

Risks and Reasons Associated with Medication Non-Adherence

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Respected sir,

Medication adherence is a well-recognized problem in the management of patients with chronic diseases needing a long-term pharmacotherapy [1]. It affects as many as 40% to 50% of patients who are prescribed medications for management of chronic conditions such as diabetes or hypertension [2]. The estimated annual cost of prescription drug-related morbidity and mortality resulting from non-optimized medication therapy was \$528.4 billion in 2016 US dollars" with a low end of \$495.3 billion and high end of \$672.7 billion [3]. Medication adherence can be conceptualized as having three major components: (a) initiation—when the patient takes the first dose of a prescribed medication; (b) implementation—the extent to which a patient's actual dosing corresponds to the prescribed dosing regimen from initiation until the last dose is taken, and (c) persistence—the time from initiation to discontinuation. WHO has classified medication adherence into five different dimensions—condition-related factors, therapy-related factors, patient-related factors, socio-economic factors and healthcare team and system-related factors [4]. A lack of emphasis on correcting poor adherence and failures in patient adherence can result in unwarranted alterations to a patient's drug regimen [5]. "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 [6]. Causes of medication non-adherence are complex and include psychosocial (e.g., alcohol use, depression, stigma), structural (e.g., distance from clinics, medication costs), therapy-related (e.g., toxicities) and health system-related barriers (e.g., lack of counselling, poor user-experience with the health system) [7]. Studies have found that patients' beliefs about medicines and their perception of their illness contribute towards poor adherence [8]. Worldwide, between 25% and 50% of patients do not take their medications as recommended. In the USA, suboptimal adherence has been associated with 125,000 deaths and 10% of hospitalizations [9]. The economic impact was also in PubMed and Scopus in September 2017, which shows an increase in total healthcare cost (>80%), pharmacy costs (70%), inpatient and outpatient costs (50%), emergency department visit and medication costs (<30%), and hospitalization costs (<20%) [10]. Nearly 70% of all medication-related hospital admissions are due to medication non-adherence alone [11]. Across South Asia, overall hypertension prevalence is estimated to be 27%. Prospective Urban Rural Epidemiology study has shown more than 50% are unaware of it and up to 80% of hypertensive patients have low adherence to medication [12]. Uncontrolled BP was found more than 50% in Bangladesh, 70% in Pakistan and almost 60% in Sri Lanka [13]. American Diabetes Association and the European Association for the Study of Diabetes guidelines in 10 developing countries from Africa (Egypt, South Africa), Middle East (Israel, Saudi Arabia, United Arab Emirates, Iran and Lebanon) and South Asia (Bangladesh, India and Pakistan) shows more than 25% and around 70% patients did not have any follow-up visit by a diabetologist or a GP,

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respectively. More than 35% patients did not receive any diabetes education [14]. In a study conducted among people with diabetes only 30% were compliant with drug regimens and the non-compliance was higher among the lower socioeconomic groups [15,16]. Poor insight was identified as a reason for non-adherence in more than 50% of studies, followed by a negative attitude toward medication in 30% and cognitive impairments in nearly 15% [17]. Patients with chronic disorders, particularly conditions such as hypertension (45% in Bengaluru, 50% in Pakistan and 60% in Mumbai) [18] and hypercholesterolemia (60% in Kuwait) [19], which often are not associated with symptoms are also more likely to be non-compliers. Patients understandably tend to become discouraged with extended therapeutic programs that do not produce cures of the conditions. The prevalence of non-adherence in elderly patients receiving polypharmacy ranged from 6% to 55%. Medication adherence was negatively associated with large caregiver burden, impaired hearing, poor cognition and greater number of drugs in elderly patients [20]. Patients with chronic diseases appear to be more adherent with once-daily compared with more frequently scheduled medication regimens [21]. Administration Timing Simplification Protocol (ATSP) was shown to be an effective strategy to improve medication adherence in cardiovascular patients [22,23]. Underuse of a drug, deprives the patient of the anticipated therapeutic benefits and possibly resulting in a progressive worsening or other complications of the condition being treated e.g. underutilization and non-adherence of warfarin among non-valvular AF patients is both prevalent and costly [24]. The statins significantly reduce morbidity and mortality in patients with CHD and in patients with hyperlipidemia, when they are used on a continuing basis (Rosuvastatin, up to 55% reduction in LDL, up to 20% lowering in triglycerides, and up to 10% increase in HDL) [25]. Underuse of antihypertensive medications may be associated with hospitalization that could have been prevented if patients had complied with their treatment regimens [26]. Overuse of a drug, mostly increases risk of ADR e.g. Medication Overuse Headache (MOH) reported with antimigraine drugs (ergots and triptans) including nausea, dizziness and coronary vasoconstriction [27]. Asthma Insight and Management (AIM) survey noted that 25% of patients rely on Short Acting Beta Agonists (SABA) monotherapy to manage their persistent asthma, many of whom use albuterol daily. Medication Event Monitoring System (MEMS) noted that 15% of patients with asthma use more than 1 canister of albuterol per month. These patients had twice the risk of an asthma-related emergency department visit or hospitalization as compared to those who filled albuterol less frequently [28]. The potential for noncompliance is greater when the treatment period is long. In a free retroviral therapy by CDC in China with HIV patients (duration 17.7 month) revealed non-adherence with progression of time. Therefore, high priority must be given to the assessment of adherence behavior as well as any necessary intervention for non-adherence during the early stages of treatment [29]. Side effects can be a problem with blood pressure medications. Some people find that the treatment may make them feel worse than the disease, which

