

**A Study On Analysis Of
Fixed Drug Combinations
Widely
Prescribed in India**

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INTRODUCTION

- Fixed Drug Combination is the combination of two different drugs in a single pharmaceutical formulation.
- They are used in the wide range of treatments particularly in chronic diseases
- They are developed to improve patients compliance and to have synergistic effect among the ingredients.

- Rational FDC'S of two drugs can be advantageous, but few combination may not be beneficial and some may be harmful to the patients.
- There is a wide range of approved FDC's have been listed in the NLEM (National list of Essential medicines) & WHO list.

Essential medicines

- The concept of essential medicines was first introduced by WHO in 1977 .
- Now been adopted by many countries, non-governmental organizations and international non-profit agencies.
- Essential medicines are those that satisfy the priority healthcare needs of majority of the population.

- It needs to be country specific in accordance to the disease burden of the nation and standard treatment guidelines
- Must be commonly prescribed by healthcare professionals and should be made available with good quality and reasonable price.
- One of the key instruments in providing balanced healthcare for a country is NLEM.

Provides the guidelines :

- Drug policies in the hospital
- Procuring and supplying of medicines in a public sector reimbursement of medicine costs
- Donating the medicines & monitoring the pricing of medicines.

- The list serves as a reference for prescribing the correct dosage form and strength
- To assess healthcare access to the population
- A source for public education and training of healthcare providers.

OBJECTIVE

To analyse the Fixed Drug Combinations commonly prescribed in India which do not comply with the FDC'S in NLEM and WHO list.

METHODOLOGY

- We collected the data of the widely prescribed FDC using CIMS, CIMS Asia.com, Medscape, Local hospital drug Formulary.
- We analysed the data comparing with the FDC in the WHO list and NLEM (National List of Essential Medicines) 2011.

FDC in the NLEM(National List of Essential Medicines) 2011

Acriflavin + Glycerin ,Aluminium Hydroxide + Magnesium Hydroxide ,Amoxicillin + Clavulanic acid ,Artesunate + Sulfadoxine + Pyrimethamine ,Artesunate + Amodiaquine, Trimethoprin + Sulphamethaxazole , Ethinylestradiol + Levonorgestrol , Ethinylestradiol + Norethisterone ,

Lamivudine + Nevirapine + Stavudine ,
Lamivudine + Zidovudine , Lamivudine +
Stavudine , Levodopa + Carbidopa , Levodopa
+ Epinephrine , Lopinavir + Ritonavir ,
Neomycin + Bacitracin , Pyrimethamine +
Sulfadoxine.

FDC in the WHO list 2011¹

Amoxicillin + Clavulinic acid ,Artemether + Lumifantrine , Artesunate + Amodiaquine , Trimethoprin + Sulphamethaxazole ,Efavirenz + Emtricitabine + Tenofovir ,Emtricitabine + Tenofovir ,Estradiol cypionate +Medroxyprogesterone acetate , Ethinylestradiol + Levonorgesterol , Ethinylestradiol + Norethisterone , Ferrous salt + Folic acid , Imipenam + Cilastatin ,

Isoniazid + Ethambutol , Isoniazid + Ethambutol + Rifampicin , Isoniazid + Rifampicin , Isoniazid + Rifampicin + Pyrazinamide , Isoniazid + Rifampicin + Pyrazinamide + Ethambutol , Lamivudine + Nevirapine + Stavudine , Lamivudine + Zidovudine , Lamivudine + Nevirapine + Zidovudine , Levodopa + Carbidopa , Levodopa + Epinephrine , Lopinavir + Ritonavir, Pyrimethamine + Sulfadoxine.

- The following drug combinations are not available in NLEM and WHO list of essential medicines.

