Prescribing trend of fixed-dose drug combinations in a tertiary hospital in Nepal

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Abstract

The objective of this study was to analyze the prescribing trend of the different fixed-dose drug combinations (FDCs) in a tertiary hospital in Nepal. A retrospective study was conducted after collecting prescriptions from patients attending Manipal Teaching Hospital, Pokhara. The rationality of FDC formulations were studied on the basis of FDCs recommended by Department of Drug Administration (DDA), Ministry of Health (MoH), Nepal and the World Health Organization (WHO). An audit of the prescriptions revealed that 40% of the prescriptions contained FDC formulations. However, FDCs in accordance with recommended DDA, MoH Nepal and WHO lists of FDCs were only 0.8% and 2.1%, respectively. The most commonly prescribed FDCs were multivitamins, cough and cold remedies and antimicrobials which constitute nearly 63% of the total FDCs prescribed. In 48.4% of the prescriptions, the prescribed FDCs contained ingredients which were not essential for the desired therapeutic effect. Nearly 98% and 95% of the FDCs prescribed did not conform to the recommended Nepal and WHO lists of FDCs, respectively. The prescription of certain FDCs, however, were justifiable and in accordance with rational drug usage.

Keywords: Prescribing pattern; fixed dose combination; essential drug list.

Introduction

Irrational prescription of drugs is of common occurrence in clinical practice.[1] The prescribing behaviour of physicians depend upon the inputs from various sources like patients, professional colleagues, academic literature, commercial publicity and government regulations. Various prescribing errors, which are very common in clinical practice, are a result of the inappropriate use of these inputs. However, such errors are preventable and for this reason ongoing prescription monitoring and studies on drug utilization patterns may help in identification as well as rectification of inappropriate prescribing in accordance with the WHO action programme on rational prescribing.[2]

Most patients are on more than one drug. The concomitant administration 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, it would be difficult to achieve patient compliance. In order to overcome this problem, many fixed-dose combinations (FDC's) have been marketed.

A fixed dose combination refers to the combination of $\geq$ 2 drugs in a single pharmaceutical formulation. Surprisingly, in spite of the formulation and existence of regulatory guidelines and the national model list of essential drugs for Nepal[3], and WHO model list of essential drugs[2], which include only 9 and 14 drug combinations, respectively (Table I & II), FDC's are used widely. Therefore, we felt a study was imperative to analyze the prescriptions for FDC's issued by Manipal Teaching Hospital, Pokhara, Nepal.

Table I: Combination of drugs recommended by Ministry of Health, Department of Drug Administration, Nepal (National list of essential drugs Nepal 1997)[3]

1. Benzoic acid + Salicylic acid
2. Ferrous salt + Folic acid
3. Ichthammol (10%) + Glycerine (5%)
4. Levodopa + Carbidopa
5. Ethinyl-estradiol + Norethisterone

6. Sodium bicarbonate (1%) + Glycerine (5%)
7. Sulfadoxine + Pyrimethamine
8. Sulfamethoxazole + Trimethoprim
9. INH + Thiacetazone

Table II: Combination of drugs recommended by World Health Organization2

1. Benzoic acid + Salicylic acid
2. Bacitracin + Neomycin
3. Levodopa + Carbidopa
4. Ethinyl-estradiol + Levonorgestrel
5. Ethinyl-estradiol + Norethisterone
6. Ferrous salt + Folic acid
7. INH + Rifampicin
8. INH + Ethambutol
9. INH + Pyrazinamide + Rifampicin
10. INH + Thiacetazone
11. Sulfadoxine + Pyrimethamine
12. Sulfamethoxazole + Trimethoprim
13. Amoxicillin + Clavulanic acid
14. Imipenem + Cilastatin

