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A STUDY ON ANALYSIS OF FIXED DRUG COMBINATIONS WIDELY PRESCRIBED IN INDIA

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ABSTRACT

Objective: Fixed Drug Combination is the combination of two different drugs in a single pharmaceutical formulations. Rational FDC'S of two drugs can be advantageous, as it is convenient in Dose Scheduling, Patient Compliance, Enhanced Effect, Minimisation of Side effects. The disadvantages are the pharmacokinetics characteristics of two drugs may not match and dose of any component may not be independently adjusted. The identification of adverse effect of particular component is difficult. FDC are widely prescribed in India for various therapeutic targets. We undertook this study to analyse the FDC commonly prescribed in India and to find out any FDC that donot comply with the [1]WHO list and [2]NLEM (National List of Essential Medicines) 2011. **Methodology:** We collected the data of the widely prescribed FDC using CIMS,CIMS Asia.com, Indian drug review, Local hospital drug Formulary. We analysed the data comparing with the FDC in the WHO list and NLEM. **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. **Conclusion:** 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 and efficacy.

KEYWORD: FDC – Fixed Drug Combination.

INTRODUCTION

Pharmacotherapy is a dynamic and ever evolving science. It requires a detailed understanding about the drug, disease and patient. A knowledge of drug action, kinetics, dosage and variability in drug response has to be considered. One among the choice of therapy is the fixed drug combination which is the combination of two or more drugs in a single pharmaceutical formulation. They are used in the wide range of treatments particularly in chronic diseases and they are developed to improve patients compliance and to have synergistic effect among the ingredients. Their use in therapeutics should have a clinically relevant justification. Rational FDC'S of two drugs can be advantageous, but few combination may not be beneficial and some may be harmful. There are many approved FDC's available in the market and are found to be useful to the patients. The rationality of FDC's is based on action of drugs by different mechanisms, difference in pharmacokinetics must not be wide, there should not be additive toxicity of the ingredients. The advantages is convenience in dose scheduling, patient's compliance, enhanced effect and minimisation of side effects. The disadvantages are the frequency of drug administration may be affected because of the difference in pharmacokinetics of the drugs, dose of any component may not be independently adjusted, identification of adverse effect of a particular component is difficult and chances of adverse drug effects are more in the combinations of drugs than the adverse drug effects caused by individual drugs. A wide range of approved FDC's have been listed in the NLEM and WHO list.

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. Essential medicines need to be country specific in accordance to the disease burden of the nation and standard treatment guidelines, they 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. It provides the guidelines for the drug policies in the hospital, procuring and supplying of medicines in a public sector, reimbursement of medicine cost, for donating the medicines, in 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. In this study we have analysed the FDC's which donot comply with the FDC'S in NLEM and WHO list.

Aim and Objective

To Analyse the Fixed Drug Combinations Widely Prescribed in India.

Methodology

We collected the data of the widely prescribed FDC using CIMS,CIMS Asia.com, Indian drug review, 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 NLEM (National List of Essential Medicines) 2011[2]

Acriflavin + Glycerin, Aluminium Hydroxide + Magnesium Hydroxide, Amoxicillin + Clavulinic acid, Artesunate + Sulfadoxine + Pyrimethamine, Artesunate + Amodiaquine, Trimethoprin + Sulphamethaxozole, Ethinylestradiol + Levonorgesterol, Ethinylestradiol + Norethisterone, Lamivudine + Nevirapine + Stavudine, Lamivudine + Zidovudine, Lamivudine + Stavudine, Levodopa + Carbidopa, Levodopa + Epinephrine, Lopinavir + Ritonavir, Neomycin + Bacitracin, Pyrimethamine + Sulfadoxine.

FDC in the WHO list 2011[1]

Amoxicillin + Clavulinic acid, Artemether + Lumifantrine, Artesunate + Amodiaquine, Trimethoprin + Sulphamethaxozole, Efavirenz + Emtricitabine + Tenofavir, Emtricitabine + Tenofavir, Estradiol cypionate +Medroxyprogesterone acetate, Ethinylestradiol + Levonorgesterol, Ethinylestradiol + Norethisterone, Ferrous salt + Foloic 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 combinatios are not available in NLEM and WHO list of essential medicines.

Available Irrational fixed drug combinations[3,4]

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 + Cyanocaobalamin, Glibenclamide + Metformin, Glimipride + Metformin, Diazepam + Propanolol, Diazepam + Imipramine, Escitalopram + Clonazepam, Simvastatin + Ezetimibe, Atorvastatin + Nicotinic acid, Atorvastatin + Ezetimibe, Rosuvastatin + Fenofibrate , Enalapril + Losartan, Metaprolol + Amlodipine, Captopril + Hydrochlorthiazide, Atenolol + Nifidipine, 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, Levocetrizine + Montelukast, Levocetrizine + Ambroxol, Cetrizine Hcl + Ketotifen.

RESULTS AND DISCUSSION

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.

Irrational FDC's containing antibiotics may lead to resistant strains of organisms which is a matter of important concern in the health care. Many of these combinations have not shown any enhanced therapeutic advantage in patients, and very often the patient is unnecessarily jeopardized with toxic reactions and also acquiring sensitization to both agents.[10] The consumers may also be imposed with financial burden due to the cost of therapy of these irrational FDC's.[8] Combinations of NSAIDs and analgesics are frequently prescribed and also are available as over the counter agents. Many of these FDC's have no rationality as both

the active ingredients have a common mechanism of action and therefore cannot potentiate the efficacy of the drug. Moreover, the combination only results in additive toxic effects like increased GI toxicity, peptic ulcer and nephrotoxicity.

In spite of the rising concern over the usage of FDC's, it gains advantage as handling and supplying the drugs at less expensive shipping costs prevent the shortage of supply of individual medicine particularly in case of communicable diseases.[12] It also reduces medication wastage. It has also been noted that FDC'S plays a better role to reverse the under-treated condition in cardiovascular patients. Thus, the 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.[9] 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. To rationalize prescribing, drug and therapeutics review committees should be constituted by the hospital. 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 and efficacy.

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