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Patient Compliance: An Untold Story or a Fairy Tale?

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Abstract

Compliance with therapy implies an understanding of how the medication is to be used, as well as a positive behavior in which the patient is motivated sufficiently to use the prescribed treatment in the manner intended, because of a perceived self-benefit and a positive outcome i.e. enhanced daily functioning and well-being. Although this is often the case, in a number of situations, the physician and pharmacist have not provided the patient with adequate instructions or have not presented the instructions in such a manner that the patient understands them. Nothing should be taken for granted regarding the patient's understanding of how to use medication, and appropriate steps must be taken to provide patients with the information and counseling necessary to use their medications as effectively and as safely as possible.

Purpose and findings of the study: Discussion and projection of drug use and monitoring status in patients of Bangladesh. The pharmacists have a vital role to play which is thoroughly discussed. Bangladesh is a highly populated country. Economic development and academic flourishment do not represent development in health sector. Both the providers and patients are responsible for irrational drug uses and patient non-compliance or non-adherence.

Materials and methods: Research conducted a comprehensive year-round literature search, which included books, technical newsletters, newspapers, journals, and many other sources. Medicine and technical experts, pharma company executives and representatives were interviewed. Projections were based on estimates such as drug end users, providers or prescribers, general theories of rational use, implication and types of different irrational uses.

Research limitation: Very few articles found in matters regarding along with a very less interest paid by general people to talk about medicine use, prescription, suggested therapy in various illness, ADRs and their management. It was very difficult to bring out facts of irrational use of drugs, non-compliance and vigilance because business mentality of the providers very little knowledge about drugs crippled the facts.

Practical and social implication: The soul of this article was to detail about patient compliance and therapeutic drug uses with appropriate guidelines. Along with students, researchers and professionals of different background and disciplines e.g. Pharmacists, marketers, doctors, nurses, hospital authorities, public representatives, policy makers and regulatory authorities have to acquire much from this article. Along with healthcare facilities, patient compliance the soul of healthcare system in a country like Bangladesh as there is a scarcity of resources, fewer access to general people for adequate and better treatment, superstition and misbeliefs about drug, treatment and treatment providers. The article should contribute an integrated guideline for patient compliance, demand pharmacovigilance and last but not the least a silvery lining to better treatment near future.

Keywords: Essential medicine; Concordance; Persistance; National drug policy

Introduction

According to the World Health Organization (WHO), non-adherence to the medical regimen consists a major clinical problem in the management of patients with chronic illness. Rates of nonadherence with any medication treatment may vary from 15% to 93% with an average estimated rate of 50%. Adherence consists of 3 essential factors.

A. Patient: Individual health literacy and involvement in the treatment decision process

B. Provider: The decided prescription drug regimens and corresponding communication barriers

C. Healthcare system: access to care, time allotted for visits and technology

Types of patients

Based on the acceptance of diagnosis and treatment initiation, patients are categorized into four types.

A. Non-compliers: Those who do not accept diagnosis and need treatment.

B. Partial compliers: Those who accept diagnosis and treatment but cannot fulfill the recommended actions sufficiently to reach targeted improvements in their health.

C. Over compliers: Those who take recommended actions in excess of targeted improvements (These patients are rare).

D. Adequate compliers: Those who follow health advice adequately to improve or control their disorder.

Types of medication taking behavior

A. Compliance: It is the conscious effort to use drugs in the manner prescribed, it is the extent to which all individuals' behavior coincides with medical & health advice. Understanding how medication should be used, with sufficient positive motivation, and intentions, looking at the perceived self- benefit and positive outcome, it can also apply to other situations such as medical device use, self-care, self-directed exercises or therapy sessions.

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B. Adherence: The extent to which a person takes medication as prescribed. WHO defines adherence as "The extent to which a person's behavior, corresponds with agreed recommendations from a health care professional". Concept of adherence is broadly viewed as related to instructions concerning medicine intake, use of medical device, diet, exercise, life style changes, rest and return for scheduled appointments.

C. Concordance: Consultative and consensual course of therapy partnership between the consumer and their doctor. It is the process by which a patient and clinician make decisions together about treatment.

D. Persistence: A person's ability to continue medical advice for the intended course, which may range from few days to life long [1].

Dimensions of Adherence: It is a multidimensional phenomenon determined by the interaction of five sets of factors- termed "dimensions" by the WHO. These dimensions are:

A. Social/economic: People who have social support from family, friends or caregivers to assist with medication regimens have better adherence to treatment. Unstable living environments, limited access to health care, lack of financial resources, cost of medication and burdensome work schedules have all been associated with decreased adherence rates.

B. Provider-patient/health care system: The relationship of the doctor-patient is one of the most important health care system-related factors impacting adherence A good relationship between the patient and health care provider, which features encouragement and reinforcement from the provider has a positive impact on adherence. Poor or lack of communication concerning the benefits, instructions for use and side effects of medications can also contribute to nonadherence, especially in older adults with memory problems.

C. Condition-related: Long term drugs administration for many chronic illnesses and adherence to such treatment regimens often declines significantly over time. This often happens when patient have few or no symptoms and the absence of them is a barrier for people to take their medication. It is important for the patient to understand the illness and what will happen if it is not treated.

D. Therapy-related: The complexity of the medication regimen which includes the number of medications and number of daily doses required; duration of therapy; therapies that are inconvenient or interfere with a person's lifestyle and side effects have been associated with decreased adherence.

E. Patient-related factors: Physical impairments and cognitive limitations may increase the risk for nonadherence in older adults. Lack of knowledge about the disease and the reasons medication is needed, lack of motivation, low self-efficacy and substance abuse are associated with poor medication adherence.