usually has no symptoms [30]. 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 (TCAs 30%, MAO inhibitors 40%, SSRIs 60%-70%, venlafaxine 70% and duloxetine 46% in Western populations) [31] and antihypertensive agents (thiazide-class diuretics, β -blockers, and centrally acting sympathoplegics reported) being implicated most frequently [32]. Situations frequently occur in which patients do not complete a full course of antibiotic therapy once they feel that the infection has been controlled. Many studies have shown that two-thirds of hypertensive patients do not achieve control. Poor adherence is probably more common in chronic conditions that are relatively asymptomatic for example hypertension [33]. The financial burden of medications may lead individuals to adopt various rationing or restrictive behaviors, such as Cost-Related Non-adherence (CRNA) to medications. The prevalence of CRNA varies between 4% and 36% in Canada [34]. Estimated prevalence of CRNA among all older adults varied from <3% in the France, Norway, Sweden, Switzerland and the UK to 16.8% in the USA. Older adults in the USA were approximately six times more likely to report CRNA than older adults in the UK [35]. It is obvious that medication errors are a pervasive problem, which is preventable. Data show that nurses and pharmacists identify anywhere from 30% to 70% of medication-ordering errors [36]. The complexity of treatment regimens is another frequently cited barrier that can be reframed as "the physicians prescribed too complex a treatment regimen". Adherence is best in patients who were prescribed 1 medication rather than multiple medications. Higher frequency of dosing also reduces adherence. While there may be reasons to avoid prescribing combination products (e.g., if they are costly), the potential to improve adherence and outcomes by reducing the number of medications and frequency of dosing should not be ignored [37,38]. About 85% of the interviewed subjects in an intercept survey said that the taste of liquid medicine is very or somewhat important to them and to their child. A nearly 80% of children complained about bad tasting medication or taste that is "too yucky" to take. Seven out of ten (70%) mothers surveyed filled 4 or more prescriptions per year with the average respondent filling 4.3 prescriptions per year for their children [39,40]. A cross-sectional study (2014-2015) in South Indian tertiary hospital reveals 17% were illiterates, 65% of them had lack of information about prescribed medications 45% patients were not aware of the side effects of the prescribed medication, more than 70% patients were not aware of what happens on missing medications regularly, nearly 65% and 60% of patients were not performing exercise and not following advice on diet respectively [41]. To help combat poor health literacy and its negative effect on medication adherence, a "shame-free" environment must be created. Possible solutions to poor patient literacy include providing the patient with pictorial and audiovisual educational material instead of written

instructions [42]. In some cases, confusion arises and mistakenly medications are given in wrong rout (e.g., swallowing suppositories, installing ear drops for otitis media to mouth, IV given to IM). A patient being prepared for Nitroglycerin patch or Pilocarpine Ocusert®. Although he had understood the instructions to apply, no instruction had been provided regarding their removal [26]. 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 are never appreciated by any patient. Patient should repeat the instructions for their better understanding and memorization and also should be encouraged to ask questions. Further, communication that ascertains patients’ needs, perspectives and values is also considered effective, as it a key feature of patient-centered care [43]. Respecting each patient’s autonomy, drawing out ambivalence about change, evoking change talk, and allowing the patient to develop and/or own the treatment plan greatly improve the odds of achieving positive clinical outcomes [44]. The provision of supplementary Patient Package Inserts (PPIs) 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 plays an important role for patient compliance [45,46]. The introduction of a video can reduce failure of adherence to safety-critical tasks and contribute to patient safety [47,48]. Motivation is the driving force underlying the wish to change behavior. Health care professionals (HCPs) reported that Empowerment, Motivation, And Medical Adherence (EMMA) supported patient-centered consultations in adults with type 2 diabetes by facilitating dialogue, reflection, and patient activity. The use of tools elicited patients’ perspectives and facilitated patient participation and shared decision-making. After 2 months, nearly 60% participants stated that they followed the goal and plan to a high or very high extent [49]. A compliance package is 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. Pharmacists’ involvement in health management is very crucial. They can follow up diagnosis, screening and daily review of drug profiles; Plan, monitor and evaluate drug programs to improve health and reduce health inequalities; Clarify and verify instruction during patient counseling; Establish protocols, set order, monitor medication profile, support and facilitate patient/drug entry during prescribing [39]. An increase in adherence rates was observed after the pharmacist intervention, followed by a gradual decrease over time. Enhancing the current intervention using an evidence-based approach and integrating big database analysis techniques to a real-time measurement of adherence could help community pharmacies improve and sustain medication adherence [50].

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