adverse effect of any one component also limits their use. FDCs are used worldwide. Ten percent of new products in Japan are FDCs, about 56% of all drugs prescribed in European countries like Spain are FDCs.<sup>2</sup>

The WHO Model list of Essential Medicines for adults contains 25 FDCs (april 2015),<sup>3</sup> while 23 FDCs are included in the National list of Essential Medicines (august 2015).<sup>4</sup> Among the commercially available FDCs, a large number of FDCs are irrational.

Data regarding the pattern of use of FDCs in developing countries like India are lacking. In a study from Ahmedabad, a total of 1170 prescriptions were collected from 24 pharmacy stores.<sup>5</sup> Out of these, FDCs were prescribed in 941 (80.3%) prescriptions. Out of the 1647 FDCs prescribed, only 95 (5.8%) and 161 (9.8%) FDCs were included in Essential Medicines Lists of the WHO (2011), National (2011) respectively.

In another study from a tertiary hospital in Goa, Nine hundred and ninety four prescriptions, containing 639 FDCs were scrutinized.<sup>6</sup> Out of 278 FDCs, only 5.4% were rational. 95% of all FDCs were brand names. In a study from Madhya Pradesh, 22% of prescriptions contained at least one irrational FDC (IFDC).<sup>7</sup> Out of this 3% of prescriptions contained  $\geq 2$  IFDCs. Most commonly prescribed irrational FDCs were multivitamin combinations, followed by antipyretic-anti-inflammatory combination.

The availability of a number of FDCs commercially coupled with a lack of awareness of their rational use, promote the overuse of FDCs in medical stores in India. Awareness and education about irrational FDCs, FDCs containing banned or controversial ingredients will help develop a rational prescribing practice among prescribers.

Though in some situations and diseases, Fixed dose combinations have some advantages but certain disadvantages like incompatible pharmacokinetics, inflexible dose ratio, increased toxicity and cost, contraindication of one component of the FDC decreased their utility in using them in most of the time. But there are lots of irrational fixed dose combinations are still marketed in Indian market. Some drug combinations are even banned.

Indian studies on use of irrational fixed dose combinations are mostly done from pharmacies. But our study looked into this matter among indoor and outdoor prescriptions of the patients admitted in a tertiary care hospital of eastern India. It will help to assess the magnitude of problem of irrational drug combination use among government hospital doctors.

Recently, Government of India has issued a notification regarding ban of 330 irrational FDC from the market,<sup>8</sup> due to pharmacokinetic mismatch or due to chance of adverse effect due to drug interaction. But prescriptions of such drugs have not been completely stopped. Some are available as over the counter. So studies need to be done to assess use of such drugs.

Also our study will compare whether any difference exists in prescription of indoor patients, regarding to use of irrational fixed dose combinations.

### Materials and methods

#### Objectives

1. To know the percentage of total number of prescribed drugs in indoor patients of general medicine department of a tertiary care teaching hospital of Eastern India, prescribed as Fixed dose combinations.

- To know the percentage of FDC, included in WHO essential medicine list and National list of essential medicine, India.
- To know the most commonly prescribed Irrational fixed dose Combinations.

**Study Design:** It was a cross sectional unicentric study, a type of prescription audit study.

Study site: College of medicine & JNM hospital, Kalyani, Nadia, West Bengal.

After obtaining clearance from the Institutional ethics committee and getting necessary permission from Head of the Department of General Medicine of the Institute, study begun. Total 615 prescriptions were taken for assessment of FDC use, the patients who were discharged from general medicine department of that hospital during the month of May 2016 .

For indoor prescriptions, copy of the bed head tickets were done on the day of patient discharge so that it will be better to assess whether any fixed dose combinations were prescribed during his/her entire hospital stay.

Then total number of FDC out of all prescription drugs were analyzed, expressed in the percentage. Number of FDC present in WHO and National essential medicine list of India were calculated, percentage of such drugs out of all FDCs calculated..

Number and percentage of irrational FDC were calculated, those which are banned as per recent order from the Drug control general of India.

**Results**

Total 615 indoor prescriptions were analyzed, out of them 283 were female and 332 were male patients. Average age of the patients was 46.55 years. Among the common diseases with which patient was admitted, cerebrovascular accident (CVA) tops the list with 90 admissions. Other common causes include Acute gastroenteritis (38 patients), COPD (26 patients), hypertension (24 patients), undiagnosed fever (18 patients).