Barriers to medication adherence

The American Heart Association lists six common barriers to medication adherence.

A. Fragmentation within the health care system. A study examining medication adherence in patients with heart failure found that adherence was significantly lower in patients who saw three or more health care providers within the same time period. Again, when patients have trouble coordinating care for their disease state (multiple disease) their adherence to treatment decreases.

B. Increasing complex drug therapies: Most elderly patients who was prescribed after a hospital discharge, the less adherent they were to those medications three months later. Many of the patients stop using their medications because they think the medications are unnecessary.

C. Poor communication between provider and patient**:** A meta-analysis study found that patients are 2.16 times more likely to stay adherent to their medications if their physician effectively communicates with them. Patients who saw physicians with effective communication techniques were more able to talk openly and honestly with their physician, therefore feeling more supported and encouraged to continue their medication regimen.

D. Unintentional patient behaviors: These behaviors include forgetting to take the medication, running out of medication and being careless about taking their medication (for example, taking a dose of the medication at the wrong time). Out of the three, the most commonly reported means of nonadherence was forgetfulness.

E. Patient physical or cognitive impacts**:** Certain physical disabilities will negatively impact medication adherence, including the inability to travel to and from the pharmacy, swallow pills, inject medications or open pill bottles. Those individuals with lower health literacy and higher physical impacts are less likely to understand the purpose of their medications and are also less likely to stay adherent to them.

F. Socioeconomic factors: Socioeconomics or the financial and/or societal status assigned to a population of individuals, can affect treatment regimens, patient understanding of those regimens and adherence to treatment. Lack of family or social support and poor mental health can also predict nonadherence.

Non-patient factors associated with Non-adherence

A. The nature of patient illness**:** Patients suffering from schizophrenia has high incidence of non-compliance due to distorted reality & lack of insight do not recognize their illness and need for treatment. Similarly, in chronic disorders like hypertension, tuberculosis etc., same pattern is observed.

B. Therapeutic regime: Multiple drug therapy like 5-6 prescribed drugs taking at different timings, taking tablets with same color, size and shape cause more confusion and skip doses. Technical difficulty in using inhalers.

C. Treatment duration: Compliance is inversely proportional to duration of treatment. In a study of long-term therapy, low compliance is observed as in bronchial asthma (50%) and hypertension (50-70%).

D. Frequency**:** Increased frequency of drug administration causes more disruption of normal routine or work schedule, hence many patients forget or inconvenienced or embarrassed. In one of the studies, compliance has improved from 59% on 8th hourly regimen to 84% with once a day regimen.

E. Adverse events: Events are like deterrents; in a study on elderly patients 40% experienced side effects of this 20% stopped medications and in this only 18-19% informed their physicians about discontinuation. In one of the surveys, over 60% are noncompliant due to adverse events. Some drugs like Anti-Hypertensive agents, Anti-depressants or Anti psychotics

cause sexual dysfunction which is frequently implicated for non-compliance.

F. Taste of medication: Can be the cause for noncompliance especially in children. Failure to comprehend the importance of therapy, as patient has limited knowledge about the illness, become non-compliant if beliefs and expectations are not met with. Poor understanding of instructions also contributes to non- compliance [2].

Types of Non-compliance

The situations most commonly associated with noncompliance with drug therapy include failure to have the prescription dispensed or renewed, omission of doses, errors of dosage, incorrect administration, errors in the time of administration and premature discontinuation.

A. Some patients for whom medication has been prescribed do not even take their prescriptions to a pharmacy and some others who do take their prescriptions to a pharmacy fail to pick them up when they are completed.

B. The omission of doses is one of the most common types of noncompliance and is more likely to occur when a medication is to be administered at frequent intervals and/or for an extended period of time.

C. Errors of dosage include situations in which the amount of an individual dose or frequency of administration is incorrect.

D. Examples of the incorrect administration of medication include not using the proper technique in using metered-dose inhalers and in some cases, giving medication by the wrong route of administration.

E. Errors in the time of administration of the drug may include situations in which medication is administered in an inappropriate relationship to meals. Certain drugs e.g., tetracycline, alendronate (Fosamax) should be administered apart from meals to achieve optimal absorption. The time of day at which a drug is administered also may be important in the use of some medications e.g., diuretics are best administered in the morning.

F. The premature discontinuation of treatment occurs commonly with the use of antibiotics as well as medications used in the treatment of chronic disorders such as hypertension.

Reasons of non compliance in elderly patients

A. Adverse effects

B. Increased or decreased sensitivity to drugs

C. Frequent change of prescriptions (prescription cascade)

D. Living alone

E. Lack of social support system,

F. Difficulty in opening the medication container that has flip off type of lid

G. Going to pharmacist/chemist due to physical problems like (osteoarthritis)

H. Impaired mobility or dexterity

I. Swallowing problems

J. Financial issues like, Low income and high cost of medications

K. Everyday inconvenience in carrying and taking of medicines

Consequences of Non-compliance

"Drugs don't work if people don't take them". This observation made by former Surgeon General C Everett Koop in his keynote address at a symposium on Improving Medication Compliance, provides a clear statement of one of the consequences of noncompliance.

A. In many cases noncompliance results in underuse of a drug, thereby depriving the patient of the anticipated therapeutic benefits and possibly resulting in a progressive worsening or other complications of the condition being treated.

B. Noncompliance also may result in the overuse of a drug. When excessive doses are employed or when the medication is given more frequently than intended, there is an increased risk of adverse reactions. These problems may develop rather innocently, as when a patient recognizes that he has forgotten a dose of medication and doubles the next dose to make up for it. Some other patients appear to believe that if the one-tablet dose that has been prescribed provides some relief of symptoms, two or three tablets will be even more effective.

