



Review Article

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ADHERENCE TO MEDICATION

Chandrashekar. K¹, Vinayak Meti¹, Saritha. M. K², Anil P Hogade³

¹Department of Pharmacology, Chettinad Hospital and Research Institute, Chennai, Tamil Nadu, India

²Department of Prosthodontics and Implantology, Chettinad Dental College & Research Institute, Chennai, Tamil Nadu, India

³Department of pharmacology, JNMC, Belgaum, Karnataka, India

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*Corresponding author

E-mail: chandrashekarshkr61@gmail.com

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ABSTRACT

Adherence to medication is defined as “the extent to which patients take medications as prescribed by health care providers”. Adherence rate is highest among patients with acute conditions, as compared with those with chronic conditions. Clinical trials report average adherence rates of only 43 to 78% among patients with chronic conditions. Adherence to medication is important because: poor adherence to medication regimen accounts for substantial worsening of disease, death and health care costs.

Key words: adherence, clinical trial, drug, patient’s compliance

INTRODUCTION

Synonyms

Concordance (or) observance (or) compliance (or) therapeutic alliance

Definition (WHO, June 2001) “The extent to which the patient follows medical instructions”

Rates of adherence reported as the percentage of prescribed doses of medication taken by patient over a specified period. Some authors include data on dose taking (taking prescribed number of pills each day) and the timing of doses (taking pills within a prescribed period) in definition of adherence. It has been found that adherence rates are higher among patients with acute conditions, as compared with those with chronic conditions. Adherence rate in chronic conditions drops after first 6 month of therapy. Average adherence rate in clinical trials range from 43 to 78 percent among patients receiving treatment for chronic conditions. Reorganization of non-adherence by physicians is poor and interventions to improve adherence have had mixed results¹.

Importance of adherence to medication

Predicts better outcomes and collecting adherence data is an essential part of clinical trials poor adherence to medication regimens accounts for substantial worsening of disease (d/t loss of efficacy (or) resurgence), death increased health care costs in USA, of all medication related hospital admissions, 33 to 69% are due to poor medication adherence with a resultant cost of approximately \$100 billion a year.

Methods of measuring adherence

Direct methods: Directly observed therapy includes measurement of level of medicine or metabolite in blood, measurement of biologic marker in blood

Indirect methods: Patient questionnaire, pill counts, rates of prescription refills; assessment of patient’s clinical

response, electronic medication monitors, measurement of physiologic markers and patient diaries.

Each method has its own advantage as well as disadvantages. “No method is considered the gold standard”. Adherence to medication regimen monitored since time of Hippocrates. Patient’s self report is a simple and effective measure of adherence.

Direct methods are expensive and burdensome to health care provider. They are good and commonly used means assessing adherence for some drugs like antiepileptic drugs such as Phenytoin or Valproic acid which will reflect adherence to regimens and sub therapeutic levels will reflect poor adherence or suboptimal dose strengths¹. Indirect methods like questioning patient, patient diaries and assessment of clinical response are easy to use. Patient’s clinical response measurement is confounded by many factors other than adherence to medication that can account for clinical outcome. Pill counts are counting the number of pills that remain in patient’s medication bottles or vials. Pill counts is not a good method of measuring adherence as it can be easily altered by the patient by discarding the medicines in bottle and also it provides no information on other aspects of taking medications, such as dose timing and drug holidays (i.e., omission of medication on three or more sequential days). Rates of refilling prescriptions are an accurate measure of overall adherence in a closed pharmacy system which ensures that refills are measured at several points in time. Electronic monitors records and stamps the time of opening bottles, dispensing drops or activating a canister. These devices provide precise detailed insights into patient’s behaviour in taking medication but however they do not document whether patient actually ingested the correct drug or correct dose. Electronic devices are costly and not used routinely. But however these devices provide most accurate and valuable data on adherence in difficult clinical situations and in setting of clinical trials and adherence research.

