ASSOCIATIONS BETWEEN THERAPEUTIC REGIMEN-RELATED FACTORS AND MEDICATION ADHERENCE IN PATIENTS ON ORAL ANTICANCER THERAPY

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ABSTRACT

Objective: Good adherence is critical for successful cancer treatment. Complex medication regimens have been found among the various therapy-related factors causing non-adherence.

Methods: In a cross-sectional questionnaire-based study of outpatients, we assessed 75 patients suffering from cancer. The objective of this study is to find associations between therapeutic regimen-related factors and medication adherence in patients on oral anticancer therapy.

Results: There was an increase in medication adherence as the length of therapy increased. About 10.76% of the patients with treatment duration <4 years showed low adherence. Low adherence was not observed with treatment duration of more than 4 years. About 6.55% of those taking up to four drugs had low adherence as compared to 14.28% taking more than 4 drugs. About 8.69% of patients taking drugs up to thrice a day showed low adherence as compared to 16.66% taking more than thrice a day. The negative association between medication regimen complexity and adherence observed in this study were in the predicted direction but did not achieve statistical significance \((p>0.05)\). The effect size was small \((d=0.28)\).

Conclusion: Complex prescription regimens reduce adherence to oral anticancer treatments, however, there are several other factors to consider than regimen simplification to increase adherence.

Keywords: Adherence, Cancer, Medication regimen complexity, Anticancer drugs.

INTRODUCTION

According to the World Health Organization (WHO), cancer is a leading cause of death worldwide. In 2020, 10 million deaths occurred due to cancer globally [1]. The transition to oral anticancer therapy has led to a new era in cancer treatment [2]. Patients generally tolerate oral anticancer therapy well. However, developing simple oral regimens that make medication as simple as feasible are crucial [3]. Studies have confirmed that the majority of patients prefer home-based oral therapy to hospital-based i.v chemotherapy [4].

Adherence is an essential component in all pharmacological therapies but is especially important in cancers. In cancer, medication adherence is critical for extending disease-free and progression-free survival. Although cancer patients have a higher motivation for drug adherence, research on adherence among cancer patients demonstrates that adherence varies from 16% to 100%, depending on the type of therapy [5].

Non-adherence has consequences for both the patient and the healthcare system [6]. The factors commonly causing non-adherence are socioeconomic, disease related, patient related treatment related, and health system related [7]. Non-adherence can arise when the medication regimen is complex which may include improper timing of drug administration or administration of multiple drugs at different times throughout the day [8].

The number of medications and the number of times per day that a patient takes a medication indicate the complexity of a pharmaceutical regimen [9]. However, medication count alone is unlikely to be an accurate indicator of regimen complexity because it ignores other factors that contribute to complexity, such as dosage forms, dose, and usage directions [10].

An increase in medication regimen complexity has been related to poor medication adherence [11]. Besides non-adherence, the complex medication regimen causes errors with dosing and drug administration [12]. Poor adherence may prove to be the most serious barrier to the efficient use of new oral anticancer agents [13].

Most of the studies have shown that adherence decreases when patients are prescribed multiple medications but some researchers have found that the adherence rises as the number of prescribed medications grows [14]. The goal of this study is to look at the associations between medication regimen complexity and adherence to oral cancer therapy.

METHODS

This is a prospective, single-group, observational study conducted from December 2019 to February 2020.

Research tool
A validated questionnaire was prepared in English and Urdu. It had three sections. Section one had the questions about the general demographic information such as age, gender, and qualification. Section two asked the questions related to drugs being used. Section three asked the questions related to medication adherence. We used the English and Urdu versions of the medication adherence tool known as general medication adherence scale (GMAS) after obtaining permission from the authors [15].

Study population
Seventy-five patients with documented cancer, attending the OPD of SKIMS Hospital, Kashmir, were selected by simple randomization for this self-report study. Authors collected the information about the duration of illness, oral anticancer drugs used, concurrent medication, besides other demographic characteristics. The authors included all the drugs the patient was taking, besides oral anticancer drug, while evaluating regimen complexity.
Inclusion criteria
Age more than 18 years, suffering from documented cancer, unsupervised domestic therapy with at least one oral anticancer drug in the treatment schedule, and willing to participate in the study were included in the study.

Exclusion criteria
Age <18 years, non-cancerous disease, under directly observed oral or parenteral anticancer therapy, and not willing to participate in the study were excluded from the study.

The objectives of the study were explained to the study participants before data collection, and their consents were sought and the questionnaires were given only to those who agreed. The confidentiality of the responders was maintained.

Statistical analysis
Analysis was done by a combination of manual calculators, VassarStats, and various other online statistical calculators.

