



ROLE OF PHARMACIST IN MEDICAL ERROR AND MEDICATION ADHERENCE – A REVIEW

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ABSTRACT

A medical error is a preventable adverse effect of care, whether or not it is evident or harmful to the patient. This might include an inaccurate or incomplete diagnosis or treatment of a disease, injury, syndrome, behavior, infection, or other ailment. As a general acceptance, a medical error occurs when a health-care provider chose an inappropriate method of care or the health provider chose the right solution of care but executed it incorrectly. Medical errors are often described as human errors in healthcare. However, medical error definitions are subject to debate, as there are many types of medical error from minor to major, and causality is often poorly determined.

Keywords: Medical errors, medication adherence, Polypharmacy.

INTRODUCTION

A 2000 Institute of Medicine report estimated that medical errors are estimated to result in about between 44,000 and 98,000 preventable deaths and 1,000,000 excess injuries each year in U.S. hospitals. Some researchers questioned the accuracy of the IOM study, criticizing the statistical handling of measurement errors in the report and reporting both significant subjectivity in determining which deaths were avoidable or due to medical error and an erroneous assumption that 100% of patients would have survived if optimal care had been provided. A 2001 study in the Journal of the American Medical Association of seven Department of Veterans Affairs medical centers estimated that for roughly every 10,000 patients admitted to the subject hospitals, one patient died who would have lived for three months or more in good cognitive health had optimal care been provided.

A 2006 follow-up to the IOM study found that medication errors are among the most common medical mistakes, harming at least 1.5 million people every year. According to the study, 400,000 preventable drug-related injuries occur each year in hospitals, 800,000 in long-term

care settings, and roughly 530,000 among Medicare recipients in outpatient clinics. The report stated that these are likely to be conservative estimates. In 2000 alone, the extra medical costs incurred by preventable drug related injuries approximated \$887 million—and the study looked only at injuries sustained by Medicare recipients, a subset of clinic visitors. None of these figures take into account lost wages and productivity or other costs.

According to a 2002 Agency for Healthcare Research and Quality report, about 7,000 people were estimated to die each year from medication errors - about 16 percent more deaths than the number attributable to work-related injuries (6,000 deaths). Medical errors affect one in 10 patients worldwide. One extrapolation suggests that 180,000 people die each year partly as a result of iatrogenic injury. One in five Americans (22%) report that they or a family member have experienced a medical error of some kind.

Difficulties in measuring frequency of errors

About 1% of hospital admissions have an adverse event due to negligence. However, mistakes are actually

much more common, as these studies identify only mistakes that lead to measurable adverse events occurring soon after the errors. Independent review of doctors treatment plans suggests that 14% of admissions can have improved decision-making; many of the benefits would have delayed manifestations. Even this number may be an underestimate. One study suggests that, in the United States, adults receive only 55% of recommended care. At the same time, a second study found that 30% of care in the United States may be unnecessary. For example, if a doctor fails to order a mammogram that is past due, this mistake will not show up in the first study. And because no adverse event occurred during the short follow-up of the study, the mistake also would not show up in the second study, because only the principal treatment plans were critiqued. However, the mistake would be recorded in the third study. If a doctor recommends an unnecessary treatment or test, it may not show in any of the studies.

Medical errors are associated with inexperienced physicians and nurses, new procedures, extremes of age, complex care and urgent care. Poor communication (whether in ones own language or, as may be the case for medical tourists, another language), improper documentation, illegible handwriting, inadequate nurse-to-patient ratios, and similarly named medications are also known to contribute to the problem. Patient actions may also contribute significantly to medical errors. Falls, for example, are often due to patients own misjudgements. Human error has been implicated in nearly 80 percent of adverse events that occur in complex healthcare systems. The vast majority of medical errors result from faulty systems and poorly designed processes versus poor practices or incompetent practitioners.

Healthcare Complexity

- Complicated technologies, powerful drugs.
- Intensive care, prolonged hospital stay.
- System and Process Design

In 2000, The Institute of Medicine released *To Err Is Human*, which asserts that the problem in medical errors is not bad people in health care—it is that good people are working in bad systems that need to be made safer. Poor communication, unclear lines of authority of physicians, nurses, and other care providers.

Disconnected reporting systems within a hospital: fragmented systems in which numerous hand-offs of patients results in lack of coordination and errors.