Some pictures of electronic monitors are shown below



Figure 1



Figure 2



Figure 3



Figure 4

Methods of measuring adherence

Following table shows methods of measuring adherence with advantages and disadvantages

Table 1: Direct methods

Test	Advantages	Disadvantage
Directly observed therapy	Most accurate	Patient can hide pills in mouth and then discard them; Impractical for routine use
Measurement of level of medicine or metabolite in blood	Objective	Variations in metabolism can give false impression of adherence
Measurement of biologic marker in blood	Objective	Requires expensive quantitative assays and collection of body fluids

Table 2: Indirect methods

Test	Advantages	Disadvantage
Patient questionnaires	Simple; inexpensive; most useful method in clinical setting	Susceptible to error with ↑ in time between visits; Results are easily distorted by patient
Pill counts	Objective; quantifiable and easy to perform	Data easily altered by patient (e.g., pill dumping)
Rates of prescription refills	Objective; easy to obtain data	Prescription refill is not equivalent to ingestion of medication; requires closed pharmacy system
Assessment of patient's clinical response	Simple; generally easy to perform	Factors other than medication adherence can affect clinical response
Electronic medication monitors	Precise; results are easily quantified; tracks patterns of taking medication	Expensive; requires return visits and downloading data from medication vials
Measurement of physiologic markers (e.g., heart rate in patients taking beta-blockers)	Often easy to perform	Marker may be absent for other reasons (e.g., ↑ metabolism, poor absorption, lack of response)
Patient diaries	Help to correct poor recall	Easily altered by patient

Barriers to adherence

Poor adherence can be due to multiple factors mainly due to patient related factors, health care provider related factors, and health care system related factors.

In one study, responses to questionnaire, typical reasons cited by patients for not taking their medications include: forgetfulness (30%) other priorities (16%) decision to omit doses (11%), lack of information (9%), emotional factors (7%) and no reason (27%)

Different barriers to adherence are listed below:

Due to poor provider-patient communication: patient has poor understanding of disease, patient has poor understanding of benefits and risks of treatment, patient has poor understanding of proper use of medication, physician prescribes overly complex regimen.

Due to patient's interaction with health care system: poor access or missed clinic appointments, poor treatment by clinic staff, poor access to medications, switching to different formulary, inability of patient to access pharmacy and high medication costs

Due to physician's interaction with health care system: poor knowledge of drug costs. Poor knowledge of insurance coverage of different formularies.

Major predictors of poor adherence to medication

Many factors are associated with poor adherence to medication². Some important factors associated with poor adherence are presence of psychological problems

(particularly depression), presence of cognitive impairment, treatment of asymptomatic disease, inadequate follow up, side effects of medication, patient's lack of belief in benefit of treatment, patient's lack of insight into the illness, poor provider-patient relationship, presence of barriers to care or medications (as listed above), missed appointments, complexity of treatment (number of daily doses, number of concurrent medications), cost of medication (or copayment or both), socioeconomic status, lack of family or social support, burdensome schedule, duration of therapy (chronic conditions), frequent changes in medication regimen, lack of immediate benefit of therapy, medications with social stigma attached to use, treatment interfering with lifestyle (or requires significant behavioural changes), long wait times, psychotic disorders and mental retardation (or developmental disability) etc.

Role of adherence to medication in clinical trials

Clinical trials are carefully planned and strictly designed experiments to give answers to very distinct clinical question: whether certain dose of certain drug is more potent than placebo. Electronic medication event monitoring system is the most reliable method of measuring adherence in clinical trials. Still today best method to measure adherence is an unresolved problem.