Materials and Methods

The patients attending Manipal Teaching Hospital, Pokhara, Nepal were randomly approached at the hospital pharmacy for their prescriptions. The patients were also interviewed regarding information not available in the prescriptions. A total of 495 prescriptions were collected during the period from January 1999 to February 2000. A specially designed form was used to record the required information from the outpatient department (OPD) drug prescription of each patient. Each prescription was subjected to critical evaluation using WHO guidelines as described in accordance with "How to investigate drug use in health facilities ?"[4] The FDC containing prescriptions were separated from the total prescriptions collected and evaluated for their rationality in line with the list of FDC's recommended by WHO[2] and Ministry of Health, Department of Drug Administration, Nepal.[3]

Results

Out of the total 495 prescriptions collected, 194 contained FDC formulations. They were further sorted out as prescriptions containing one, two and three FDC's. These were 160 (82.4%), 28 (14.4%) and 6 (3.0%), respectively. Out of these 194 prescriptions, only 2 (1.0%) and 5 (2.5%) contained FDC's as recommended by Nepal and the WHO essential drug list, respectively. In 2% of the FDC containing prescription one ingredient was present at least two times as a part of FDC formulation.

The total number of FDC formulations prescribed was 233 and all of them were prescribed in brand names (trade names). Out of these, 2 (0.8%) and 5 (2.1%) FDC's were in accordance with the recommended WHO and Nepal list of FDC's, respectively. The most commonly prescribed were multivitamins 73 (31.3%), cough and cold remedies 40 (17.1%), antimicrobials 34 (14.5%), antacids 25 (10.7%), analgesics 14 (6%), antiasthmatics 9 (3.8%), antidiarrhoeals 5 (2.1%), antihypertensives 3 (1.2%) and others 30 (12.8%).

Discussion

A report by Shewade *et al* [4] had documented that almost 61.3% of the FDC's prescribed at JIPMER, Pondicherry, India was in accordance with those listed in the WHO recommended list of FDC's. It is evident from the present study that there are only 0.8% and 2.1% of FDC's which are in accordance with Nepal and WHO recommended list of FDC's.[2,3] In health units in Nepal, an average of 56% drugs were prescribed by brand names[5] and FDC formulations may contribute largely (46.6%). Potential advantages of FDC's include reduced side-effects (levodopa with carbidopa), increased patient compliance (anti-tubercular drug combination), synergy and increased efficacy (combination of sulfamethoxazole with trimethoprim or sulfadoxine with pyrimethamine for the prophylaxis and treatment of falciparum malaria)[6] and reduced cost. Potential disadvantages[7] include inflexible fixed-dose ratio, incompatible pharmacokinetics, increased toxicity and physician and pharmacists' ignorance of contents.

The most widely prescribed FDC's not having any rational basis are the multivitamin combinations (31.3%) and cough and cold remedies (17.1%). WHO has deleted the combination of vitamins from its list with the comment that vitamins are considered part of nutrition and vitamin combinations should not be used indiscriminately. The cough mixtures contain expectorants, cough suppressants, antihista-mines, sympathomimetics, alcohol and other CNS depressants without any rational basis.

In the United States, a fixed-dose 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 though 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 alone or one drug must act to reduce the incidence of adverse effects caused by the other.[8]

Therefore, the drug combinations which are not included in the WHO list of FDC's but meet the above criteria may also be designated as justified and rational eg, combination of more than one antihypertensive agents for the successful control of moderate to severe hypertension[9], the combination of potassium sparing and potassium losing diuretics, combination of ß-lactam antibiotics with ß-lactamase inhibitors[10], antacids containing a mixture of aluminium and magnesium salts, dermatological preparations which normally contain two drugs in the vehicle, combination of theophylline with ß-adrenergic agonists for synergistic effects in asthma.[11] Nearly 98% and 95% of the FDC's prescribed did not conform to the recommended Nepal and WHO list of FDC's. However, certain FDC formulations were justified and were rational. So a critical reappraisal is required by the practitioners and consensus reached at their local/national scientific forums followed by an appeal to the regulatory authorities to weed out irrational FDC's from the market. Further, medical professionals should be trained on concepts of essential drugs and rational drug use.[12]

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