

Original research article

Evaluation of prescription for rational use of fixed dose drug combinations

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Abstract

This study was conducted to study about the rationality of the different fixed dose drug combinations (FDC) prescribed by Doctors. A retrospective study was conducted after collecting prescription from patients attending private clinics and Government hospitals. The rationality of FDC formulations was studied on the basis of FDCs recommended by WHO in its list of essential drugs. Audit of the prescriptions reveals that 75% of the prescriptions contained FDC formulations. However, FDCs in accordance with recommended WHO list of FDCs were only 11%. The most common prescribed were antimicrobials and analgesics which constitute nearly 30.5% of the total FDCs prescribed. In 52% of the prescriptions, the prescribed FDCs contained ingredients which were not essential for the desired therapeutic effect. 80% of the FDCs prescribed did not conform to the recommended WHO list.

However, the use of certain FDCs was highly justified and rational.

Keyword: Prescription audit, fixed dose drug combination.

Introduction

The prescription order is an important transaction between the physician and the patient. The prescribing behavior of physician depends upon the input from various sources like patients, professional colleagues, academic literatures, commercial publicity and Government regulations. Various prescribing errors are result of ineffective use of these inputs and are very common in clinical practices. Some lacunae in medical education, lack of continuing medical education leading to ignorance, inappropriate role of seniors are also some of the factors. However the continuous monitoring of prescriptions and drug utilization studies may help to identify the problems involved in therapeutic decision and promote the rational prescribing.

Most patients are on more than 1 drug. The concomitant use of two or more drugs adds to the complexity of individualization of drug therapy. The dose of each drug should be adjusted to achieve the optimal benefit otherwise patient compliance is difficult to achieve. To obviate the latter problem, many fixed dose combinations (FDCs) are marketed. An FDC refers to the combination of two or more drugs in single formulations. Surprisingly even in the presence of regulatory guidelines and WHO model list of essential drugs which includes only 12 drug combinations (Table 1) FDCs are being used widely. Therefore, a study has been carried out for the rational use of FDCs by analysing the prescriptions issued by Government hospitals private nursing homes and general practitioners of Gaya district.

Materials and Methods

The patients attending private clinics and Government hospitals were randomly approached either outside the clinic or at chemist shop with a request to have their prescriptions

photocopied. In the present process the patients were also interviewed to have information not found in the prescriptions. The study was conducted from December 19 to January 2020. The FDC containing prescriptions were separated from the total prescriptions collected and evaluated for their rationality according to the list of FDC recommended by WHO.

Table 1:

Categories of FDC Prescribed	Percentage
Antibiotics	16.15
Analgesics	14.35
Multivitamins	14.61
Antihypertensive	9.23
Cough & Cold remedies	7.69
Antidiarrhoeal	7.96
Antihistaminic	4.60
Others	14.30

Results

Out of the total 280 prescriptions collected, 210 contained FDC formulations. They were further sorted out prescriptions containing one, two three and four FDCs. These were 84 (30%), 89 (31.78%), 3 (1%), respectively. Out of these 210 prescriptions only 42 (20%) contained FDCs as recommended by the WHO in its list of essential drugs.

In 54% of the prescriptions, the prescribed FDCs contained ingredients which were not essential for the desired therapeutic effect. In 11.43% of the FDC containing prescription, one ingredient was present at least two times both as a part of FDC formulation and as a single drug.

The total number of FDC 44 (11.28%) formulations prescribed were 390. Out of these FDCs were in accordance with recommended WHO list of FDCs. The most commonly prescribed were antimicrobials (16.15%), analgesics (14.35%), multivitamins 14.16% and antihypertensive (9.23%), cough and cold remedies 7.69%, antidiarrhoeal 7.94%, antiasthmatic 4.6% and others 14.3% (Table 1)

Discussion

It is evident from the present study that there was only 11.28% of FDCs that are in accordance with the WHO recommended list of FDCs. Potential advantages of FDCs include reduced side effects (levodopa with carbidopa), increased patient compliance (anti tubercular drug combination), synergy and increased efficacy (combination of oestrogen and progesteron), synergy and increased efficacy (combination of oestrogen and progesteron in oral contraceptives, combination of sulfamethoxazole and trimethoprim, pryme thamine and sulfadoxine for the treatment and prophylaxis of falciparam malaria) and reduced cost. Potential disadvantages include inflexible fixed dose ratio, incompatible pharmacokinetics increased toxicity and physician and pharmacists ignorance of contents.

Table 2:

Combination drugs recommended by World Health Organisation.