C. Numerous hospital admissions and nursing-home admissions are related to noncompliance. Hypertension is the most frequently studied disease with regard to compliance. In one study it is reported that the underuse of antihypertensive medications may be associated with hospitalization that could have been prevented if patients had complied with their treatment regimens. The statins (e.g., atorvastatin [Lipitor], simvastatin [Zocor]) have been shown to significantly reduce morbidity and mortality in patients with coronary heart disease and in patients with hyperlipidemia, when they are used on a continuing basis.

D. It has been observed that about one-half of patients with schizophrenia are noncompliant in using their medications and experience a relapse of symptoms within a year of initiation of antipsychotic treatment. The inadequate control of schizophrenia has, in some situations, been associated with violent actions [3].

Factors associated with Non-compliance

A. Disease: The nature of the patient's illness may, in some circumstances, contribute to noncompliance. In patients with psychiatric disorders, the ability to cooperate as well as the attitude toward treatment may be compromised by the illness and these individuals may be more likely than other patients to be noncompliant. Patients with chronic disorders, particularly conditions such as hypertension and hypercholesterolemia, which often are not associated with symptoms are also more likely to be noncompliers. Patients understandably tend to become discouraged with extended therapeutic programs that do not produce cures of the conditions. Even when cures can be anticipated as a result of long-term therapy, problems still can occur as exemplified by patients with tuberculosis who frequently become noncompliant as the treatment period continues.

B. Therapeutic Regimen

a) Multiple Drug Therapy: It generally is agreed that the greater the number of drugs a patient is taking, the higher is the risk of noncompliance. For example, many elderly patients are taking five or six or more medications several times a day at different times. In addition, some elderly

patients may experience lapses of memory that make noncompliance even more likely. Even when specific dosage instructions for the medications are provided, problems still can occur. The similarity of appearance (e.g., size, color, or shape) of certain drugs may contribute to the confusion that can exist in the use of multiple drugs. The observations in an editorial provide a perspective that is helpful in understanding the challenge for the patient who is to take a number of medications

b) Frequency of Administration: The administration of medication at frequent intervals makes it more likely that the patient's normal routine or work schedule will have to be interrupted to take a dose of medication, and in many cases the patient will forget, not want to be inconvenienced, or be embarrassed to do so.

c) Duration of Therapy: The potential for noncompliance is greater when the treatment period is long. As noted earlier, a greater risk of noncompliance should be anticipated in patients with chronic disorders, especially if discontinuation of therapy is not likely to be associated with prompt recurrence of symptoms or worsening of the illness. Noncompliance with regimens for the treatment of tuberculosis is a major reason for the development of resistance to multiple antitubercular agents and is a very important problem for many patients with this infectious disease.

d) Adverse Events: The development of unpleasant effects of a drug is a likely deterrent to compliance. In some situations, it may be possible to change the dosage or use alternative drugs to minimize adverse events. However, in other cases such alternatives may not exist, and the benefits expected from therapy must be weighed against the risks. Particularly disconcerting are those situations in which the development of adverse events makes patients feel worse than they did before therapy was initiated, as often occurs in hypertensive patients. The adverse events (e.g., nausea, vomiting, hair loss) associated with the use of many antineoplastic drugs are sufficiently distressing to a number of patients with cancer that they do not take their medication in the manner intended. The ability of certain drugs to cause sexual dysfunction is a reason for noncompliance by some patients, with the antipsychotic agents, antidepressants, and antihypertensive agents being implicated most frequently.

e) Patients may be asymptomatic or Symptoms subside**:** Patients may feel better after taking the drug and feel that they no longer need to take it once the symptoms subside. Situations frequently occur in which patients do not complete a full course of antibiotic therapy once they feel that the infection has been controlled. This practice increases the likelihood of a recurrence of the infection and increased resistance of the microorganisms causing the infection, and patients must be advised to take the full course of antibiotic therapy.

f) Cost of Medication**:** Noncompliance may occur with the use of drugs that have a relatively low cost; however, it might be anticipated that patients may be even more reluctant to use the entire prescribed quantity of more-expensive agents. The expense involved has been cited by some patients as the reason for not having prescriptions dispensed at all, whereas in other cases the medication is taken less frequently than intended or prematurely discontinued because of the cost.

g) Administration of Medication**:** Although patients may fully intend to comply with instructions, they may inadvertently receive the wrong quantity of medication because of incorrect measurement of medication, use of inappropriate measuring devices, or incorrect use of medication-administration devices. The inaccuracy of using teaspoons to administer liquid medications is well known and is compounded by the possibility of spillage and asking the patient to measure a fraction of a teaspoonful. This problem has been long recognized, but problems still occur. The importance of providing the patient with measuring cups, or calibrated droppers for the use of oral liquids is evident. Some patients do not use metered-dose aerosol inhalation devices correctly, and this could result in inadequate control of the conditions (e.g., asthma) for which their use is intended. The provision of oral instruction by the pharmacist has resulted in better patient understanding and performance of the correct steps for inhaler use.

h) Taste of Medication**:** Medication taste problems are encountered most commonly with the use of oral liquids by children. Getting a child to take a dose of medication may be such a difficult task for a parent that doses may be missed or administration of the drug discontinued as soon as the parent sees any sign of improvement. Experiences such as these have resulted in initiatives to flavor liquid medications so that they are acceptable to children. FLAVO has used more than three dozen flavors in the development of a medication flavoring formulary system that has been used successfully in pharmacies around the country. This system also has been extended for use in medications prescribed for pets.

C. Patient/Health Professional Interaction-These observations are equally important with respect to the interaction between the pharmacist and the patient. The following factors are among those that could influence compliance adversely if inadequate attention is given to the scope and quality of the interaction with the patient.