- The impression that action is being taken by other groups within the institution.
- Reliance on automated systems to prevent error.
- Inadequate systems to share information about errors hamper analysis of contributory causes and improvement strategies.
- Cost-cutting measures by hospitals in response to reimbursement cutbacks.

- Environment and design factors. In emergencies, patient care may be rendered in areas poorly suited for safe monitoring. The American Institute of Architects has identified concerns for the safe design and construction of health care facilities.
- Infrastructure failure. According to the WHO, 50% of medical equipment in developing countries is only partly usable due to lack of skilled operators or parts. As a result, diagnostic procedures or treatments cannot be performed, leading to substandard treatment.
- The Joint Commissions Annual Report on Quality and Safety 2007 found that inadequate communication between healthcare providers, or between providers and the patient and family members, was the root cause of over half the serious adverse events in accredited hospitals. Other leading causes included inadequate assessment of the patients condition, and poor leadership or training.

Competency, Education, and Training

- Variations in healthcare provider training & experience,
- Failure to acknowledge the prevalence and seriousness of medical errors.
- The so-called July effect occurs when new residents arrive at teaching hospitals, causing an increase in medication errors according to a study of data from 1979-2006.

Human Factors and Ergonomics

Sleep deprivation has also been cited as a contributing factor in medical errors. One study found that being awake for over 24 hours caused medical interns to double or triple the number of preventable medical errors, including those that resulted in injury or death. The risk of car crash after these shifts increased by 168%, and the risk of near miss by 460%. Interns admitted falling asleep during lectures, during rounds, and even during surgeries.

- Fatigue,
- Depression and burnout.
- Diverse patients, unfamiliar settings, time pressures.
- Complications increase as patient to nurse staffing ratio increases.
- Drug names that look alike or sound alike.

Examples of errors

- Misdiagnosis of an illness, failure to diagnose or delay of a diagnosis. This type of error could be a direct mistake of a doctor or caused when the doctor is acting on incorrect information supplied by some other person.
- Giving the wrong drug or (wrong patient, wrong chemical, wrong dose, wrong time, wrong route)
- Giving two or more drugs that interact unfavorably or cause poisonous metabolic byproducts

- Wrong-site surgery, such as amputating the wrong limb
- Retained surgical instruments. In particular, gossypiboma, resulting from a surgical sponge being left behind inside the patient after surgery
- Patients implementation of drugs and treatments
- Using race as a diagnosis, not a factor
- Transplanting organs of the wrong blood type
- Incorrect record-keeping
- Misdiagnosis of psychological disorders
- Regarding mental illnesses, sufferers of dissociative identity disorder usually have psychiatric histories that contain three or more separate mental disorders and previous treatment failures. The disbelief of some doctors around the validity of dissociative identity disorder may also add to its misdiagnosis.
- Studies have found that bipolar disorder has often been misdiagnosed as major depression. Its early diagnosis necessitates that clinicians pay attention to the features of the patients depression and also look for present or prior hypomanic or manic symptomatology.
- The misdiagnosis of schizophrenia is also a common problem. There may be long delays of patients getting a correct diagnosis of this disorder.
- The DSM-5 field trials included test-retest reliability which involved different clinicians doing independent evaluations of the same patient -- a new approach to the study of diagnostic reliability.

Most common misdiagnoses

A 2009 meta-analysis identified the 5 most commonly mis-diagnosed diseases as: infection, neoplasm, myocardial infarction, pulmonary emboli, and cardiovascular disease. Physician familiarity with this information is variable.

Outpatient vs. inpatient

- Misdiagnosis is the leading cause of medical error in outpatient facilities.
- Ever since the National Institute of Medicines groundbreaking 1999 report, *To Err is Human*, found up to 98,000 hospital patients die from preventable medical errors in the U.S. each year, government and private sector efforts have focused on inpatient safety.
- After an error has occurred
- Mistakes can have a strongly negative emotional impact on the doctors who commit them.
- Recognizing that mistakes are not isolated events
- Some doctors recognize that adverse outcomes from errors usually do not happen because of an isolated error and actually reflect system problems. There may be several breakdowns in processes to allow one adverse outcome. In addition, errors are more common when other demands compete for a physicians

attention. However, placing too much blame on the system may not be constructive.

