

FACTORS AFFECTING RATIONAL DRUG USE (RDU), COMPLIANCE AND WASTAGE

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Abstract

Irrational drug use and unused drug waste are considerable problems in the modern world. The main aim of this review is to evaluate the different aspects and indicators of rational drug use from a clinical pharmacist perspective. Pharmacists are in the ideal position to make the patient aware of rational drug use and to reduce pharmaceutical waste. The factors affecting rational drug use are similar for unused drugs and drug wastage. The result of irrational drug use affects not only the recovery of the patient but also the society socially, economically, and culturally. Most of the irrational use problems may be able to be solved by appropriate education.

Key words: Rational drug use, Unused drugs, Compliance.

Akılci İlaç Kullanımını (AİK), Uyunc ve İlaç İsrafını Etkileyen Faktörler

Akılci olmayan ilaç kullanımı ve kullanılmayan ilaçların israfı modern dünyanın önemli problemleri arasındadır. Bu derleme çalışmasındaki ana amaç, klinik eczacı bakış açısı ile, akılci ilaç kullanımını etkileyen faktörleri değerlendirmektir. Eczacılar toplumu akılci ilaç kullanımına teşvik etmek ve ilaç israfını önlemek ve bu konularda eğitim ve yönlendirme yapmak konusunda ideal bir konumdadırlar. Akılci ilaç kullanımı ve ilaç israfını etkileyen faktörler çok benzerdir. Akılci olmayan ilaç kullanımı sadece iyileşme sürecini değil, aynı zamanda toplumu da ekonomik ve kültürel olarak da etkilemektedir. Akılci olmayan ilaç kullanım problemleri uygun eğitimle çözümlenebilir.

Anahtar kelimeler: Akılci ilaç kullanımı, Kullanılmayan ilaçlar, Uyunc.

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INTRODUCTION

As a global issue, rational drug use is a multifaceted subject. The role of governments, drug authorities, society, manufacturers, the educational system, media, patients and other health care workers cannot be denied. The responsibility of health care professionals has assumed great significance, and in recent decades, the pharmacist's role in therapy has expanded. Many factors have an influence on prescribing and have expanded the pharmacist's role from a passive dispenser to an active participant in the therapeutic decision-making team (1).

All the services performed by pharmacists practicing in hospitals, community pharmacies, nursing homes, home-based care services, clinics and any other setting where medicines are prescribed and used, are included in the remit of clinical pharmacy (2).

Promoting the correct and appropriate use of medicinal products and devices is the main goal of clinical pharmacy activities. The clinical pharmacist's activities can be summarized as following: consulting, selection of drugs, drug information, formulation and preparation, drug use studies and research, pharmacokinetics/ therapeutic drug monitoring, clinical trials, pharmaco-economy, dispensing & administration, teaching & training. The aims of these activities are to maximize the clinical effect of medicines, to minimize the risk of treatment-induced adverse events and to minimize the expenditures for pharmacological treatments for the national health systems and for the patients (2,3).

The pharmacy profession plays a key role in reducing medical errors by making appropriate interventions at each stage. By first recording potential harm to the patient, appropriate pharmacy interventions to increase patient safety can be made; these interventions are recognized as key steps in the medication-use process (4).

The aim of this review is to evaluate the different aspects and indicators of Rational Drug Use (RDU) from a clinical pharmacist perspective. The role of the pharmacist in RDU is important for all healthcare providers. Pharmacists are in the ideal position to make the patient aware of rational drug use, to improve the patient's quality of life, and also to reduce pharmaceutical waste.

RATIONAL DRUG USE

Correct and appropriate use of medicines is one of the most important facets in the therapy of a disease. Focusing on terminology, it should be noted that in 1985 at the Nairobi Conference WHO defined the term 'RDU' as "where patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements for an adequate period of time, and at the lowest cost to them and their community" (5, 6). Pharmaceutical care and clinical pharmacy services have evolved to ensure RDU while aiming to reduce waste and increase the patient's quality of life.

RDU is closely related to the continuous support of drug information. Every step of the decision making process for RDU requires adequate drug information. Drug information must be objective, accurate, complete, up-to-date, accessible and serviceable; but it also must be continually improving (7).

When RDU cannot be achieved, drug wastage, environmental pollution, increased mortality and morbidity, increased adverse drug reactions and hospitalization, and wasted economical resources will result.

From correct diagnosis to rational therapy, several factors affect the improvement of health status. In terms of medical therapy the real determinant is the patient. It is a paradox that patients remain largely passive in consultations while needing to be active in their own medicines management and behavior changes. The general approach in consultations remains giving advice with the expectation that health-care professional's expertise will lead to patient

compliance. Health-care professionals are frustratingly aware that this approach does not work efficiently, but continue to struggle with it for want of a better strategy (8). To make patients stick to the therapy, some approaches have evolved such as compliance, adherence and concordance.