1. Failure to Comprehend Importance of Therapy**:** Patients usually know relatively little about their illnesses, let alone the therapeutic benefits and problems that could result from drug therapy. Therefore, they establish their own beliefs and expectations with respect to their drug therapy. If the therapy does not meet these expectations they are more likely to become noncompliant. Poor Understanding of the Instruction: Prescriptions that state that medication should be taken as directed can be the source of misunderstanding as well as serious consequences. For example, many prescriptions are written and labeled to indicate how many doses are to be taken each day with no additional clarification as to how the doses are to be scheduled. How should instructions to take one tablet three times a day be interpreted? Does this mean every 8 h or with meals, or possibly some other schedule? If the drug is to be given with meals or at a specified time before or after meals, it

usually is assumed that the patient eats three meals a day. Yet this is not always the case.

2. In some cases, the uncertainty or confusion on the part of the patient is such that medications are given by the wrong route of administration (e.g., instilling oral pediatric antibiotic drops into the ear for an ear infection or administering suppositories by the oral route).

3. A patient being prepared for an electrocardiogram was observed to have 20 transdermal nitroglycerin patches at various locations on his body. Although he had understood the instructions to apply one patch a day, no instruction had been provided regarding their removal.

Non- compliance detection

Current detection methods include indirect measures, such as self-report, interview, therapeutic outcome, pill count, change in the weight of metered-dose inhaler canisters, medication-refill rate, insurance prescription claims databases and computerized compliance monitors, and direct measures, such as biological markers, tracer compounds, and assay of body fluids. In general, the direct methods of detection have a higher sensitivity and specificity than the indirect methods. However, all of these methods have their limitations. To help overcome limitations of the assessment methods and to provide corroborative information, it is recommended that at least two different detection methods be used to measure compliance.

Indirect methods: Self-reports and interviews with patients are the most common and simplest methods of attempting to determine compliance with therapy. Pill counts are another detection method used to measure compliance and frequently are used in clinical drug studies. A patient's compliance with a medication regimen can be assessed by the difference between the number of dosage units initially dispensed and the number remaining in the container on a return visit or during an unscheduled home visit. However, pill dumping (i.e., attempts by patients to misrepresent their compliance by discarding medication) is common, and several studies have shown that return counts grossly overestimate actual compliance rates [2].

Direct methods: Biological markers and tracer compounds indicate patient compliance over an extended period. For example, measurement of glycosylated hemoglobin in patients with diabetes mellitus gives an objective assessment of metabolic control during the preceding 3-month period. Tracer compounds small amounts of agents with long half-lives such as phenobarbital have been added to drugs in some studies and measured in biological fluids as pharmacological indicators of compliance.

Improving compliance

Pharmacists have a particularly valuable opportunity to encourage compliance since their advice accompanies the actual dispensing of the medication, and they usually are the last health professional to see the patient prior to the time the medication is to be used.

A. Identification of Risk Factors-These factors should be considered in planning the patient's therapy so that the simplest regimen that is, to the extent possible, compatible with the patient's normal activities can be developed.

B. Development of Treatment Plan-The more complex the treatment regimen, the greater is the risk of noncompliance, and this must be recognized in the development of the treatment plan. The use of longer-acting drugs in a therapeutic class, or dosage forms that are administered less frequently, also may simplify the regimen. The treatment plan should be individualized on the basis of the patient's needs, and when possible, the patient should be a participant in decisions regarding the therapeutic regimen.

C. Patient Education- One of the findings of the report of the Office of the Inspector General is "education is the best way to improve compliance". Complex terms and unnecessary jargon that can interfere with patient understanding should be avoided. Patients should be asked to repeat the instructions for administering their medications to show that they understand them, and they also should be encouraged to ask questions.

D. Oral communication/counseling- Oral communication is the most important component of patient education because it directly involves both the patient and the pharmacist in a two-way exchange and provides the opportunity for the patient to raise questions. For such communication to be most effective it should be conducted in a setting that provides privacy and is free of distractions.

E. Written communication- It is also desirable and sometimes required to provide supplementary written instructions or other information pertaining to the patient's illness or drug therapy, and many pharmacists provide patients with medication instruction cards or inserts. Information that pertains to the specific medication/formulation being dispensed is preferred to information that applies to a therapeutic class of agents or a general statement that applies to all dosage forms of a particular medication. The provision of supplementary written information appears to be most effective in improving compliance with short-term therapeutic regimens (e.g., antibiotic therapy). For drugs used on a long-term basis, written information as a sole intervention has not been shown to be sufficient for improving patient compliance.

F. Audio-visual materials- The use of audio-visual aids may be particularly valuable in certain situations because patients may be better able to visualize the nature of the illness or how their medication acts or is to be administered (e.g., the administration of insulin, the use of a metered-dose inhaler). An increasing number of health-care professionals have used such aids effectively by making them available for viewing in a patient waiting area or consultation room and then answering questions the patient may have.

G. Controlled therapy- It has been proposed that hospitalized patients be given the responsibility for self- medication prior to discharge. Usually, patients go from a complete dependence on others for the administration of their medication while hospitalized to a situation in which they are given the full responsibility when discharged, often with the assumption that they know about their drugs because they were taking them in the hospital. The suggested arrangement would permit patients to start using the medications on their own before discharge, so that health-care professionals can more directly identify problems or situations that might undermine compliance, and answer patient questions.

H. Patient Motivation- Information must be provided to patients in a manner that is not coercive, threatening, or demeaning. The best intentioned, most comprehensive educational efforts will not be effective if the patient cannot be motivated to comply with the instructions for taking the medication. The physician-patient interaction has been characterized as a negotiation. This concept may be extended further by the development of contracts between patients and health-care providers in which the agreed-upon treatment goals and responsibilities are outlined.