Placing the practice of medicine in perspective

Essayists imply that the potential to make mistakes is part of what makes being a physician rewarding and without this potential the rewards of medical practice would be less: if I left medicine, I would mourn its loss as I've mourned the passage of my poetry. On a daily basis, it is both a privilege and a joy to have the trust of patients and their families and the camaraderie of peers. There is no challenge to make your blood race like that of a difficult case, no mind game as rigorous as the challenging differential diagnosis, and though the stakes are high, so are the rewards.

Disclosing mistakes

Forgiveness, which is part of many cultural traditions, may be important in coping with medical mistakes.

Disclosure to oneself

Inability to forgive oneself may create a cycle of distress and increased likelihood of a future error. However, those who coped by accepting responsibility were more likely to make constructive changes in practice, but to experience more emotional distress. It may be helpful to consider the much larger number of patients who are not exposed to mistakes and are helped by medical care.

Disclosure to patients

Patients are reported to want information about what happened, why the error happened, how the errors consequences will be mitigated, and how recurrences will be prevented. Detailed suggestions on how to disclose are available. A 2005 study by Wendy Levinson of the University of Toronto showed surgeons discussing medical errors used the word error or mistake in only 57 per cent of disclosure conversations and offered a verbal apology only 47 per cent of the time.

Patient disclosure is important in the medical error process. The current standard of practice at many hospitals is to disclose errors to patients when they occur. In the past, it was a common fear that disclosure to the patient would incite a malpractice lawsuit. Many physicians would not explain that an error had taken place, causing a lack of trust toward the healthcare community. In 2007, 34 states passed legislation that precludes any information from a physicians apology for a medical error from being used in malpractice court (even a full admission of fault). This encourages physicians to acknowledge and explain mistakes to patients, and keeping an open line of communication. The American Medical Associations Council on Ethical and Judicial Affairs states in its ethics code:

- Situations occasionally occur in which a patient suffers significant medical complications that may have resulted from the physicians mistake or judgment. In these situations, the physician is ethically required to inform the patient of all facts necessary to ensure understanding of what has occurred. Concern regarding legal liability which might result following truthful disclosure should not affect the physicians honesty with a patient.

From the American College of Physicians Ethics Manual: In addition, physicians should disclose to patients information about procedural or judgment errors made in the course of care if such information is material to the patients well-being. Errors do not necessarily constitute improper, negligent, or unethical behavior, but failure to disclose them may. However, there appears to be a gap between physicians attitudes and practices regarding error disclosure. Willingness to disclose errors was associated with higher training level and a variety of patient-centered attitudes, and it was not lessened by previous exposure to malpractice litigation. Hospital administrators may share these concerns.

Consequently, in the United States, many states have enacted laws excluding expressions of sympathy after accidents as proof of liability; however, excluding from admissibility in court proceedings apologetic expressions of sympathy but not fault-admitting apologies after accidents.

Disclosure to non-physicians

In a study of physicians who reported having made a mistake, disclosing to non-physicians sources of support may reduce stress more than disclosing to physician colleagues. This may be due to the physicians in the same study, when presented with a hypothetical scenario of a mistake made by another colleague, only 32% physicians would have unconditionally offered support. It is possible that greater benefit occurs when spouses are physicians.

Disclosure to other physicians

Discussing mistakes with other doctors is beneficial. However, doctors may be less forgiving of each other. The reason is not clear, but one essayist has admonished, Dont Take Too Much Joy in the Mistakes of Other Doctors.

Disclosure to the physicians institution

Disclosure of errors, especially near misses may be able to reduce subsequent errors in institutions that are capable of reviewing near misses. However, doctors report that institutions may not be supportive of the doctor.

- Use of rationalization to cover up medical errors
- Based on anecdotal and survey evidence, Banja states that rationalization (making excuses) is very common

amongst the medical profession in covering up medical errors. Common excuses made are:

- Why disclose the error? The patient was going to die anyway.
- Telling the family about the error will only make them feel worse.
- It was the patients fault. If he wasnt so (obese, sick, etc.), this error wouldnt have caused so much harm.
- Well, we did our best. These things happen.
- If were not totally and absolutely certain the error caused the harm, we dont have to tell.
- By harm or not harm to patient
- A survey of more than 10,000 physicians in the United States came to the results that, on the question Are there times when its acceptable to cover up or avoid revealing a mistake if that mistake would not cause harm to the patient?, 19% answered yes, 60% answered no and 21% answered it depends. On the question Are there times when it is acceptable to cover up or avoid revealing a mistake if that mistake would potentially or likely harm the patient?, 2% answered yes, 95% answered no and 3% answered it depends.