Definition of the Terms Compliance, Adherence and Concordance

Instead of compliance or adherence, some researchers are using the term concordance to acknowledge the more active role that the patients should play in negotiating the treatment regimen. The term compliance is defined as: “the extent to which the patient follows the health professionals’ advice and takes the treatment” (8, 9, 10). Compliance can be perceived as obeying the advice. The definition of patient adherence is “the extent to which a person’s behavior (taking medication, following a diet, and/or executing lifestyle changes) corresponds with agreed recommendations from a health-care provider” (8, 11). Adherence was the first term that was used to acknowledge patient involvement in therapy decisions. The term concordance is defined as “an agreement reached after negotiation between a patient and a healthcare professional that respects the beliefs and wishes of the patient in determining whether, when and how medicines are to be taken and the primacy of the patient’s decision is recognized” (8, 12). As can be seen, concordance recognizes a more active patient role.

Patient preference is important, since it directly translates into patient satisfaction. In this regard, patient satisfaction is highly correlated with being compliant with the treatment regime and improved patient care (13).

Patients also show immense variation in their desire for a degree of involvement and shared decision making. A national survey in the United States of America (USA) showed that about half of population prefer to leave decisions ultimately to their doctor whilst nearly everyone wants to be offered choices and asked their opinion (14). Some patients may perceive as oppressive a decision-making approach inflexibly imposed by practitioners (15). While the majority of patients prefer patient-centered communication, some say they actually do not like it and want more directive styles with clear and strong advice (16). However, health consumers seem to gain satisfaction from a more patient-centered approach (8).

The term compliance is sometimes used in general for all of the above concepts, and has been taken to mean the patients adherence to therapy leading to the realization of RDU. The actual and scientific meaning of compliance, adherence and concordance have been given above, but generally terms compliance, adherence and concordance are used interchangeably and this has generated some confusion (17).

In Turkish, there are no words corresponding separately to the terms compliance, adherence and concordance. In this review, the term compliance will be used for all of these expressions, meaning the patients’ application of therapy in real life.

Linguistically and culturally, compliance, adherence and concordance may have variants but the factors affecting both RDU and these concepts are tried to be summarized in below.

FACTORS RELATED TO COMPLIANCE

Patient and therapy

If the steps of diagnosis, prescription, and dispensing of medical treatment are correctly followed, the most important part of RDU, the key determinant role, is the acceptance of therapy by patient (18).

Many variables play a role in compliance for any given medical regimen, and for any given patient. Due to the complexity of the variables determining compliance, they can be divided into different groups as below:

The illness

The potency of the drug, hospitalization due to the illness, and diagnosis of the problems caused by the illness has shown to have no correlation with the degree of compliance (19,20). Also there is no consistent evidence indicating that sicker patients have better compliance with their therapy than healthier ones (21).

Sociological factors

According to most studies, there is no consistent correlation between socio-economic status, age, sex, education, occupation, income, or marital status and compliance. (19,20,22,23). However, these factors can be determinants when a specific region, condition and population are selected. For example, elderly patients do not usually comply to the medical regimen; but this is not only related to age alone, it is also probably related to memory and sensory impairments (24). So compliance and demographic data do not correlate with each other, they only may have predictive value.

Patients' knowledge of their disease

It has been observed that educational attempts alone individually do not demonstrate any consistent effect on compliance (25); especially in chronic conditions, patients need to know all aspects of their illness, symptoms, what happens if the therapy is not accepted and necessary changes on life style.

Patients' knowledge of their medications

Patients' information about the purpose of the drugs that have been prescribed for the patient can decrease compliance errors. In addition, according to one study, when the patient knows the name of the drug that has been prescribed, there are fewer errors in drug-taking (22). In a study conducted in the United Kingdom it was found that exploring how patients' drugs worked for them was effective in revealing their beliefs about medicines, and often led naturally on to a candid account of actual use (26).

The medical regimen

Polypharmacy (the use of multiple medications) increases compliance errors (27). Multiple medication signifies the complexity of the regimen and discourages the patients from complying (22,28,29). A simplified drug regimen is more effective in ensuring compliance. Planning the drug administration time around the patients' daily routine, like bedtime, after or before meals leads to better compliance (21).

Medication Side Effects

Side effects are a reason for noncompliance. Patients should be informed about the side effects of the drug that have been prescribed (30). However, if the patients know what they will experience, it can be easier to accommodate for (21).

