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Drug Utilization Pattern of Fixed Dose Combinations Prescribed for Patients of Psychiatric Disorder in Psychiatric Department in A Tertiary Care Teaching Hospital

Medical Science

KEYWORDS : Drug utilization, fixed dose combinations, WHO, essential medicine list.

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ABSTRACT

Introduction: Prescription order is an important transaction between the physician and patient. It brings into focus the diagnostic acumen and therapeutic proficiency of the physician with instruction for palliation or restoration of the patient's health.

Psychiatric disorders are one of the major causes of morbidity. WHO estimated that globally over 450 million people suffer from mental disorders. For the treatment of psychiatric disorders, a wide array of psychotropic drugs is available. Psychiatrists are now very keen to use newer psychotropic medications in psychiatric practice which require vast study on their utilization and consequences on real life effectiveness and safety in actual clinical practice. There are very few studies which have evaluated the prescription pattern of fixed dose combinations and their safety profile in psychiatric patients from India. This leads to prompt us to design the present study.

Aims & Objective: Primary aim was to analyze the drug utilization pattern of fixed dose combinations prescribed for patients of psychiatric disorder in psychiatric department in J.L.N medical college & Associate group of Hospitals.

Material & Methods: After taking prior approval from Institutional Ethics Committee, this study was carried a for 6 months duration (1st Apr 2015 - 30th Sep 2015) in J.L.N. Medical College & Associate groups of Hospitals Ajmer. We randomly collected 135 copies for each month and a total of 810 carbon copies of prescription of patients who had visited the OPD of the psychiatric department of this college, fulfilling the inclusion and exclusion criteria were selected for study. Data were analysed as per our aims & objective.

Result: We found that that of total medicine formulations prescribed, 5.75% (177) were in the form of fixed dose combinations (FDCs). All the medicine formulations prescribed were from Rajasthan Essential Drug list (RMSC-EDL) and were essential according to state essential drug list.

Conclusion: In our study FDC occupies (5.75 %) only a small fraction of total drugs prescribed. This is a sign of good prescribing. It is the high time that health care professionals, pharmaceutical companies and regulatory authorities should join hands and prescribe guidelines for the manufacture and sale of FDCs.

Introduction

Prescription order is an important transaction between the physician and patient. It brings into focus the diagnostic acumen and therapeutic proficiency of the physician with instruction for palliation or restoration of the patient's health. [1]

The prescribing behavior of physician depends upon the input from various sources like patients,[2] commercial publicity,[3] professional colleagues, academic literature,[4] and Government regulations.[5] Ineffective use of these inputs can result in a wide variety of prescribing errors.[6]

Now a days prescribing pattern is changing and it has become just an indication of medicine with some instructions of doses without considering its rationality. [7]

The rationality of prescribing pattern is of utmost importance because, bad prescribing habits includes misuse , overuse and underuse of medicines which can lead to unsafe treatment, exacerbation of the disease, health hazards, economic burden on the patients and wastage of resources. Examples of irrational use of medicines include: polypharmacy, inadequate dosage, and use of antimicrobials even for non-bacterial infections, excessive use of injections when oral forms are available and inappropriate, self-medication and non-compliance to dosing regimes. [8]

Irrational prescribing is a habit that is difficult to cure. However, prevention is possible. There is some evidence that interventions such as short problem-based training course in pharmacotherapy and rational use focused workshops can improve prescription behavior and skills. However, irrational prescribing can be avoided by sticking to the ideal prescription writing and by following P-drug concept. [9]

Psychiatric disorders form an important public health priority. [10] Of the top ten health conditions contributing to the Disability Adjusted Life Years (DALYs), four are psychiatric disorders. [11] These disorders are one of the major causes of morbidity. Mental illness is associated with high levels of health service utilization and associated costs, and in developing countries these costs are mostly paid by the patient. [12]

WHO estimated that globally over 450 million people suffer from mental disorders. Currently mental and behavioral disorders account for about 12 percent of the global burden of diseases. This is likely to increase to 15 percent by 2020. Major proportions of mental disorders come from low and middle income countries. [13]

Mental disorder is defined by *Diagnostic and statistical manual of mental disorders* (5th ed.) **DSM-V** as a syndrome characterized by clinically significant disturbance in an individual's cognition, emotion regulation, or behavior that reflects a dysfunction in the psychological, biological, or developmental processes underlying mental functioning. Mental disorders are usually associated with significant distress in social, occupational, or other important activities. [14]

For the treatment of psychiatric disorders, a wide array of psychotropic drugs is available. During the past two decades, the development of newer drugs like Selective Serotonin Reuptake Inhibitors (SSRIs) and atypical anti–psychotics have drastically changed the drug therapy protocols. Psychiatrists are now very keen to use newer psychotropic medications in psychiatric practice which require vast study on their utilization and consequences on real life effectiveness and safety in actual clinical practice. [15]

Various factors like cost of drugs, local paradigms, etc. play a role in the selection of drug therapy and hence, affect the outcome. It is impossible to give suggestions for improving the attitude of physicians regarding the pattern of prescription without the knowledge of utilization pattern of drug.