Cause-specific preventive measures

Traditionally, errors are attributed to mistakes made by individuals who may be penalized for these mistakes. The usual approach to correct the errors is to create new rules with additional checking steps in the system, aiming to prevent further errors. As an example, an error of free flow IV administration of heparin is approached by teaching staff how to use the IV systems and to use special care in setting the IV pump. While overall errors become less likely, the checks add to workload and may in themselves be a cause of additional errors.

A newer model for improvement in medical care takes its origin from the work of W. Edwards Deming in a model of Total Quality Management. In this model, there is an attempt to identify the underlying system defect that allowed the opportunity for the error to occur. As an example, in such a system the error of free flow IV administration of Heparin is dealt with by not using IV heparin and substituting subcutaneous administration of heparin, obviating the entire problem. However, such an approach presupposes available research showing that subcutaneous heparin is as effective as IV. Thus, most systems use a combination of approaches to the problem.

In specific specialties

The field of medicine that has taken the lead in systems approaches to safety is anaesthesiology. Steps such as standardization of IV medications to 1 ml doses, national and international color coding standards, and development of improved airway support devices has made anesthesia care a model of systems improvement in care.

Pharmacy professionals have extensively studied the causes of errors in the prescribing, preparation, dispensing and administration of medications. As far back as the 1930s, pharmacists worked with physicians to select, from amongst many options, the safest and most effective drugs available for use in hospitals. The process is known as the Formulary System and the list of drugs is known as the Formulary. In the 1960s, hospitals implemented unit dose packaging and unit dose drug distribution systems to reduce the risk of wrong drug and wrong dose errors in hospitalized patients; centralized sterile admixture services were shown to decrease the risks of contaminated and infected intravenous medications; pharmacy computers screened each patients medication list for drug-drug interactions and, pharmacists provided drug information and clinical decision support directly to physicians to improve the safe and effective use of medications. Pharmacists are recognized experts in medication safety and have made many contributions that reduce error and improve patient care over the last 50 years. More recently, governments have attempted to address issues like patient-pharmacists communication and consumer knowledge through measures like the Australian Governments Quality Use of Medicines policy.

Legal procedure

Standards and regulations for medical malpractice vary by country and jurisdiction within countries. Medical professionals may obtain professional liability insurances to offset the risk and costs of lawsuits based on medical malpractice.

Methods to improve safety and reduce error

Medical care is frequently compared adversely to aviation: while many of the factors that lead to errors in both fields are similar, aviations error management protocols are regarded as much more effective.

- Patients informed consent policy
- patients getting a second opinion from another independent practitioner with similar qualifications
- voluntary reporting of errors (to obtain valid data for cause analysis)
- root cause analysis
- Electronic or paper reminders to help patients maintain medication adherence
- systems for ensuring review by experienced or specialist practitioners
- hospital accreditation
- Reporting requirements
- In the United States reporting medical errors in hospitals is a condition of payment by Medicare. An investigation by the Office of Inspector General, Department of Health and Human Services released January 6, 2012 found that most errors are not reported and even in the case of errors that are reported and

investigated changes are seldom made which would prevent them in the future. The investigation revealed that there was often lack of knowledge regarding which events were reportable and recommended that lists of reportable events be developed.

Misconceptions of medical error

Common misconceptions about adverse events are the following, and in parentheses are the arguments and explanations against those misconceptions:

- Bad apples or incompetent health care providers are a common cause. (Although human error is commonly an initiating event, the faulty process of delivering care invariably permits or compounds the harm, and is the focus of improvement.
- High risk procedures or medical specialties are responsible for most avoidable adverse events. (Although some mistakes, such as in surgery, are harder to conceal, errors occur in all levels of care. Even though complex procedures entail more risk, adverse outcomes are not usually due to error, but to the severity of the condition being treated.). However, USP has reported that medication errors during the course of a surgical procedure are three times more likely to cause harm to a patient than those occurring in other types of hospital care.
- If a patient experiences an adverse event during the process of care, an error has occurred. (Most medical care entails some level of risk, and there can be complications or side effects, even unforeseen ones, from the underlying condition or from the treatment itself.