Patients' beliefs and attitudes towards health and illness

The foundations of patients' beliefs are formed by personal experience, along with the experiences of their acquaintances. These beliefs could either be true or misleading, based on objective truth or on misconception. Especially in asymptomatic conditions, such as following a diagnosis of hypertension, misunderstanding can be a particular problem, when the usual explanations may not be accepted as valid. Sociological studies show that patient beliefs about medicines arise from many sources and can affect use substantially. The acceptance level of patients of their illness and therapy is reflected in the way that conditions are described, particularly when discussing their initial diagnosis. When informing the patients about their illness, the language and tone used could indicate major underlying tensions. Using personal pronoun for medications and illnesses described, such as "my" (implying ownership, rather than 'it', implying distance), is a sign of acceptance. Appropriate adjustments such as comfortably habitual medication use indicate the acceptance of illness. Reluctance to accept their situation could be reflected by anger and/or denial, which hinder other lifestyle changes, as well as medication use (26).

According to the literature, when the patient has the following beliefs and attitudes, compliance is better (30,31):

- Susceptibility to the illness or its complications,
- The belief that the illness or complications of it can lead to severe consequences for life,
- The belief that the therapy will decrease the effect and complications of illness
- Absence of obstacles like side effects, high cost, inaccessibility to therapy to engage in the medical regimen.

Involvement of the spouse and family support

Support of family members and spouse towards the illness or the medical regimen is a very important variable influencing compliance (21). Especially in pediatric populations, the mother's attitude and the physician are the real determinants (32,33,34). Disorganized family, strife, and emotional turmoil lead to increase in risk for noncompliance (35,36). On the other hand, social support and close and stable relationship in the family helps in compliance (37).

The Doctor-Patient Relationship

It is of vital importance that the patient and doctor have good communications. Agreement about what is expected of the patient and dependence on instructions regarding therapy increases compliance (22,38). Research indicates that compliance is more likely to be improved if (33,34,39):

- Expectations of the patient are being met
- There is a perception of warmth and empathy in the patient-doctor communication
- Explanation of diagnosis is made
- Addressing questions and concerns of the patient

Psychiatric Factors

The ways in which patients characteristically deal with stress or illness may partially determine their degree of compliance (21). Psychological aspects of the illness concept is a variable in compliance. According to Lipowski, illness concepts can be described in eight different ways whereby the individual gives meaning to their illness, injury or disability (25): illness as challenge, illness as enemy, illness as punishment, illness as weakness, illness as relief, illness as strategy, illness as irreparable loss or damage, illness as value.

Significance of illness depends on personal experience and knowledge. Perception of the illness is predominantly conscious. However, this perception is also partly subconscious, and can function as a cognitive nucleus affecting emotional or motivational responses (40).

Adequate information

Surveys show that satisfaction with information provided about illness and the medical regimen can increase compliance. However, most patients indicate lack of information provided in consultation (41, 42). On the other hand, patients remember about 60% of what they have been told (8, 43). The information remembered depends upon salience and the time in the consultation when it was imparted. The most likely words to be remembered are the first things said (8, 44).

Special patient and disease groups

Different disease conditions need different approaches when it comes to RDU and compliance. Chronic illnesses should be handled individually due to their specific treatment options, life style changes etc. Patients with chronic conditions have a higher rate of noncompliance due to long-term and complex medical therapy that calls for changes in existing behavioral patterns (43).

Examples of these chronic disease and studies related to them can be seen below:

Cardiovascular diseases

In the present day, one of the leading causes of death is cardiovascular disease. Researchers estimate that some form of cardiovascular disease can be observed in one fifth of the population. Noncompliance is a considerable reason for the increasing number of deaths related to cardiovascular disease (43). For example, since in hypertension it is not subjectively observable that the therapy improves the health situation of the patient the individual receiving therapy tends to be noncompliant or only partially compliant (45).

Diabetes

Recent estimates indicate there were 171 million people in the world with diabetes in the year 2000, and this is projected to increase to 366 million by 2030 (46). Research suggests that diabetes care is mostly performed by patients themselves, at a rate of 95%. More than simply administering medication, diabetes necessitates complex and strict life style changes. In addition to fairly rigid dietary and exercise plans, patients should be properly taking doses of insulin and/or oral anti-diabetic medications (43). So, the complex nature of therapy leads to high rates of noncompliance (8,43). Education about self care and convincing patients to comply with medical regimens are highly essential for this patient group (47). Especially, foot care, insulin taking and other crucial topics have to be focused on.

Elderly and multiple chronic conditions

It appears extremely difficult to achieve RDU in this group. The existence of multiple chronic conditions leads to poly-pharmacy (48). Polypharmacy can easily result in drug-related problems (DRPs), including untreated indications, drug use without an indication, improper drug selection, subtherapeutic dosage, overdosage, medication error, medication nonadherence, drug interactions, adverse drug reactions, adverse drug withdrawal events, and therapeutic failure (49).