There are very few studies which have evaluated the prescription pattern of fixed dose combinations and their safety profile in psychiatric patients from India. In view of this, the present study is designed.

Aims & Objective: Primary aim was to analyze the drug utilization pattern of fixed dose combinations prescribed for patients of psychiatric disorder in psychiatric department in J.L.N medical college & Associate group of Hospitals.

Material & Methods

After taking prior approval from Institutional Ethics Committee, we carried a retrospective non-interventional study of 6 months duration (1st Apr 2015 - 30th Sep 2015) in J.L.N. Medical College & Associate groups of Hospitals Ajmer.

We randomly collected 135 copies for each month and a total of 810 carbon copies of prescription of patients who had visited the OPD of the psychiatric department of this college, fulfilling the inclusion and exclusion criteria were selected for study. Patients suffering from a psychiatric illness were included whereas diseases other then psychiatric illness and those cases in which diagnosis is not certain were excluded. The minimum sample size required in this study is 810 cases at 95 % confidence interval and 10 % allowable error to verify the expected proportion 30 % depression which was the most common group of psychiatric conditions found in patients attending psychiatry outpatient department as per the seed article.

Data was analyzed as per our aims & objective.

Statistical analyses

Statistical analyses were done using computer software (SPSS version 20 and primer). The qualitative data were expressed in proportion and percentages and the quantitative data expressed as mean and standard deviations. The difference in proportion was analyzed by using chi square test and significance level for tests were determined as 95 % ($P< 0.05$).

Observation

Total number of 810 Prescriptions were studied, the M: F ratio was 1.86:1. Out of total patients, 527 (65.06 %) were males whereas 283 (34.93%) were females.[Table-1].

In this study, number of drugs belongs to various categories (anxiolytics, antidepressants, anti-psychotics, anti-convulsants, mood stabilizers, GIT medications, Vitamines & minerals etc.) were prescribed for various psychiatric disorder.

In present study, we observed the prescribing pattern of FDC of above prescribed medicines. We also observed their status in essential medicine list (EML) of WHO & National essential medicine list (NEML).

It is evident from table-2, that Of total medicine formulations prescribed, 5.75% (177) were in the form of fixed dose combinations (FDCs); among them 17.51% (31) were form the EML as well as NEML where as 82.49% (146) were outside the EML as well as NEML. Among the analgesic- antipyretics, 41.55% medicine formulations were in the form of FDCs and none of them is included in NEML or in WHO EML. Among the GIT drugs 15.15% (30) of the medicine formulations were in the form of FDCs and neither of them was included in both of EML, WHO or National. Among the antimicrobials (AMAs) 50% FDCs were from the EML & NEML. In the group of Vitamins and minerals drugs, FDCs 55.56 % (30) were from the NEML as well as WHO EML, and it is mainly due the fact that multivitamins, was the most frequently prescribed agent among the group.

36.87% (1134) of total medicine formulations, were matching, with those listed in WHO Model List of Essential Medicines (EML) whereas 60.47%(1860) of total medicine formulations, were matching with those listed in National Model List of Essential Medicines (NEML) whereas remaining 63.13 % (1942) and 39.53 % (1216) medicine formulations are considered as non-essential, as they are not mentioned in WHO EML or in NEML respectively. Of total non-essential medicine formulations, 82.49 % (146) were in the form of fixed dose combinations according to both WHO EML and NEML. (Table-3).

All the medicine formulations prescribed were from Rajasthan Essential Drug list (RMSC-EDL) and were essential according to state essential drug list.

Discussion: Bringing information on patterns of existing practice together with information on appropriate practice is an essential component of efforts to improve healthcare. This is possible only when each and every prescription in the hospital is audited by a prescription auditing team.