Medication adherence

In medicine, compliance (also adherence or capacitance) describes the degree to which a patient correctly follows medical advice. Most commonly, it refers to medication or drug compliance, but it can also apply to other situations such as medical device use, self care, self-directed exercises, or therapy sessions. Both the patient and the health-care provider affect compliance, and a positive physician-patient relationship is the most important factor in improving compliance, although the high cost of prescription medication also plays a major role. Compliance is commonly confused with concordance. Concordance is the process by which a patient and clinician make decisions together about treatment.

Non-compliance is a major obstacle to the effective delivery of health care. Estimates from the World Health Organization (2003) indicate that only about 50% of patients with chronic diseases living in developed countries follow treatment recommendations. In particular, low rates of adherence to therapies for asthma, diabetes, and hypertension are thought to contribute substantially to the human and economic burden of those conditions. Compliance rates may be overestimated in the medical

literature, as compliance is often high in the setting of a formal clinical trial but drops off in a real-world setting. Major barriers to compliance are thought to include the complexity of modern medication regimens, poor health literacy and lack of comprehension of treatment benefits, the occurrence of undiscussed side effects, the cost of prescription medicine, and poor communication or lack of trust between the patient and his or her health-care provider. Efforts to improve compliance have been aimed at simplifying medication packaging, providing effective medication reminders, improving patient education, and limiting the number of medications prescribed simultaneously.

Terminology

An estimated half of those for whom treatment regimens are prescribed do not follow them as directed. Until recently, this was termed non-compliance, which was sometimes regarded as meaning that not following the directions for treatment was due to irrational behavior or willful ignoring of instructions. Today, health care professionals more commonly use the terms adherence to or concordance with a regimen rather than compliance, because these terms are thought to more accurately reflect the diverse reasons for patients not following treatment directions in part or in full. However, the preferred terminology remains a matter of debate. In some cases, concordance is used to refer specifically to patient adherence to a treatment regimen that is designed collaboratively by the patient and physician, to differentiate it from adherence to a physician only prescribed treatment regimen. Despite the ongoing debate, adherence is the preferred term for the World Health Organization, The American Pharmacists Association, and the U.S. National Institutes of Health Adherence Research Network.

Concordance also refers to a current UK NHS initiative to involve the patient in the treatment process to improve compliance. In this context, the patient is informed about their condition and treatment options. They are involved with the treatment team in the decision as to which course of action to take, and partially responsible for monitoring and reporting back to the team. Compliance with treatment is improved by:

- Only recommending treatments that are effective in circumstances when they are required
- Selecting treatments with lower levels of side effect or fewer concerns for long-term use
- Prescribing the minimum number of different medications, e.g., prescribing a single antibiotic that addresses two concurrent infections (though risking contributing to antibiotic resistant species development)
- Simplifying dosage regimen by selecting a different drug or using a sustained release preparation that needs fewer doses during the day

- Discussing possible side effects, and whether it is important to continue medication regardless of those effects
- Advice on minimising or coping with side effects, e.g., whether to take a particular drug on an empty stomach or with food
- Developing trust so patients don't fear embarrassment or anger if unable to take a particular drug, allowing the doctor to try a better tolerated alternative

Societal impact

A WHO study estimates that only 50% of patients suffering from chronic diseases in developed countries follow treatment recommendations. This may affect patient health, and affect the wider society when it causes complications from chronic diseases, formation of resistant infections, or untreated psychiatric illness. Compliance rates during closely monitored studies are usually far higher than in later real-world situations. For example, one study reported a 97% compliance rate at the beginning of treatment with statins, but only about 50% of patients were still compliant after six months.

Compliance issues

1. Prescription fill rates

While a health care provider visit with a patient may result in the patient leaving with a prescription for medication, not all patients will fill the prescription at a pharmacy. In the U.S., 20-30% of prescriptions are never filled at the pharmacy. There are many reasons patients do not fill prescriptions including the cost of the medication, doubting the need for medication, or preference for self-care measures other than medication. Cost may be a barrier to prescription drug adherence, but convenience, side effects and lack of demonstrated benefit are also significant factors to a complex situation. A US nationwide survey of 1,010 adults in 2001 found that 22% chose not to fill prescriptions because of the price, which is similar to the 20-30% overall rate of unfilled prescriptions. However, analysis by health insurers suggest that patient co-payment requirements can be reduced to \$0 with little or no improvement in long-term adherence rates.