In addition to these, elderly patients have difficulty in remembering, understanding the therapy and reading written labels and prescriptions (50, 51). Noncompliance among elderly is estimated to be high, because of the difficulties noted above. When the elderly individual has a spouse, a family member or a care-giver to assist with their medical regimen, it improves the compliance of this patient group (48).

Pharmacist interventions, home visits, medicine reminder cards, pill organizers, and medication summaries can be beneficial in terms of therapy compliance in the elderly. According to studies, interventions increase the compliance and decrease drug related problems in elderly (49, 52).

Psychiatric disorders

One of the groups which can be hard to manage is the psychiatric group. Because generally, they tend to be unaware about the need for therapy, compliance rates are very low. It has been observed by researchers that when the condition is under control, the patient is more likely to abandon the anxiolytic or depression treatment procedure (50, 53). Self-adjustment of the dosage of benzodiazepines is another dangerous habit that patients on anxiolytics fall into (54,55). Torun et al. observed that in patients with anxiety, when the effects of the medication decrease, the compliance of the patient also decreases (56). In a study conducted in Turkey, most patients with depression and anxiety admitted having been noncompliant. About 30% of these noncompliant patients quit the therapy on the premise that "I can get by without medication". This shows that if patients feel better, the risk of noncompliance will manifest itself. So these patients' compliance must be monitored frequently. Also, it is known that one in seven of these patients stop taking medication because of the side effects (57). Interventions by the pharmacist have positive effects on the patients using psychotropic agents (49).

AIDS (Acquired immune deficiency syndrome)

AIDS is a worldwide epidemic which has affected millions of people. It has quite a complex drug therapy. Innovations in effective AIDS therapy including HAART (highly active antiretroviral therapy) provides the possibility of significantly controlling the effects of AIDS. Failure in treatment is mainly caused by low compliance rates with the HAART regimen (58). Because of the complex nature of the disease and its therapy, patients struggle to understand the importance of compliance to treatment. Abandonment of drug regimen due to side effects is also possible, if the patient does not consider the life-prolonging effect of the regimen. Education given by a pharmacist or other health care professional about the disease and the therapy has vital significance in AIDS (43).

Pediatrics

A determinant of compliance in pediatric conditions is the parents attitude toward the illness and the therapy. Actually, the patients are often passive due to dependence on an adult care giver, and are less likely to follow a medical regimen than adults who are active in managing their condition (59). Acceptance of the family improves compliance in pediatric patients (60).

REASONS FOR NONCOMPLIANCE AND IRRATIONAL DRUG USE

Noncompliance is a complicated problem which has many variables in itself. Due to this variability, the reasons for noncompliance are numerous. The presence of one or more variables, can lead to noncompliance to the medical regimen. Reasons for noncompliance can be divided into groups to which the variables belong (6, 61):

Doctor and healthcare professional related reasons

At the top of the health chain is the doctor. Good communication between doctor and patient is of vital importance, so that many of the reasons for noncompliance originating from misunderstanding can be avoided.

Inadequate information about the disease, therapy options, medication etc. provided by the doctor is an important factor. Not to check the patient's understanding and recall can result in noncompliance also (62,8). When the patients do not know the mechanism of action and common side effects of the drug, they tend to abandon the therapy (8,48). The pressure to shorten the consultation and avoid an in-depth investigation of the patients concerns is another cause (63). The right atmosphere, warmth and empathy are important but are not always easily achieved (8). Giving suboptimal time to the patient can trigger noncompliance (62).

Deficient training of the medical students can result in inappropriate prescribing. In addition to this, to satisfy the patients' expectations and demands for quick relief, health care professionals can prescribe drugs irrationally (62). Lack of information about pharmacotherapy in the clinical setting is a key issue (64). Mistakes in diagnosis and errors in the medication regimen can also be a reason for irrational drug use and noncompliance (62). The patients' lack of trust in the doctor and the impression that she/he is not genuinely interested in them as patients can be another reason for noncompliance (65).

Dispensing system and pharmacist related reasons

The dispensing of medication is a huge responsibility. The pharmacists as dispensers have to be aware of this responsibility. A defective system for drug supply, and a disorganized dispensing and counseling process can be a cause of noncompliance (62). In some countries like Turkey, patients can buy drugs without the need of a prescription, and self medication is practiced (7). Moreover, the presence of a large number of medications on the market is another problem (62). Also pharmacists may advise inappropriate over the counter (OTC) medication consciously (seeking profit) or unconsciously. Sometimes the patient does not want to use extra drugs and can give up taking drugs, thus causing noncompliance (7).