Available Irrational fixed drug combinations

Norfloxacin + Metronidazole , Norfloxacin + Tinidazole , Ciprofloxacin + Tinidazole , Ofloxacin + Tinidazole , Ofloxacin + Metronidazole , Ofloxacin + Ornidazole , Ofloxacin + Ornidazole + Lactobacillus , Loperamide + Simethicone , Azithromycin + Ambroxol , Roxithromycin + Serratiopeptidase , Roxithromycin + Ambroxol, Amoxycillin + Cloxacillin , Cefadroxil + Clavulanic acid ,

Cefalexin + Probenacid , Fluconazole +
Tinidazole, Metronidazole + Diloxanide Furoate,
Metronidazole + Nalidixic acid , Doxycycline +
Tinidazole , Cefixime + Azithromycin , Cefixime +
Ofloxacin , Cefixime + Clavulanate , Nimesulide +
Racemethionine , Nimesulide + Paracetamol ,
Nimesulide + Chlorzoxazone , Nimesulide +
Paracetamol + Tizanidine , Mefenamic acid +
Drotaverine , Paracetamol + Drotaverine ,
Nimesulide + Tizanidine , Ibuprofen + Tramadol
Hcl , Nimesulide + Serratiopeptidase , Nimesulide
+ Serratiopeptidase + Paracetamol ,

Diclofenac + Tizanidine , Diclofenac +
Paracetamol , Diclofenac + Paracetamol +
Serratiopeptidase , Diclofenac + Paracetamol +
Tizanidine , Aceclofenac + Paracetamol +
Serratiopeptidase , Aceclofenac + Paracetamol,
Aceclofenac + Tizanidine ,Mefanamic acid +
Tizanidine , Pregabalin + Mecobalamin , Folic
acid + Cyanocobalamin , Glibenclamide +
Metformin , Glimipride + Metformin , Diazepam +
Propanolol , Diazepam + Imipramine ,
Escitalopram + Clonazepam ,Simvastatin +
Ezetimibe , Atorvastatin + Nicotinic acid ,
Atorvastatin + Ezetimibe ,

Rosuvastatin + Fenofibrate , Enalapril + Losartan,
Metoprolol + Amlodipine , Captopril +
Hydrochlorthiazide , Atenolol + Nifedipine ,
Domperidone + Rabeprazole , Lansoprazole +
Domperidone , Rabeprazole + Levosulpride ,
Rabeprazole + Itopride , Ranitidine +
Dicyclomine, Ranitidine + Domperidone ,
Omeprazole + Cinitapride , Ranitidine +
Domperidone + Simethicone, Ondansetron +
Rabeprazole , Domperidone + Esomeprazole ,
Itopride + Pantoprazole , Fexofenadine +
Montelukast , Ketotifen + Salbutamol ,
Levocetirizine + Montelukast , Levocetirizine +
Ambroxol, Cetrizine Hcl + Ketotifen.

RESULTS

- From the analysis of the data we found that around 70 FDC do not comply with the criteria developed by essential medical list of WHO or NLEM of India or both. Out of the 70, 23 were with antibiotics, 20 with analgesics and remaining with sedatives, antihistamines and vitamin preparation.

DISCUSSION

The rationality of FDCs is based on :

- ❖ Action of drugs by different mechanism
- ❖ The difference in pharmacokinetics must not be wide
- ❖ There should not be additive toxicity of the ingredients

Advantages

- Convenient in Dose Scheduling
- Patient's Compliance
- Enhanced Effect
- Minimisation of Side effects

- Handling & supplying the drugs at minimum shipping costs
- Prevents the shortage of supply of individual medicine
- Reduces medication wastage
- Reverses the under-treated conditions

DISADVANTAGES

- The pharmacokinetics characteristics of two drugs may not match.
- Dosage alteration of a drug is possible only with Dosage alteration of the other drug.
- The identification of adverse effect of particular component is difficult.

- The frequency of drug administration may be affected (Difference in pharmacokinetics of the drugs).

- Chances of adverse drug effects are more in combinations of the drugs than the adverse drug effects caused by individual drugs.

- Irrational FDC's containing antibiotics - resistant strains of organisms & toxic reactions.
- Most important aspect of FDC is the evidence of efficacy and safety when two or more drugs are given as a single formulation.

CONCLUSION

- Careful monitoring and censoring the pharmaceutical industry can reduce the irrational drug combinations .
- Clinical pharmacists should play a major role in imparting awareness and knowledge to the public regarding the FDC's.
- ADR reporting and pharmacovigilance should be made mandatory and more effective in the health care centres.
- The post graduate students and the Doctors in medical colleges should be trained and encouraged to assess the new drug combinations.

- Hence we claim the FDC are valuable therapy and also widely prescribed and they need to be developed based on the rationality of pharmacokinetic and pharmacodynamic parameters and clinical studies are needed to evaluate the safety.

Key word:

FDC – Fixed Drug Combination and efficacy.

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