2. Course completion

Once started, patients seldom follow treatment regimens as directed, and seldom complete the course of treatment. Cost and poor understanding of the directions for the treatment (referred to as health literacy) are major barriers to completing treatments. As mentioned previously, the World Health Organization (WHO) has estimates that only 50% of people complete long-term therapy for chronic illnesses as they were prescribed, which puts patient health at risk.

A wide variety of packaging approaches have been proposed to help patients complete prescribed treatments. These approaches include formats that increase the ease of remembering the dosage regimen as well as

different labels for increasing patient understanding of directions. For example, medications are sometimes packed with reminder systems for the day and/or time of the week to take the medicine. With the objective to support patient adherence to medicinal therapy, a not-for-profit organization (Healthcare Compliance Packaging Council of Europe/HCPC-Europe) was set up between the pharmaceutical industry, the packaging industry and representatives of European patients organizations. The mission of HCPC-Europe is to assist and to educate the healthcare sector in the improvement of patient compliance through the use of packaging solutions. A variety of packaging solutions have been developed by this collaboration to aid in patient compliance.

The failure to complete treatment regimens as prescribed has significant negative health impacts worldwide. Examples of the rate and consequences of non-compliance for selected medical disorders is as follows:

- Diabetes non-compliance (98% in US) is the principal cause of complications related to diabetes including nerve damage and kidney failure
- Hypertension non-compliance (93% in US, 70% in UK) is the main cause of uncontrolled hypertension-associated heart attack and stroke
- Asthma non-compliance (28-70% worldwide) increase the risk of severe asthma attacks requiring hospitalization.

Polypharmacy is the use of multiple medications by a patient, especially when too many forms of medication are used by a patient, when more drugs are prescribed than is clinically warranted, or even when all prescribed medications are clinically indicated but there are too many pills to take (pill burden). Furthermore, a portion of the treatments may not be evidence-based. The most common results of polypharmacy are increased adverse drug reactions, drug-drug interactions and higher costs. Polypharmacy is most common in the elderly but is also widespread in the general population. Polypharmacy is most common in people with multiple medical conditions. Combination therapy is the use of multiple drugs specifically to treat a single medical condition; monotherapy is the use of a single drug.

Pill burden

Pill burden is a term that refers to the number of tablets, capsules or other dosage forms that a patient takes on a regular basis. High pill burden decreases compliance with drug therapy, resulting from the need to take a large quantity of pills or other forms of medication on a regular basis. It also increases the possibility of adverse medication reactions (side effects) and drug-drug interactions. High pill burden has also been associated with an increased risk of hospitalization, medication errors, and increased costs for both the pharmaceuticals themselves and for the treatment of adverse events. Finally, pill burden is a source of dissatisfaction for many patients.

High pill burden is commonly associated with antiretroviral drug regimens to control HIV, but can be seen in other patient populations. For instance, adults with multiple chronic conditions such as diabetes, hypertension, lymphedema, hypercholesterolemia, osteoporosis, constipation, and clinical depression can often be prescribed more than a dozen different medications daily. The adverse reactions of these combinations of drugs are not reliably predictable. Obesity is implicated in many of the aforementioned conditions, and it is not uncommon for a clinically obese patient to receive pharmacologic treatment for all of these. Because chronic conditions tend to accumulate in the elderly, pill burden is a particular issue in geriatrics.

Reducing pill burden is recognized as a way to improve medication compliance. Common approaches for reducing pill burden include selecting fixed dose combination drug products, products with long-acting active ingredients, and sustained release/extended release formulations when appropriate. Some combinations of drugs may be available in certain strengths as a single pill, called a fixed dose combination. One notable example of a fixed dose combination drug product is the antiretroviral drug product Atripla, which combines 3 drugs (efavirenz + emtricitabine + tenofovir) into one pill.

The selection of long-acting active ingredients over short-acting ones may also reduce pill burden. For instance, ACE inhibitors are used in the management of hypertension. Both captopril and lisinopril are examples of ACE inhibitors. However, lisinopril is dosed once a day, whereas captopril may be dosed 2-3 times a day. Assuming that there are no contraindications or potential for drug interactions, using lisinopril instead of captopril may be an appropriate way to limit pill burden. Similarly, sustained release/extended release drug formulations reduce pill burden by reducing the dosing frequency. The same active ingredient is present in both the immediate-release form and the sustained release form.