It is a component of medical audit that does monitoring and evaluation of the drug prescribing patterns and suggests necessary modifications in prescribing practices to achieve rational therapeutic practice as well as cost effective health care. [16]

In this study we found that number of male patient was more than female. Nearly similar results were also observed in previous carried studies.[17, 18] This may be due to the reason that males in the Indian Scenario had to deal with lots of burdens in their day to day life, be it the pressure of family sustenance, work pressure, social pressure, or burden of financial debts etc. Moreover the lifetime prevalence rate of substance abuse is much high in males as compared to females, thus leading to increased incidence of psychiatric illness in males.

Essential status of prescriptions: Essential medicines and rational use of medicines are two sides of a coin – inseparable from each other and mutually dependant. Increase in the use of essential medicines makes the medicine therapy more rational.

A fixed dose combination refers to the combination of two or more drugs in a single pharmaceutical preparation.[19] It is widely accepted that most drugs should be formulated as single compounds. Fixed ratio combination products are acceptable only when the dosage of each ingredient meets the requirement of a defined population group and when the combination has a proven advantage over single compounds administered separately in therapeutic effect, safety or compliance. [20] FDCs are highly popular in the Indian pharmaceutical market and have been particularly flourishing in the last few years.

The rationality of FDCs should be based on certain aspects such as [21]

The drugs in the combination should act by different mechanisms.

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The pharmacokinetics must not be widely different.

The combination should not have supra-additive toxicity of the ingredients.

Most FDCs have the following demerits:

Dosage alteration of one drug is not possible without alteration of the other drug.

Differing pharmacokinetics of constituent drugs pose the problem of frequency of administration of the formulation.

By simple logic there are increased chances of adverse drug effects and drug interactions compared with both drugs given individually.

In our study most of the fixed dose combinations were of analgesic-antipyretic preparations and gastrointestinal drugs preparations.

Out of total FDCs 41.55% (91/177) belongs to analgesic antipyretic group and none of these FDCs matches with that of WHO EML and NEML respectively thus considered as non essential. The FDCs included were of combination of paracetamol with ibuprofen and diclofenac. Apart from these, fixed dose combinations of Diclofenac + Paracetamol + Chloroxazone and Naproxen + Domperidone were also prescribed.

The difference in the mode of action of ibuprofen and paracetamol makes it an effective fixed dose combination for anti-inflammatory, antipyretic and analgesic property and commonly prescribed in conditions like pain in acute injuries, post-operative pain and pain following dental procedures.

Ibuprofen 400 mg is the standard therapeutic dose with a proven efficacy of analgesic and anti-inflammatory action. However, paracetamol is combined with ibuprofen to attain superior analgesic, anti-inflammatory and antipyretic profile. USFDA has regulated a circular to health professional to prescribe only those combinational drugs with paracetamol (acetaminophen) with dose as low as 325mg. USFDA's recommendation to all the healthcare professionals clearly states the unavailability of data to show the additional benefits of taking more than 325 mg of paracetamol per dosage unit that outweighs the added risks for liver injury.

In India, a variety of NSAID combinations are available, often as Over-the-counter products. [22] These combinations are the easiest way of selling two drugs when one (or even none) may be needed for the patient. These 'combined' pills are marketed with slogans like "Ibuprofen for pain and Paracetamol for fever" and "Ibuprofen for peripheral action and paracetamol for central action"! Recently, combinations of NSAIDs with rantidine, omeprazole and other proton pump inhibitors are also being marketed with the ostensible reason that the gastric adverse effects of NSAIDs can be prevented by using these combinations. It is indeed very unfortunate that the medical fraternity in India have fallen prey to such gimmicks. The gullible patient then has to pay for the doctors' complacence in terms of extra cost and extra adverse effects.

There is no synergism when two drugs acting on the same enzyme are combined. Thus combining two NSAIDs or NSAID with analgesics like paracetamol may not improve the efficacy or potency of treatment. If at all, it only adds to the cost of therapy and more important, to the adverse effects.[21,22] and the 'muscle relaxants' in some of these combinations are of questionable efficacy.

In the group of GIT drugs most of the FDCs prescribed were of proton pump inhibitors with antiemetics. All these FDCs do not match with WHO EML or NEML thus considered as non-essential combinations. Proton pump inhibitors reduce gastric acid secretion in conditions with hyperacidity, which brings symptomatic relief. There is no justification of combining these drugs with antiemetic drugs. Domperidone or Ondansetran as part of prescription in conditions of hyperacidity is not always required as it is not always associated with vomiting. Even in Gastro-esophageal reflex disease Domperidone is an inferior choice. In drug therapy for GERD proton pump inhibitors represent excellent drugs followed by H_2 Blockers. Therefore there is no justification of combining antiemetic with excellent drug like proton pump inhibitor or H_2 Blocker in conditions of hyperacidity.