A. Compliance Aids

a) Labeling- The importance of the accuracy and specificity of the information on the label of the prescription container has been noted. Auxiliary labels that provide additional information regarding the use, precautions, and/or storage of the medication also will contribute to the attainment of compliance. The inclusion of pictograms in labeling and patient information leaflets has been demonstrated to have a positive effect in the acquisition and understanding of information regarding medications prescribed for patients with limited literacy skills.

b) Special Medication Calendars and Drug Reminder Charts**:** Various forms, such as medication calendars, have been developed and are designed to assist patients in self-administering drugs. In addition to their use in helping patients understand which medication to take and when to take it, the forms on which patients are to check the appropriate area for each dose of medication they take, can be evaluated by the pharmacist or physician when the patients return for more medication or have their next appointment.

c) Special Medication Containers, Caps and Systems**:** Specially designed caps for prescription containers also have been developed to facilitate compliance, and include features such as a digital timepiece that displays the time and day on which the last dose of medication was taken, and an alarm and flashing light when it is time to take the next dose. Containers/caps that contain all or some of these features include The Prescript Time Cap, The Pill Timer, and Remind Cap Closures. The use of microelectronic medication monitors (Medication Event Monitoring System) in the caps of prescription containers has been described earlier. For patients with vision impairment or who otherwise have difficulty reading information on prescription labels, products such as Talking Rx, ScripTalk, and Aloud Talking Prescription Labels have been developed to play a prerecorded message when activated. Instructions for using the medication are recorded in a small electronic unit or microchip that is attached to the bottom of the container or embedded in a label.

d) Compliance Packaging- A compliance package has been defined as a prepackaged unit that provides one treatment cycle of the medication to the patient in a ready-to-use package, and a comprehensive review of the use of such packaging as a patient education tool has been published.

1. This type of packaging usually is based on blister packaging using unit-of-use dosing and is designed to serve as a patient-education tool for health professionals and to make it easier for patients to understand and remember to take their medications correctly at home. Specially designed packaging for oral contraceptives was one of the first initiatives of this type and has been valuable in increasing patient understanding of how these agents are to be taken.

2. Special packages of certain corticosteroids (eg, Medrol Dosepak) also have been designed to facilitate the use of steroids in dosage regimens that may be difficult to understand or remember [4].

3. The medicine on time system is an example of a packaging system that provides unit-of-use dosing with specific labeling in a plastic card that is set up like a calendar. In addition to simplifying the use of medications for patients who self-administer their medications, these systems also have been very useful in the distribution and administration of medications in assisted living and other patient-care facilities.

4. A possible negative effect of drug packaging on patient compliance is seen with the use of the child-resistant containers. Some patients, particularly the elderly and those with conditions like arthritis and parkinsonism, have difficulty opening some of these containers and may not persist in their efforts to do so. There also may be difficulty opening some foil-packed drugs. Pharmacists should be alert to problems of this type and, when appropriate, suggest use of standard containers or caps.

e) Dosage Forms- New dosage forms of certain drugs also have been developed, in large part in recognition of problems of noncompliance. For example, the development of longer-acting, controlled-release dosage forms of numerous medications (eg, calcium channel blocking agents) has permitted less frequent administration of these agents, which facilitates compliance. The use of transdermal delivery systems permits less-frequent administration of the drugs (eg, nitroglycerin, fentanyl) given by this route.

Monitoring Therapy

1. Self-Monitoring- Patients should be apprised of the importance of monitoring their own treatment regimen and, in some situations, the response parameters.

2. Pharmacist Monitoring- The pharmacist's role in minimizing noncompliance does not end when the prescription is dispensed. Pharmacist follow-up with telephoned or mailed refill reminders has been found to increase compliance. One approach in which both health professionals and patients have collaborated effectively in reviewing/monitoring the use of medication has been the brown bag program. The Administration on Aging and National Council on Patient Information and Education (NCPIE) have encouraged older consumers to put all their medicines in a bag and take them to their health professional for a personalized medicine review.

3. Directly Observed Treatment (DOT)- Even when many of the steps described earlier have been taken, noncompliance may still result. Many of the recommendations for improving patient compliance are included in a comprehensive set, Recommendations for Action to Advance Prescription Medicine Compliance that has been developed by NCPIE. Bottom line is "no single strategy or programmatic focus showed any clear advantage compared with another. Comprehensive interventions combining cognitive, behavioral, and affective components were more effective than single-focus interventions.

Benefits of patient compliance

The improvement of compliance will result in a situation in which all parties benefit. Most importantly patients benefit from the enhancement of the efficacy and safety of their drug therapy. Pharmacists benefit because there is an increased recognition and respect for the value of the advice and service that they provide. Pharmaceutical manufacturers benefit from the favorable recognition that accompanies the effective

and safe use of their drugs as well as from the increased sales resulting from the larger number of prescriptions being dispensed. Finally, society and the health care system benefit as a result of fewer problems associated with noncompliance. Although an increase in compliance will result in more prescriptions being dispensed and a higher level of expenditures for prescription medications, this increase in costs will be more than offset by a reduction in costs (eg, physician visits, hospitalizations) attributable to problems due to noncompliance (US Public Health Service).

General Health Matters of Bangladesh

Bangladesh is considered a developing country with more than 75% of the total (142 million) population living in rural areas [5]. Though majority of the population live in rural areas, the government healthcare system remains a very minor source of health care there. Around 26% of professional posts in rural areas remain vacant and there is high rate of absenteeism (about 40%). Treatments in the rural areas are mainly (about 45%) provided by unqualified health personnel including medical assistants, mid-wives, village doctors, community health workers in comparison to that by qualified medical graduates (only 10-20%). Over-prescribing and inappropriate prescribing are very common in the country due to unethical practices of both health professionals and drug manufacturers.