Health System Related Reasons

It is really important that the health care facilities be easily accessible. Inadequate access to medical facilities and care is attributed as a reason for poor compliance (66). Economic problems of patients who do not have health insurance can also be a reason for irrational drug use and noncompliance (43, 67). On the other hand it has been observed that in Turkey, people with the health insurance can demand prescriptions from health care professionals more easily and put pressure on the doctors to write prescriptions for them. (3, 7). Some of the items on the prescription are reimbursable. Patients may easily give up using medicines which are reimbursed. The government is perusing a policy of imposing restrictions on more expensive medicines in order to reduce the drug budget. Each day more medicines are being excluded from the reimbursable medicine list to reduce the somewhat needless burden of medical expenses.

Patient Related Factors

As real determinants of compliance, patient characteristics predominate. In general, none of demographic factors such as age, marital status, living alone, sex, race, income, occupation, number of dependents, intelligence, level of education, or personality type have been shown to be consistently related to compliance (43). However, these factors can have a considerable effect. Especially age and mental awareness are significant factors in the process of compliance (3). Elderly patients have poor compliance rates as mentioned before (48, 51). Difficulty in reading is another factor which might affect compliance. Unless the patient can read the label on the medicine container, the directions for using the medicine, or even the prescription, he/she is not likely to be compliant with therapy (51). Patient dissatisfaction, seen as active questioning or being anxious about therapy, is also an indicator of noncompliance (3). When the patients get ill, they tend to be anxious and anxiety can adversely affect cognition (8). The habit of storing medicines in various places in the home may result in unintentional noncompliance (68). Patients taking drugs for multiple chronic illnesses can easily get mixed up and forget to take their medication (43).

It is of crucial importance that the patients understand what their problem is and what they have to do to apply their therapy. The patients cannot comply with treatments unless they clearly understand the treatment directions (51). They tend to forget a major proportion of the information which they learnt during consultations with the health care professional (43). Belief that side effects will occur, the drug is useless or the illness is unimportant etc. can be a reason for noncompliance (65).

Disease Related Factors

Characteristics of the disease may affect the patient and their compliance with the therapy. Acute diseases can get worse, if the proper treatment is not applied. However, it is especially in chronic diseases where failure to comply can be seen more often. Compliance to therapy is influenced by the nature of the disease such that patients tend to quit the medical regimen unless they feel the symptoms of the disease. Diseases like hypertension which develop without symptoms can be a reason for noncompliance (8,43). Due to long term or life-long treatment needs, chronic patients can be noncompliant either partially or completely, depending upon the state of the disease (57).

In psychiatric diseases such as anxiety and depression, patients are more likely to abandon the therapy when they feel better (57).

Therapy or drug related factors

Features of the drug therapy can be the reason for noncompliance. Complex therapy and long term usage are frequently cited as a cause for being noncompliant (66). Improper timing of drug administration is more likely to occur if the medical regimen is complex and requires the administration of several medications continually, or at unusual times during the day. This situation can disturb the patient and can cause him/her to quit the medication or get confused about the drugs (43, 69). Side-effects of the drugs are another big problem in compliance. Intolerance of the side-effects can lead the patient to abandon the drug, especially if a multiple drug regimen exists (69). In addition, factors such as, difficulties in swallowing, tableting errors (pills which are too small or too big), bad taste, drugs which have passed the expiration date, can result in noncompliance (65,66,69,70).

Besides this, generic substitution of the original drugs is an additional challenge for the patients. The patients may feel insecure about the situation, and it was even observed that some patients took the brand product as well as the non-branded substituted product at the same time

(71). Also, some patients were of the opinion that cheaper generic drugs were counterfeit and stopped taking their medication (72).

Drug Manufacturers Related Reasons

Sometimes, factors related to pharmaceutical companies can influence compliance. Advertisements for OTC drugs can convince people to buy the product, but finally most of this kind of OTC use results in the patient stopping taking the “real” medication (7). Promotional activities of the pharmaceutical manufacturers may affect rational prescribing and also compliance in turn (62, 73). The quality of the containers is an aspect often neglected, but a study conducted in Texas University indicated that if patients do not like the container, they may choose to keep the drugs elsewhere and consequently they may lose the information on the label, and in the end noncompliance occurs (12). If the medication package insert, product information leaflet and/or label of the medicine are not clear, then the patient cannot understand the written directions and becomes confused (7, 65).

Environmental Reasons

The environment where the patient has lived and grown up may be a factor to be taken in consideration. Family, friends and societies that have negative beliefs about drug use can influence the patients’ usage. Discouragement of medicine taking is an important reason for noncompliance (60). On the other hand, in a context where there is excessive medication use, this can lead to irrational use of medication (66).

Above all, if the patients are elderly mentally or cognitively impaired, the presence of a helper or a family member who remembers to collect their medications, decreases the rate of noncompliance (7,51, 60). Also, if the patient is pediatric, the parents will determine the usage of the medication and their attitudes will predominate. Noncompliance is inevitable, unless the parents are aware of the importance of the therapy and the disease (59, 60).