In our study, just two antimicrobials were prescribed. Out of which one fixed dose combination is present in both NEML and WHO EML and considered essential and one does not matches and considered non-essential. The essential FDC was Amoxicillin + Clavulanic acid combination and Non-essential was Ofloxacin + Ornidazole combination. Though claimed to be broad spectrum, combining (antiamoebic) with fluoroquinolone (antibacterial) is irrational because patient suffers only from one type of diarrhoea. Using this combination adds to cost, adverse effects and may encourage resistance.[22]

Among Vitamins & Minerals 55.56% of FDCs were from the EML & NEML. The vitamins and minerals FDCs used were mostly of Vitamin B complex and iron with folic acid. Combination of ferrous salt with folic acid is included in WHO model list of essential medicine and in national list of essential medicine. Calcium preparations were not included in national list of essential medicine as well as WHO model list of essential medicine.

There are alarming increases in irrational FDCs in recent years and pharmaceutical companies manufacturing these FDCs are luring physicians to prescribe their products by unethical means. Instead of investing money in research and development to develop new molecule, most companies create and manufacture so called novel product by just combining two or more drugs.

Irrational FDCs also impose unnecessary financial burden on consumers. Medical practitioners who prescribe such combinations could be the centre of controversy when subjected to litigation, as these combinations do not find mention in standard text or reference books and reputed medical journals. Pharmaceutical manufacturers, however, continue to reap the benefits of huge sales, and therefore continue to promote combinations with vigor.

Conclusion

All the drugs were prescribed by generic name and were from RMSC-EDL, this indicates the good prescription habit. Prescribing medicines by official names avoids the confusion and makes the drug therapy rational and cheaper.

In our study FDC occupies (5.75 %) only a small fraction of total drugs prescribed. This is a sign of good prescribing. But majority of FDC (82.49%) were from outside the essential list of medicines (WHO EML & NEML). This practice should be decreased and more drugs should be prescribed from essential list of medicines (WHO EML & NEML).

Further we have studied the prescribing pattern of psychotropic drugs in government medical set-up. Hereby doc-

tors can prescribe only those medicines which were from RMSC- EDL and available in Hospital Drug Store under MNDY(Mukhya Mantri Dava Vitran Yojna).

In our study this government policy was totally followed and all drugs were from state essential drug list. This is an extremely advantageous policy for common people as it ensures health compliance for all without implicating financial burden on patients. Therefore this policy should be followed in other states also.

It is the high time that health care professionals, pharmaceutical companies and regulatory authorities should join hands and prescribe guidelines for the manufacture and sale of FDCs.

Table 1. Sex Ratio- As a Whole- (Total No. of Prescriptions-810)

Sex	Number Of Prescriptions	Percentage (%)
Male	527	65.06
Female	283	34.93
Total	810	100

The M: F ratio was 1.86:1.

Table-2: Essential Status of Fixed Dose Combinations (FDCs.) System/ Drug Category Wise. [National Essential Medicines List -2015(NEML) & WHO List of Essential Medicines-2015 (WHO EML)].

System / Drugs	Total No. of Medicine Formulations	FDCs	%	Essential		Non Essential	
				NEML	WHO EML	NEML	WHO EML
GIT	198	30	15.15	0	0	30 (100%)	30 (100%)
NSAIDs	219	91	41.55	0	0	91 (100%)	91 (100%)
Antibiotics	2	2	100	1 (50%)	1 (50%)	1 (50%)	1 (50%)
Vitamins & Minerals	428	54	12.61	30 (55.56%)	30 (55.56%)	24 (44.44%)	24 (44.44 %)
Total	847	177	5.75	31 (17.51)	31 (17.51)	146 (82.49)	146 (82.49)

Table-3 Essential Status of Medicines and Fixed Dose Combinations (FDCs.) in accordance with 19thWHO List of Essential Medicines-Apr 2015[WHO EML] and National List of Essential Medicines-2015[NEML])

	19thWHO List of Essential Medicines-Apr 2015[WHO EML].		
Parameter	Medicine Formulations (2899)	FDCs(177)	Total(3076)
Essential	1104(38.08%)	30(16.95%)	1134 (36.87%)
Non-Essential	1795(61.92%)	147(83.05%)	1942 (63.13%)
	National List of Essential Medicines-2015[NEML		
Parameter	Medicine Formulations	FDCs	Total
Essential	1830(63.13%)	30(16.95%)	1860(60.47%)
Non-Essential	1069(36.87%)	147(83.05%)	1216(39.53%)

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