Regulatory Regime

A. The Directorate General of Drug Administration (DGDA): DGDA is the drug regulatory authority of Bangladesh, which is under the Ministry of Health and Family Welfare. DGDA regulates all activities related to import and export of raw materials, packaging materials, production, sale, pricing, licensing, registration, etc. of all kinds of medicine including those of Ayurvedic, Unani, and Herbal and Homoeopathic systems.

B. The Pharmacy Council of Bangladesh (PCB): PCB was established under the Pharmacy Ordinance in 1976 to control pharmacy practice in Bangladesh.

C. The Bangladesh Pharmaceutical Society (BPS): It is affiliated with international organizations International Pharmaceutical Federation and Commonwealth Pharmaceutical Association. The National Drug Policy (2005) states that the WHO's current Good Manufacturing Practices (GMP) should be strictly followed and that manufacturing units will be regularly inspected by the DDA. Other key features of regulation are restrictions on imported drugs; a ban on the production in Bangladesh of around 1,700 drugs which are considered non-essential or harmful; and strict price controls, affecting some 117 principal medicines.

Misbeliefs and superstitions in health seeking behavior

In our society cultural beliefs, attitudes and superstition greatly influence the pathogenesis of disease and also health seeking behavior. Majority of the parents are not aware about the illness of their infants due to lack of knowledge basically due to poor educational background. Data of different authors in Bangladesh have been reviewed to assess the magnitude of morbidities & health seeking behavior of under five children. Various studies show that common disease of under five children are gastroenteritis, pneumonia, diarrhea, skin infection, helminthiasis, abdominal pain, dental problem & chronic suppurative otitis media [6]. Another study in Bangladesh on health seeking behavior of the parents of under five children found that majority sought treatment from Homeopaths and nonqualified allopath's. Only a few of them received modern allopathic treatments. Bangladeshi women report low but increasing use of antenatal care, as well as low rates of delivery in a health facility or with the assistance of a skilled provider. Although almost half of women reported having one or more complications during pregnancy that they perceived as life threatening, only one in three sought treatment from a qualified provider. More than three-fourths of women with the time-sensitive complications of convulsions or excessive bleeding either failed to seek any treatment or sought treatment from an unqualified provider. The principal reason cited for failing to seek care for life-threatening complications was concern over medical costs, and pronounced socioeconomic disparities found for maternal care-seeking behavior in both urban and rural Bangladesh [7].

Prescription patterns of drugs

Despite legal prohibitions, numerous drugs with similar or no significant benefits are available in the market. As a specific example, there are seven members of the angiotensin-converting enzyme (ACE) inhibitors available in the country. The efficacies and chemical structures of these molecules are more or less similar, but their price vary significantly. The drug policy clearly prohibits the production of multi-ingredient preparations of vitamins and minerals with the exception of B-complex vitamins. But a mixture of 32 vitamins and minerals including selenium, vanadium, molybdenum, tin and many other unnecessary ingredients has been marketed in the country for a few years, violating the principles of the NDP. The need for these trace elements in Bangladesh is not established whereas nutritional deficiencies are mainly related to vitamins A and B-complex, iron, calcium, iodine and zinc. Irrational prescription and use of antibiotics are rampant throughout the country, with an estimated half of all antibiotics being sold without prescriptions. Self-medication is widespread, and all types of medicines can be purchased without a prescription. There are about 30,000 illegal and 80,000 unlicensed drug stores operating in the country. It is alleged that both legal and illegal drug dealers are engaged in selling fake, smuggled and adulterated medicines in the country.

Inappropriate uses of prescription drugs

The drug use studies involving outcomes, adverse reactions and bioavailability in Bengali population has never been seriously looked into in Bangladesh. Like all other developing countries, irrational and inappropriate use of medicines is very common in Bangladesh. Recent study showed that about half of the antibiotics were sold without any prescriptions, and even ordinary people without any knowledge of medicine asked the drug seller for specific antibiotics. Moreover, self-medication is a common practice among laypeople. Unjustified combination of vitamins and minerals are still extensively available violating the principles of NDP, which restricts the production and marketing of these types of combination products. Recently, many pharmaceutical manufacturers have launched one such combination containing 32 ingredients including selenium, vanadium, molybdenum, tin and other less important or unnecessary minerals. But the socio-demographic conditions of Bangladesh clearly out-weighs the justification of this type of combination products as most of the nutritional deficiencies are caused due to Vitamin A or B-complex, iron, calcium, iodine, or zinc deficiency. Deficiencies due to selenium, vanadium or tin are seldom diagnosed in Bangladesh, if ever. British pharmacopoeia clearly indicates that there is no justification for prescribing multiple ingredient vitamin preparation. In addition, drug like syntocinon (a hormonal injection which is given to pregnant

women to ease labor) is being sold or used indiscriminately in-home deliveries in rural Bangladesh, which is readily available without prescription there.

Misuse of OTC drugs

In real sense, there is no 'prescription only drug' in Bangladesh at present. One can get any drugs from anywhere. Only need is money; no prescription indeed. Over the counter (OTC) drugs have emerged recently as drugs of serious misuse across Bangladesh, and other neighboring countries. One report estimates that there are four million drug misusers in the South Asian region, with Bangladesh accounting for nearly 500,000. Self-medications in a population with low literacy level like Bangladesh are very challenging, which poses risks such as incorrect diagnosis, absence of knowledge of alternative treatments, irrational use of drugs and neglecting side effects and drug interactions. Study showed that around 30- 40% of disadvantaged population including the women, elderly, ethnic minorities, poor / ultra-poor undertake self-medications for managing illness.