STUDIES RELATED IRRATIONAL DRUG USE

Irrational drug use is a hazardous habit and as a consequence many different problems arise. Ineffectiveness in treatment and lack of safety of the therapy, exacerbation or prolongation of disease, distress and harm to the patient, increase in the cost of the therapy, and wastage of resources are the main hazards caused by irrational drug use (62,74).

One study from Tanzania indicates that less than one in four patients correctly use prescribed medical treatments (75). Reports exist from many developing countries describing patterns of drug use in a range of health settings, including hospitals, health centers, private practitioner practices, and pharmacies. These reports routinely highlight similar problems in drug utilization: poly-pharmacy (due both to multiple prescriptions and the prescribing of fixed combination drugs); too frequent and unnecessary use of antibiotics, injections, or vitamins; use of incorrect medications to treat specific problems; and so forth (73, 76). In addition to these, hoarding expired or surplus medicines in the home, taking or giving them to friends and family members are frequently observed problems that may lead to accidental or inappropriate ingestion (18, 70). Besides this, people can give advice about medicine to friends and family, and vice versa patients can seek advice from family and friends who are not health-care professionals. Use of medication without medical consultation may result in serious health problems. In countries like Turkey, people can buy drugs without prescription (except for controlled drugs), and so self-medication rates have been reported to be high, and can be the cause of wasted resources, the emergence of resistant strains of microorganisms, and serious adverse reactions and toxicity (3, 68). Drugs are purchased with and without prescriptions and

are stored in different places in the home. Some places in the home are not suitable for keeping drugs and can easily cause the degradation of the drug (68). Use of an ineffective or inappropriate drug, for example antibiotics in upper respiratory tract viral infections, is also a common problem. Usage of medication without any clear proven beneficial effect can cause serious health related problem (7). Confusion over which medication is which is often seen elderly (43). Unnecessarily use of expensive medications result in wastage of economic resources (7).

There are some studies conducted in Turkey and other countries related to irrational drug use as described briefly below (43):

- Approximately 125,000 people with treatable cases die each year in the USA because they do not take their medication properly. A review of drug use indicated the following:
- 12-20% of patients use other people's medicines.
- Approximately 1/4 of all nursing home admissions are related to improper self-medication.
- 60% of all patients cannot identify their own medications.
- 14-21% of patients never fill their original prescriptions, neither do they get a repeat prescription or refill the original prescription
- 30-50% of all patients ignore instructions concerning their medication.

In a study conducted in Saudi Arabia, 37% of Saudi households indicated that they never checked the expiration date of a medication prior to administration. Self-medication was prevalent among households participating in this study, with a mean of 20.6% of Saudi households citing that family members took drugs prescribed for their friends or other family members and 43.9% purchased medical products based on the advice of friends or family members (77).

Özçelikay et al researched drug usage of university students in Ankara. Results showed that 90.2% of participating students took medication without seeing a healthcare professional. Also, 13.1% of the participants said that they stopped taking medication when feeling better, and disposed of the surplus medicines; 6.7% of students discontinue the therapy and give medications to others, while 6.0% of them hoard surplus medicines (78).

Results of a study which was conducted in a university hospital in Ankara, showed that 28.6% of the patients discontinue the therapy before the specified time; 34.9% of them did not read medication package inserts; and 28.3% of them did not check the expiry date of the drugs. Drug use on the advice of relatives or friends was admitted by 25.6% of the participants and 22.6% of them gave advice to others. 44.8% of subjects said that they unused drugs at home [18]. A study conducted in Kayseri in Turkey found that there was unused analgesic medication in the houses of 84.6% of those surveyed. (79).

A study performed at two military bases in December 2006 concluded that 61.6% of the respondents are fully compliant to treatment regimens; 18.6% of subjects complete all the medications prescribed; 49.1% store medication and when expired dispose of them; 42.9% keep the medications in a medicine cabinet or special drawer; and 42,2% keep them in refrigerator. Moreover, 88.4% of the participants are sensitive about the expiration date of the medications (6).

An investigation conducted in different regions of the northern United Arab Emirates concluded that 45% of the participants admitted using stored medicines without medical consultation, while 55% of them only used drugs after medical consultation. Among the latter group, only 57% of the participants completed the treatment course. The habit of sharing medicines with family members, relatives and friends was cited by 86% of the sample studied throughout the study period (68).

In Bangladesh a report of a small study at local level showed that polypharmacy rates are quite high, and can cause serious health problems. Especially in drug supply, irrational drug use continues to exist (73). A study from Belgium indicated that 1/3 of the medicines found at

home are stored in unsuitable conditions. The patients are not aware that drugs can be easily degraded if the appropriate storage conditions are not met (81).