At risk demographic groups

Patients at greatest risk of polypharmacy consequences include the elderly, psychiatric patients, patients taking five or more drugs concurrently, those with multiple physicians and pharmacies, recently hospitalized patients, individuals with concurrent comorbidities, low educational level, and those with impaired vision or dexterity.

Adverse reactions and interactions

Every medication has potential adverse side-effects. With every drug added, there is an additive risk of side-effects. Many medications have potential interactions with other substances. As a new drug is prescribed, the risk of interactions increases exponentially. Doctors and pharmacists aim to avoid prescribing medications that interact; often, adjustments in the dose of medications need

to be made to avoid interactions, such as with warfarin, as it may lose its effect.

Thoughtful versus thoughtless polypharmacy

A patient with a complex or even an ostensibly straightforward illness whose personal pharmacopoeia reads like a drug store pharmacy is not necessarily receiving poor treatment. A carefully followed patient with whom a physician is using additive drug choice and dosage range on a trial and error basis may lead to a treatment program that, for a real example, includes two antidepressants, three antihypertensives, a beta blocker, a calcium channel blocker, a bone saving bisphosphonate, an antiepileptic, a stomach saving H2 blocker, aspirin, prostaglandin blocker, lactoferrin, a calcium-magnesium supplement and herbal preparations.

Two generally true circumstances underlie the theory of thoughtful, therapeutic polypharmacy: (1) Drugs given for a single somatic locale act on biochemical mechanisms present throughout the body such that their nonlinear interactions can produce an (unknown except empirically) global physiological state of health; (2) The more independent variables, handles, to manipulate, the greater the likelihood of finding and stabilizing a small available parametric space of healthy function while minimizing unwanted effects.

The use of multiple pharmaceuticals to treat a single illness is often the result of a healthcare practitioner attempting, usually through trial and error, to obtain the highest efficacy through the concept of drug synergy. Often certain medications can interact with others in a positive way specifically intended when prescribed together to achieve a greater effect than any of the single agents alone. This is particularly prominent in the field of anesthesia and pain management, where atypical agents such as antiepileptics, antidepressants, muscle relaxants, NMDA antagonists, and other medications are combined with more typical analgesics such as opioids, prostaglandin inhibitors, NSAIDs and others. This practice of pain management drug synergy is known as an analgesia sparring effect. In anesthesia, particularly IV anesthesia and General anesthesia, multiple agents are almost always required, including hypnotics or analgesic

inducing/maintenance agents such as Versed or Diprivan, usually an opioid analgesic such as morphine or Demerol, a paralytic such as vecuronium, and in inhaled general anesthesia generally a halogenated ether anesthetic such as sevoflurane or desflurane.

Misuse

It is not uncommon for those dependent or addicted to substances to enter or remain in a state of polypharmacy misuse. One of the best examples includes those who chronically or acutely binge on amphetamines or other psychostimulants (particularly those with long half lives such as the amphetamines and methylphenidate). Because these agents have the effect of reducing or eliminating sleep for long periods of time, when sleep is finally desired or in an effort to reduce the crash, hypnotics such as benzodiazepines, sometimes opiates, and less frequently barbiturates are used to induce sleep. Another classic example of concurrent polypharmacy misuse is the speedball, a solution of typically cocaine and heroin in the same syringe which is injected together. Other combinations like amphetamines, methylphenidate and morphine, oxycodone, hydrocodone etc. are also used and sometimes taken orally. The classic combination of cocaine and heroin injection has resulted in numerous high profile deaths as the stimulant effect of cocaine (which has a notably short half-life) last much shorter than the depressant effects of opiates, which can then induce respiratory depression, respiratory arrest, and death.

CONCLUSION

The present review concluded that clinical pharmacists performing drug therapy reviews and the teaching of physicians and their patients about drug safety and polypharmacy, as well as collaborating with physicians and patients to correct polypharmacy problems. This led to a marked improvement in interactions and cost. Similar programs are likely to reduce the potentially deleterious consequences of polypharmacy. Such programs hinge upon patients and doctors informing pharmacists of other medications being prescribed, as well as herbal, over-the-counter substances and supplements that occasionally interfere with prescription-only medication.

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