RESULTS
There were 58.7% of males (n=44) and 41.3% of females (n=31). About 53.3% (n=4) were up to 30 years old, 66.66% (n=50) were 31–60 years, and 28.00% (n=21) above 60 years. About 45.33% (n=34) were literate and 54.66% (n=41) were illiterate (Table 1).

About 81.33% (n=61) were taking up to four drugs per day and 18.66% (n=14) were taking more than 4 drugs per day. About 92.00% (n=69) were taking drugs up to 3 times a day and 8.00% (n=6) 4 times a day or more. About 86.66% (n=65) were on anticancer therapy for up to 4 years and 13.33% (n=10) for more than 4 years (Table 2).

Those taking up to four drugs 6.55% (n=4) had low adherence, 55.73% (n=34) medium, and 37.70% (n=23) high adherence. Those taking more than 4 drugs 14.28% (n=2) had low adherence, 57.14% (n=8) medium, and 28.56% (n=4) high adherence. Those taking drugs up to thrice a day 8.69% (n=6) had low adherence, 57.97% (n=40) medium, and 33.33% (n=23) high adherence. Those taking drugs 4 times a day or more 16.66% (n=1) had low adherence, 33.33% (n=2) medium, and 50.00% (n=3) high adherence. Those with treatment duration up to 4 years, 10.76% (n=7) had low adherence, 53.84% (n=35) medium, and 35.38% (n=23) high adherence. Those with treatment duration more than 4 years, 70.00% (n=7) had medium, and 30.00% (n=3) high adherence (Table 3).

The associations between the dependent variable and predictors are insignificant (p>0.05) (Tables 4 and 5).

DISCUSSION
Oral anticancer therapy has many advantages over intravenous therapy, including convenience and ease of administration. However, because the doctors are unable to monitor the patient, unsupervised domiciliary treatment may result in non-adherence.

The patient is considered non-adherent when the doses of the prescription to which the patient has consented are skipped, extra doses are taken, or doses are taken in the wrong quantity or at the wrong time [16]. Non-adherence is linked to several factors, including treatment regimen characteristics, the patient, the patient’s social environment, and the clinician-patient relationship. Knowing the factors that contribute to non-adherence can help physicians spot situations where adherence is likely to be poor [13].

The complexity of the regimen is inversely related to adherence across the spectrum of therapeutic classes. The finding that once-daily regimens had much higher compliance than 3 and 4 times daily regimens supports the idea of simplicity. Even a once-daily dose, however, does not guarantee full compliance [17].

The present study found an increase in medication adherence as the length of therapy increased. About 10.76% of the patients with treatment duration <4 years showed low adherence. Low adherence was not observed with treatment duration of more than 4 years. About 6.55% of those taking up to four drugs had low adherence as compared to 14.28% taking more than 4 drugs. About 8.69% of patients taking drugs up to thrice a day showed low adherence as compared to 16.66% taking more than thrice a day. The negative correlations between medication regimen complexity and adherence observed in this study were in the predicted direction but did not achieve statistical significance (p>0.05). The effect size was small (d=0.28).

In a systemic review of associations between dose regimens and medication compliance, compliance was found significantly higher...
for once daily versus 3 times daily (p=0.008), once daily versus 4 times daily (p<0.001), and twice daily versus 4 times daily regimens (p=0.001); however, there were no significant differences in compliance between once-daily and twice-daily regimens or between twice-daily and 3 times daily regimens [17].

In a study on adherence to hormonal therapy on breast cancer, approximately a quarter of the women with breast cancer were found non-adherent [18].

During imatinib therapy in patients with chronic myeloid leukemia, one-third of patients were considered to be non-adherent. Only 14.2% of patients were perfectly adherent with 100% of prescribed imatinib taken [19].

In a study on tamoxifen therapy in breast cancer, adherence during the 1st year of treatment was 87% but declined to 50% after 4 years [20].

Some studies about chronic diseases found that a longer duration of the disease resulted in good compliance and newly diagnosed patients had poor compliance [21].

**CONCLUSION**

In addition to the number of drugs and frequency of drug administration, various other therapy-related factors are involved in poor or non-adherence to oral anticancer drugs. Medication regimen complexity is a modifiable factor. Adherence will improve if a prescription regimen that needs fewer drugs and fewer administrations per day is created. Interventional programs such as education, psychological support, and simplification of complex medication regimens can improve adherence. Oral cancer chemotherapy can be effective only if adherence is optimized.

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**AUTHORS’ CONTRIBUTIONS**

The author compiled the data and after analyzing it the article was structured.

**CONFLICTS OF INTEREST**

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**ETHICAL APPROVAL**

Yes.

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