Out of 615 patients, 317 patients (51.55%) had received 1 or more combination drugs and 298 patients (48.45%) were treated without any FDC.

Overall 4547 drugs were prescribed among all patients, out of which 484 were FDCs (10.64% of all drugs). So number of FDC s prescribed per patient was 484/615= 0.79. Number of drugs prescribed per patient was 4547/615= 7.39.

Out of 484 FDC, 71 combination drugs (14.67% of all FDC s prescribed) are included in National list of essential medicine 2015. Only 52 FDC (10.74% of all FDCs prescribed) are from WHO essential medicine list. 17 FDC (3.51%) were from the list which are banned combination as per recent notification by DCGI in 2016.

Among the FDC prescribed in this study, which are present in NLEM are amoxicillin-clavulanate (in 33 prescriptions), piperacillin-tazobactam (in 19), ferrous sulphate- folic acid (16), imipenem-cilastatin(2) and levodopa-carbidopa(1).

Among them piperacillin-tazobactam are not included in WHO essential medicine list.

Order of frequency	Combination	Number of prescriptions	Route of use
1	Salbutamol-ipratropium	72	Inhalation/nebulizer
2	Aspirin-atorvastatin	37	Oral/ Ryle’s tube
3	Sucralfate-oxetacaine	36	Oral

4	Amoxicillin-clavulanate	33	Intravenous
4	Meropenem- sulbactam	33	Intravenous
5	Omeprazole-domperidone	29	oral
5	Ampicillin- sulbactam	29	Intravenous
6	Citicoline- piracetam	23	Oral/Ryle’s tube
7	Piperacillin-tazobactam	19	Intravenous
7	Amoxicillin-sulbactam	19	Intravenous
8	Telmisartan-amiodipine	17	Oral
9	Ferrous sulphate- folic acid	16	Oral
10	Cefoperazone- sulbactam	15	Intravenous

**Table1: List of most frequently used fixed dose combinations**

Other combination used are ticarcillin-tazobactam injection (8 patients), ticarcillin-clavulanate (6), cefepime- tazobactam(7), escitalopram-clonazepam tablet (6), cefixime-azithromycin tablet (6), frusemide- spironolactone (5).

Among the irrational combinations, we have found use of aceclofenac- paracetamol in 4 patients, ibuprofen- paracetamol in 2, azithromycin-cefixime in 6, clidinium-drotaverine-chlordiazepoxide in 2, salbutamol-bromhexine in 1, rosuvastatin-vitamin D in 2. Out of 484 FDCs prescribed, these 17 FDCs are currently not approved by DCGI.

**Discussion**

Though fixed dose combinations have certain advantages, combining any two drugs should not be encouraged due to pharmacokinetic and pharmacodynamic difference of two drugs.

This study showed that just more than 10% of all drugs prescribed were FDC. Number of FDC per prescription was less than 0.8, which was far better than previous studies done in Ahmedabad and Madhya Pradesh.

But like other previous studies, here also most of the combination drugs were not from the National list of essential medicine 2015 and WHO essential medicine list 2015. Physicians should be made aware of the list of such combination essential medicines as they are generally cheaper and more widely available, i.e., replacing cefoperazone-tazobactam with cefoperazone sulbactam, which is present in national list of essential medicine but the former is not.

From the list of top 10 most commonly used combination drugs, there were 6 antimicrobial combinations, all of them were combination of beta lactam-beta lactamase inhibitors. Though 3 of them (amoxicillin-clavulanate, piperacillin-tazobactam, cefoperazone-sulbactam) are present in National list of essential medicine 2015, we found that other combinations are also used. Recently DCGI (Drug control General of India) notification banned many combination drugs and 3.57% of the combination drugs prescribed in this study were from that list. Most common irrational prescription was cefixime-azithromycin combination. Physicians should be made aware of these combination drugs, which should not be prescribed now. This is possible by continuous medical education about rational use of drugs.

**Conclusions:**

In this study, though there were few prescriptions of irrational combinations, the number is quite less than other similar studies. Num-

ber of fixed dose combinations per prescription was less than 1. Only around 10% of the combination drugs were from National list of essential medicine 2015 and WHO essential medicine list 2015. Physicians should be made aware of this and should be encouraged to write more combination drugs from the essential medicine list and stop writing the irrational combinations.

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