A study conducted in the psychiatry department of a teaching hospital in Turkey among patients taking medications due to anxiety and depression reported that 76.2% of anxiolytic drug users and 51.4% of the antidepressant users admitted that they had quit the therapy. 60.7% stated that they had a record of noncompliance. Of these noncompliant patients, 29.5% stopped taking the medication on the premise that, "I can cope without medication", and 14.3% stopped the medication because of the side effects they experienced. The patients specifically stated that when they felt better, they stopped their medications. Some of them also admitted that they changed the dosage of the medication by themselves without consulting a healthcare professional, and they quit the therapy when they experienced side effects (57).

A research conducted among elderly patients reported that 78% of the participants used drugs that had helped their friend, 82% self-medicated, 32% were glad to use medication, and that 27.3% of subjects kept their medications in an unspecified cabinet (48). In a study that examined the medication awareness of a Turkish population, it was reported that 20% of the population bought medication without prescription. They also stated that they bought medication on the advice of friends, relatives, pharmacist-pharmacy technicians, or based on their own experience (81).

Sorensen et al. studied risk factors via home visits in New South Wales and Western Australia. During the home visit, irrational drug use was observed to be related to potential risk factors which were identified as poor adherence, expired medications, multiple prescribers and dispensers, medication hoarding, multiple storage locations of drugs, lack of a medication administration routine, the presence of discontinued medication repeats, and the patient's understanding of generic versus trade names (82).

NONCOMPLIANCE, UNUSED DRUGS AND MEDICINE WASTAGE

With the increase in the number of patients with chronic diseases in the world, drug usage has increased greatly. As a part of the global problem of irrational drug use, unused drugs and medicine wastage are often neglected. However it is becoming a huge issue to handle.

Definition of an unused drug is "a drug which is purchased, whether according to a prescription or not, but which is not administered (83). Unused drugs compose a risk to public health through poisoning and suicide when not protected, when allowed to accumulate in the home and to pollute the environment through poor disposal (84). Hoarding is a habit can cause unused drugs to build up in the home. Hoarding was defined in cases where multiple drugs were retained in the home, particularly when drugs were no longer needed or had expired (82).

Hoarding and the related presence of the unused drugs at home finally leads to wastage of the medication. The definition of medication wastage is "any drug product, either dispensed by a prescription or purchased over-the-counter that is never fully consumed" (77). This phenomenon may be because of the patients' poor compliance, excessive and irrational prescribing, or the lack of control over the sales of prescription medications in the community pharmacy (85, 86).

Medicine wastage not only causes unnecessary economical loss in the health system, it also causes environmental pollution if the drugs are not disposed of properly, in addition to higher suicide and poisoning rates. There are many studies indicating that living animals which were exposed to medicine contaminated media underwent anatomical, physiological, reproductive and behavioral changes (87).

Statistics related to unused and expired medicines can be summarized as follows (88):

- In the USA, in 2007, of the 4 billion prescriptions filled elderly patients wasted more than \$1 billion worth of drugs.

- A major source of accidental poisoning of children results from medicines found at home, and 36% of these cases occur in the grandparents' homes.

In Turkey, patients can buy many medications without a prescription. However, 70% of the people with health insurance prefer to consult a doctor and apply pressure on the doctor to write prescription which includes the drugs the patient wants. This pressure is often exerted to make the doctor prescribe drugs that are believed to be useful 'just in case' they may be needed. Doctors cannot resist this irrational pressure (89). The phenomenon also enhances the accumulation of unused and waste medicines.

The number of studies related to unused and waste medicines has risen in the last decade. Although medicine-return campaigns underestimate the real wastage, since people tend to flush drugs down the toilet or dispose of them with household rubbish, they can be beneficial as a reflection of real drug wastage (90). Some of the studies related to the subject can be seen below:

In Great Britain, the incidence of medication wastage was found to be substantial. Published research suggests that 50% of patients are noncompliant with the dosage of their prescription medicines. According to the results, 51% of medicines in the household were not currently being used. 40% of the medications found at home had expired. Another survey indicated that each year nearly 33% of the population of England could not complete the course of a prescribed drug regimen. In addition to this, nearly 25% of adults surveyed in the same study admitted to having unused medicines in their homes (77).

Sorensen et al. studied medicine related risk factors using home visits, and found that the average number of current medications taken by the patients in the study was 9.9; whereas the average number of medications found in the home was 14.7 (82). A study conducted in Ankara showed the result that the rate of unused drugs was 61.3% (6).

Leach et al. conducted a survey of prescribed medicines in homes in England and Wales. The average home had 2-3 medicine containers; 56% of these drugs were being used currently, 6% of them were in occasional use, and 28% were never used. 20% of all oral antibiotics identified in the study were found to be wasted (91).