Lack of availability and accessibility of essential medicines

Though the official documents showed that about 80% of the people of Bangladesh had sustainable access to affordable essential drugs in Bangladesh, there are numerous evidences of frequent and persistent unavailability of essential drugs in the government health facilities [8]. Most of the inpatients (86%) reported paying for medicines from outside. As with rural areas, unavailability of essential drugs the urban government health facilities is often very common. Theft and illegal sale of essential medicines from the government hospitals are very common. Officials in-charge of hospital drug stores sell these drugs to local pharmacies instead of supplying to the poor patients. And it is obvious that those activists neither think nor contributes to patient compliance. Reasons of adverse drug reactions in Bangladesh.

1. Self-medication
2. Poly pharmacy
3. Aggressive promotion and push sell of drug products
4. Unethical practice of healthcare providers
5. Irrational use of antibiotics, steroids and other drugs
6. Registration of more combination products where alternative options are there
7. Distribution/purchase of medicine from any unauthorized source
8. Improper storage and distribution of drugs

Role of pharmacist in the management of ADRs

As seen through various studies and the basic concept of pharmaceutical care, a pharmacist plays a pivotal role in the identification, detection, prevention, and management of drug-drug interactions, drug-food interactions and ADRs. Pharmacist can carry out such activities in inpatient setting, while taking part in viewing charts during ward rounds, and during medication management while dealing with prescriptions. Since pharmacists have a vast knowledge on drugs and therapeutics, their ability to discover and deal with ADRs is quite important. Keeping in view the reporting of ADRs, according to a study carried out by [9] on the prevalence of ADRs, a pharmacist's participation enhances reporting rate with higher caliber. The intervention of pharmacists by organizing lectures and group discussions thus providing information about the importance, seriousness, preventability and necessity of reporting shows heightened improvement of knowledge, attitude and perception about ADRs. All health professionals play their respective roles in balancing between benefits and risks of medication when it is introduced in the market. However, the expertise of a pharmacist about a drug, especially if newly marketed, play a more important role in ADRs reporting to the authorities which helps in either withdrawing the product from the market or cause labelling changes. Pharmacists working in community pharmacy have an added advantage of detecting and reporting ADRs while dealing with on the counter prescriptions and herbal products. In a community pharmacy, a pharmacist may not have direct and definite patient list but the patients coming to the same pharmacy to refill their prescription gives the pharmacist an opportunity to detect a possible ADR that the patient might be experiencing and can help in the management and the reporting of the said ADR.

Therapeutic compliance reports of Bangladesh

A. Patients with Rheumatic Heart Disease: Therapeutic compliance among patients with rheumatic heart disease in National Center for Control of Rheumatic fever and Heart disease, Dhaka, Bangladesh. The mean adherence was determined at 50%. This was less than the adherence level determined by Harrington, in an aboriginal community in Australia [10].

B. Compliance to Anti-hypertensive Medications: A multi-center study done by WHO in the year 2001, revealed that 45% of elderly people in Bangladesh and India suffered from hypertension. 40% of them are aware of their disease and only 10% are compliant to treatment. In the year 2007 a study done in Rajshahi, Bangladesh revealed that 85% of the hypertensive population were non-adherent to their antihypertensive medications [11].

C. Type 2 Diabetes Mellitus Patients' Compliance: The importance of management of type 2 diabetes with pharmacologic and non-pharmacologic therapies varies in cost and risk. A study in BIRDEM, Dhaka found that among the diagnosed Type 2 people 14% take both insulin and oral medication and 58% take oral medications only. It was found the intake of oral medication was 89% and for injectable medication only 50%. Here also the insulin intake was high in urban area due to cost and availability of the drug in local market. Around 24% respondents was found took herbal medications for controlling diabetics which is lower in cost [12].

D. Cost of non-compliance among diabetes patients: In this cross-sectional study, 220 patients with diabetes were recruited from logs of diabetes clinics in Mirzapur, Bangladesh. Participants were asked about self-care practices and health complications and comorbidities associated with diabetes. The most commonly reported health effect was vision impairments such as blurring, dim vision or blindness (66%), followed by poor wound healing (29%) and dizziness (28%). Sexual dysfunction was reported among 13% of men (5% of the entire sample). In examining comorbidities, hypertension was most commonly self-reported in 45% of participants, followed by heart disease and depression (19 and 16%, respectively) [13].

E. Antibiotic Resistance: Recent study showed that about half of the antibiotics were sold without any prescriptions, and even ordinary people without any knowledge of medicine asked the drug seller for specific antibiotics [14]. Rural people do not always do what the prescribers advise them to do. Financial

ability, however, is not the sole influence, as it was observed that people who could pay did not always purchase all the prescribed drugs and this survey finding also complies with previous results. Among all other causes of antibiotic resistance there could be three causes those are responsible for antibiotic resistance; first, inappropriate prescriptions which are prevalent in the country due to poor consulting period (a mean of only 54 seconds was recorded in a Bangladeshi study in 1994) of doctors in Bangladesh and it is estimated that more than half of medicines are inappropriately prescribed, dispensed or sold. Second, because patients often travel long distances and incur large expenses for medical care, they are unlikely to return for follow-up visits, and finally, because many drugs are expensive, indigent patients purchase incomplete regimens whenever possible and discontinue treatment when symptoms disappear but before the pathogen is eliminated.