1. Benzoic acid + salicylic acid
2. Bacitracin + neomycin
3. Levodopa + carbidopa
4. Ethinylestradiol + levonorgestrel
5. Ethinylestradio + norethisterone

6. Folic acid + ferrous salt
7. Isoniazid + ferrous salt
8. Isoniazid + ethambutol
9. Isoniazid+pyrazinamide+rifampicin
10. Isoniazid + Thiacetazone
11. Pyrimethamine + sulfadoxine
12. Sulfamethoxazole + trimethoprim

The most widely prescribe FDCs which are not having any rational basis are the analgesics 14.35% multivitamin combinations 14.61% and cold and cough mixtures 7.69%. The combination analgesic are extremely popular. There is little evidence that any analgesic combination is better than its individual components alone. However many patients are benefitted with combination probably because individual component may not have complete anti inflammatory, analgesic and antipyretic activity. WHO has deleted the combination of vitamins from its list with the comment that vitamins are considered part of nutrition and vitamin combination should not be used indiscriminately. The cough mixtures contain expectorants, cough suppressans, antihistamines, sympathomimetics, alcohol and other CNS depressants without any rational basis.

In the United State, a fixed does combination of drugs is considered a new drug and as such must be approved by the Food and Drug Administration (FDA) before it can be marketed, even through the individual drugs are available for concurrent use. To be approved certain conditions must be met. The two drugs must act to achieve a better therapeutic response than either drug along or one drug must act to reduce the incidence of adverse effects caused by the other.

Therefore the drug combinations which are not included in the WHO list of FDCs but meet the above crieteria can also be designated as justified and rational for example combination of more than one antihypertensive agents for the successful control of moderate to sever hypertension, the combination of potassium sparing and potassium losing diuretics, combinations of β lactam antibiotics with β lactamase inhibitors, antacid containing a mixture of aluminium and magnesium salts, dermatological preparations which normally contain 2 drugs in the vehicle combinations of theophylline and adrenergic agonist for synergistic effect in asthma. Nearly 80% of the FDCs prescribed effect in asthma. Nearly 80% of the FDCs precribed did not conform to the recommended who list of FDCs. However, certain FDC formulations were justified and rational. So a critical reappraisal is required by the practitioners and consensus at their local national scientific forums followed by an appeal to the regulatory authorities to weed out irrational FDCs from the market.

References:

1. Benet LZ. Principles of Prescribed order writing and patients compliance instructions. In Hardman JG, Limbird LE, Molinoff PB, Ruddon RW, Gilman AG, editors Goodman and Gilman's The Pharmacological Basis of Therapeutics 9th ed. New York, Mc Graw Hill 1996, 1617-706.
2. Ansair KU, Singh S. Pandey RC Evaluation of prescribing patterns of doctors for rational drug therapy, Indian J. Pharmacol 1998, 30-43-6.
3. Singh S, Ansari KU, Kastury N, Pandey RC An audit of Prescription for rational use of antibiotics Indian J Clin Pharmacol Therap 1997, 18, 77-81.
4. Bapna JS, Shewade DG, Pradhan SC. Training medical professionals on the concepts of essential drugs and rational drug use. Br J Clin Phrmacol 1994:37-399-400.
5. WHO technical report series No. 867-1997.

6. Gupta N, Ansari KU, Fixed dose drug combinations their uses, regulations and future prospects antiseptic 1991, 88-384-7.
7. Arnold K. Trends in the development of chemotherapy for parasitic drugs. South East Asian JI of Tropical Medicine & Public Health 1978;9; 177-82.
8. Beares WT. Analgesic combinations In Lasagna, editor Combination drugs. Their uses and regulation New York Stration International Medical Book Corporation 197552-72.
9. Nies AS Principles of therapeutics In Gilman AG, Roll TW Nies As, Taylor Peditors Goodman and Gilmans The pharmacological Basis of Therapeutics 8th ed. New York Poergamon Press, 1991-72.
10. Fagan TC. Remmbering the lesions of basisc pharmacology, Arch Intern Med 1994154,1430-1.
11. Sensakovic JW, Smith LG Beta Lactamase inhibitor combinations Med Clin North America 1995, 79, 695, 703.
12. Anderson KE, Pereson CGA editors symposium Antihistamine xanthenes and adenosine, Amsterdam, Excerpta Medica 1985.
13. Rishi RK, Sangeetas Surendra K. Tailang M. Prescription Audit Experience in Garhwal (Utranchal India Triop Dist. 2003, 33 ; 76-19)

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