If the problem is considered from an economic perspective, the cost of the medication wasted and the proper disposal cost are extremely high. In addition, the utilization of medical time is another indirect result. Governments, health care providers, and consumers have to work together to find ways to control these unnecessary costs while continuing to provide quality health care for their nations (77). The global view shows that medication waste is a huge problem. Medication wastage is an extravagant burden on the economies of many countries.

The economic aspects of medicine wastage can be summarized in the light of the research summarized below:

In Great Britain, the medicines returned to pharmacies each year for disposal is worth around £230 million and it is estimated that a great deal more is disposed of by patients themselves, often in environmentally harmful ways like being disposed of with household rubbish or flushed down the toilets (74, 91). According to another report in England, the annual value of unused medicine return was estimated to be £100 million in 2007 (8). However, this figure almost certainly underestimated the full cost of drug wastage, as it is based only on unused drugs that are actually returned (robust data). It is estimated that as much as 10 per cent of all prescribed medications are wasted and this would mean up to £800 million worth of drugs are wasted annually just in primary care. Moreover, the full cost of wastage is not just the cost of the drugs themselves. Governments also have to pay for returned drugs to be destroyed (92).

A study conducted in Saudi Arabia and the Gulf countries showed that families in Saudi Arabia and other Gulf countries spent a total of \$150 million on medications that were never consumed (77). In another study conducted in Canada, antihypertensive drugs followed by analgesics/anti-inflammatory agents were most commonly associated with medication wastage in terms of total dollar value. The results parallel comparable studies conducted in Israel and Algeria (93, 94). In a relatively small state like Oklahoma, it is estimated that between \$2.3 and \$7 million worth of unused prescription drugs are destroyed in nursing homes annually (77). As

much as \$1 million worth of prescription drugs are wasted each year in San Mateo County – a small county in California, USA with a population of 718,451. This wastage is partly attributed to patients dying or their medications being changed by health care professionals (95).

In 1996, a study conducted in Alberta, Canada calculated drug returns over a two month period and noted that people making returns brought back an average of 60% of the drugs from the original prescription drugs. The dollar value of these medicines was over \$700,000 over a two month period, when extrapolated to include the whole province (96). According to a similar study from Houston, Texas conducted over a six month period in 2002 for oral tablets and capsules alone, the wastage for the state was estimated at \$53 million (97). Based on research conducted in the United Kingdom in 2004, medication wastage was estimated at between £30 and £90 million per annum (90). The Pharmaceutical Management Agency of New Zealand assumed an expenditure of \$565 million for medications in 2005 (98). 6% of this value equates to the \$34 million dollars potentially wasted in New Zealand [89]. In a survey carried out in England and Wales, an estimate suggests that roughly £23 million of prescription medication (%5-6 of the total) are wasted each year (91).

Public health expenditure was 13.7 billion TL (Turkish Liras) in 2002, while it increased to 35.3 billion TL in 2007. In the same years, the total Social Security Agency (SGK) health expenditure was 7.6 billion TL and 20 billion TL respectively. Furthermore, in 2008 the SGK's health expenditures rose to 30 billion TL. In 2008, the market for prescription medicine increased at a rate of 9 per cent to 12 billion TL (9.3 billion dollars). Drug expenditure per person was \$136 (7).

According to a report from the Ankara Trade Chamber about medication wastage, it was assumed that 7% of unused drugs in pharmacies are disposed of because of expiration, while 60% of the medication kept at home expires without even being used. The cost of this medicine wastage was around 500 million dollar in Turkey in 2006 (99).

In 2007, the value of drugs sold was \$14 billion in Turkey and medication expenditure per person was \$200. Financing the social security foundations is a macroeconomic problem in Turkey, and the SGK budget accounts for 8.6 billion TL of the total. The total drug-related outlay of the SGK is around 40-50% of the whole SGK expenditure (6).

A cross-sectional study among elderly people in 2001 estimated that 2.3% of all drug costs are related to medication wastage. In the USA, this would represent over \$1 billion in medication wastage in the elderly population (100). Considering that there is an aging population, this value will be greater in the future.

To sum up, multiple studies investigating the presence of unused drugs highlight the high global rate of wastage. Health authorities have to try to solve this problem immediately before a permanent hazard results. To appreciate the real extent of medicine wastage, the economic aspects of the problem should be reviewed.

CONCLUSION

To conclude, this review has sought to emphasize the reasons and factors impinging on RDU, compliance. To improve RDU, doctors and pharmacists should be educated well enough to accurately inform the public because many irrational drug-related problems can be solved by education. The need of the public for relevant education should be highlighted. Pharmacists are the most accessible health-care professional for the patient, and have an important role in improving RDU habits and compliance. It is obvious that, improvement attempts in RDU will also decline the waste of medicinal products and will help to save the environment.

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