Role of pharmacist in patient compliance

The pharmacist could be a coordinator between different members of healthcare team and the patients. Thus, involvement of pharmacists in health management system is becoming very crucial day by day. Pharmacists are involved in providing health care facilities as well as suggesting medical staff on proper selection of drugs. They also plan, monitor and evaluate drug programs to improve health and reduce health inequalities. Hospital pharmacists ensure that medicines are managed safely and effectively so that they are appropriate for the age, sex, body weight and clinical status of the patient. Community pharmacists on the other hand come in direct contact with the public and they not only dispense medications but also counsels' patients regarding general health topics such as diet, exercise, stress management, over-the-counter medications etc. Some community pharmacists also provide specialized services to help patients with diabetes, asthma, smoking cessation, drug addiction, and patients with high blood pressure. Pharmacists can prevent drug interaction, counsel patient regarding the disease and medication e.g. providing information, advice and assistance about medication and therapy due to their access of interpersonal communication. Thus, pharmacists can play a key role in preventing drug abuse by providing clear information about the adverse effects of medications. A pharmacist is one of the inevitable members of healthcare team who can help in achieving the goal of rational use of drugs by following good pharmacy practices and can also combat counterfeit drugs due to their pharmaceutical expertise. To reduce the potential medication error, 'Medication Safety Alerts' outlined the roles of pharmacists at different stages of medication use as below:

A. Prescribing Stage

1. Clarify and verify if not sure or not clear
2. Establish protocols and order sets
3. Monitor all medication profiles
4. Maintain open communication channels with physicians
5. Educate physicians about dangerous abbreviations
6. Provide input to patients' medication regimens
7. Encourage physicians to use protocols and preprinted order forms
8. Support and facilitate implementation of computerized physician order entry systems
9. Support use of a personal digital assistant for clinical information resources

B. Dispensing Stage

1. Automatic dispensing
2. Reorganize drug storage and shelving to separate drugs with similar names
3. Redesign workflow to achieve efficiency and to facilitate safety checking
4. Make use of computerized clinical information
5. Be more vigilant with high-risk medications and high-risk patients, e.g., establish a system of double checks
6. Communicate clearly with nurses and patients

C. Transcribing and Adminstering Stages

1. Support and facilitate use of electronic medication administration records (MARs)
2. Ensure that each patient's MAR is updated in a timely manner when pharmacy service is not available
3. Check and compare each patient's MAR at least daily to ensure that orders are interpreted correctly and carried out
4. Support the use of point-of-care dispensing cabinets
5. Support the use of bar coding for patients, orders and drugs for administration

D. Monitoring Stage

1. Follow up laboratory results and/or blood level monitoring
2. Screen automatic stop orders for drugs that require reactivation
3. Perform daily review of drug profiles to spot potential problems
4. Establish rapport and effective communication with nurses
5. Engage Patients

Recommendations

A. Leadership- While the rest of the world has made great advancements to enhance the consumer experience, healthcare organizations have been slower to change their ways, making patients conform to the needs of the system. Evolution requires a change in culture, philosophy, and technology. Greater visibility into processes is ensuring control, quality and safety measures within hospitals, clinics, model pharmacies and any healthcare settings.

B. Medical Records Management- Leveraging the improvements in technology to link databases and systems with automated forms yields timelier reporting and tracking of patient records of history, medication and provider's instruction. Continue monitoring is the soul of compliance and control. From artificial intelligence to machine learning, health systems should be exploring all kinds of innovations to move healthcare forward. Predictive analytics, evidence-based practice automation, digital disruptors, and non-traditional players apply to and accelerate patient experience initiatives.

C. Infection Control- Being able to identify problems earlier, ordering the proper testing and infection treatments, followed by the ability to monitor and report the cases with accuracy.

D. Reduction in Medication Errors- Capturing information electronically to eliminate human errors and misunderstandings in prescriptions. Medication errors are caused by mistakes in prescribing, dosing, and administration, both in inpatient and outpatient settings. All four types of errors like Prescription errors, Transcription errors, Dispensing errors and Administration errors are rectified and officially reported by hospital pharmacists. Along with these, Prescription Reviewing, Medication Reconciliation, incidents of Adverse Drug Reactions (ADR) should also monitored to ensure rational drug use for patients.

E. Staff Training and Professional Credentialing- The ability for the human resources department to have greater reporting capabilities to determine license validity and visibility into license expiration. Non-compliance can be improved by simply reminding patients to take their medication. More information means a more compliant patient. As with the reminder services, the concept of providing information to improve compliance has been a highly appealing solution. Although understanding the condition and treatment is important, provision of information alone does not often provide the solution. There have been studies in chronic conditions such as asthma, hypercholesterolemia and diabetes that have seen drastically improvement of compliance.

F. Quality Monitoring- Henry Ford says "Quality is doing right when no one is looking". Capturing real time data to analyze the current quality efforts taken and compare them to other hospitals. In a world where clinicians have more demands and less time, one thing patients desire most often gets lost: connection. Patient experience leaders struggle to help busy practitioners understand that listening and building relationships can impact not only satisfaction scores, but also compliance and outcomes.

G. Patient satisfaction Observation: Concern over the quality of health care services in Bangladesh has led to loss of faith in public and private hospitals, low utilization of public health facilities, and increasing outflow of Bangladeshi patients to hospitals in neighboring countries. Under the circumstances, assessment of the country's quality of health care service has become imperative, in which the patient's voice must begin to play a greater role. There is little effort to involve them in measuring satisfaction or defining health service standards. Consequences of patient dissatisfaction can include patients not following treatment regimen, failing to pursue follow-up care and, in extreme cases, resorting to negative word-of-mouth that dissuades others from seeking health care from the system. Service orientation of doctors was found to be the strongest factor influencing patient satisfaction in hospitals.

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