Average adherence rate in clinical trials range from 43 to 78%. Some trials consider rates of greater than 80% to be acceptable, whereas others consider rate of greater than

95% to be mandatory for adequate adherence. Even under guaranteed best conditions in clinical studies adherence is incomplete³. Only 80% of stratified and randomized participants adhere to medication satisfactorily. Even under optimal conditions 20% of the study population don't follow the protocol. If this is not recognized, at least 20% of untreated patients will be considered as treated and therefore bias the study results. Adherence to medication data are needed to avoid erroneous conclusions of trial results. High levels of non-adherence in a clinical trial increase the risk of a type 2 error. For a comparative study with a power of 95% to show a difference between two groups at the 5% level and to accommodate a mean adherence rate of 50%, the number of subjects in each group must be increased about fourfold. Finally overall adherence rate in clinical trials is about 80% and transferring these results to patients with treated in a routine setting would lead to an untrue conception of reality³.

Adherence to medication in clinical care

Measuring adherence in clinical routine work is more difficult than measuring in clinical trials because it is unclear whether informing a patient about goal of adherence study will influence patient's behaviour or not. Hence observer bias becomes worse if, additional information about the consequences of non-adherence is taken. Consequently, when investigating compliance the biasing conditions of routine care cannot be modified, and efficacy results must be biased.

Steps necessary for implementing adherence control in clinical routine: Cheaper and more sophisticated compliance measuring devices are needed, all the involved healthcare partners should be appropriately aware of the importance of non-adherence, the patient should learn to accept compliance measurement as a valuable treatment service and Physician should learn to use compliance control as an aid to control treatment.⁴

Strategies for improving adherence to medication regimen

Numerous strategies have been employed in improving adherence but none of them have shown effective results. Followings are some of the important strategies in improving adherence.

Identify poor adherence, Emphasize the value of regimen and effect of adherence, Educate and support patient, Elicit patient's feelings about his or her ability to follow the regimen, and if necessary, design supports to promote adherence. Provide simple, clear instructions and simplify the regimen as much as possible (e.g., by reducing number of drugs and frequency of administration; using drugs with longer duration of action; using modified-release formulation; using depot injections; using single dose of drug as IM injection of penicillin to treat gonorrhoea or large oral dose of amoxicillin 3g to treat UTI), Encourage the use of medication taking system, Using electronic medication reminders (as alarm, warnings, reminders, software for instructions etc), Use rational fixed drug combination (FDC) whenever possible, Consider more efficacious and safer drugs (when side effect is the cause for non-adherence), Listen

to patient, and customize the regimen in accordance with patient's wishes, Supervised administration (administration of drug by doctor, nurse, or other attendant), Effective patient-doctor communication, Obtain help from family members, friends, and community services when needed, Consider for more "forgiving medications".

Over adherence to medication (over compliance)

20% patients take more drug than prescribed (even increasing the dose by 50%). In diseases where precise adherence with frequent or complex regimens is important, e.g. In glaucoma where sight is at risk, patients responds obsessively by clock-watching in a state of anxiety to avoid slightest deviation from timed administration of correct dose, to the extent that their daily life becomes dominated by this single purpose⁵.

Doctor compliance

It is defined as "the extent to which behaviour of doctors fulfils their professional duty: Not to be ignorant, to adopt new advances when they are sufficiently provided, to prescribe accurately, to tell patients what they need to know, to warn, i.e. to recognise the importance of act of prescribing, in hospital studies, error rates in drug administration ranges from 15-25%.

CONCLUSION

A collaborative approach to care augments adherence. Patients with difficulty in maintaining adequate adherence need intensive strategies. It can be enhanced by emphasizing the value of patient's regimen, making simpler regimen, and customizing the regimen to patient's lifestyle. Poor adherence to medication regimen contributes to worsening of disease, death and increased health care costs. "Non-adherence always should be considered in evaluating potential causes of inconsistent or nonexistent response to therapy". New technologies such as reminders through cell phones or personal digital assistants etc may help in improving adherence. Cost-effectiveness of drug treatment depends on drug intake, improving compliance enhances efficacy of treatment and optimizes the investment of all the healthcare partners.

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