

Medicines information and adherence in HIV/AIDS patients

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Summary

Background: Providing written medicines information is being legislated in an increasing number of countries worldwide, with the patient information leaflet (PIL) being the most widely used method for conveying health information. The impact of providing such information on adherence to therapy is reportedly unpredictable. Therapy for human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS) and related opportunistic infections usually involves polytherapy and complex regimens, both of which are risk factors for non-adherence. The objective of this study was to assess the impact of medicines information on adherence to chronic co-trimoxazole therapy in low-literate HIV/AIDS patients.

Methods: Two different PILs were designed for co-trimoxazole tablets and were available in both English and isiXhosa. Participants were randomly allocated to a control group (receiving no PIL), group A (receiving a 'complex PIL') and group B (receiving a 'simple PIL' incorporating pictograms). At the first interview, demographic data were collected and the time, date and day that the participant would take his/her first tablet of the month's course was also documented. In a follow-up interview adherence to therapy was assessed using two methods; self-report and tablet count.

Results: The medicines information materials incorporating simple text and pictograms resulted in significantly improved adherence to therapy in the short term, whereas a non-significant increase in adherence was associated with the availability of the more complex information. This was shown by both the self-reported assessment as well as the tablet count.

Conclusion: This research suggests that appropriately designed written material can have a positive impact in improving adherence and, together with verbal consultation, are essential for enabling patients to make appropriate decisions about their medicine taking.

Introduction

According to the Joint United Nations Programme on HIV/AIDS (UNAIDS) 2004 report of the global AIDS epidemic, an estimated 40 million people worldwide are infected with HIV. More than 95% live in low- and middle-income countries and approximately 70% of these people (28.1 million) live in Sub-Saharan Africa (1). With the high levels of HIV infection, as well as the escalation of deaths from AIDS, South Africa is very much in the spotlight. The epidemic has become a serious development issue, with extremely far-reaching social, political and economic implications. Currently, it is estimated that 4.8 million South Africans are infected with HIV/AIDS and 18 000 people die of AIDS every month, while 600 people die every day (1).

HIV is a virus that weakens the body's immune/defence system to such an extent that even mild opportunistic infections can result in death. Drug therapy for HIV/AIDS and related opportunistic infections is often complex, invariably involving polytherapy and is long term, all factors that have been shown to impact negatively on adherence. Non-adherence in HIV/AIDS patients has extremely serious consequences, making it vital to ensure good comprehension of medicines information in an effort to optimize adherence. Pneumocystis carinii pneumonia (PCP) is the most common, life-threatening opportunistic infection. It is caused by a parasite, which almost always presents itself as a lung infection, but can often spread to other organs (2). For the purpose of this research study, usage of co-trimoxazole tablets was reviewed as they are used both for the prevention and treatment of PCP. A constant concentration in the blood should be maintained, necessitating a high degree of adherence (2).

The limited literacy skills of a large proportion of the South African population present a significant barrier to accessing and understanding medicines information necessary for the degree of adherence required for a successful therapeutic outcome. The challenge we as healthcare providers (HCPs) face is to communicate this information in an appropriate, understandable form commensurate with the patient's literacy skills, and, in addition, to ensure that it is acceptable in terms of the patient's culture, beliefs, attitudes and expectations. Written patient education material is made available to patients in the form of patient information leaflets (PILs), brochures and booklets. Unfortunately, in developing countries such as South Africa, much of this literature probably goes unused as a significant proportion of the population may not be able to read it and therefore will likely fail to obtain necessary preventative and therapeutic health services (3–5). Such individuals often do not understand what the HCP has said and are reluctant to ask for clarification or indicate that they do not understand. Complications in therapy may arise, as the inability to read and understand written information can interfere with adherence to a recommended regimen (4, 6).

Poor patient adherence to prescribed therapy has evolved worldwide into a major public health problem, as it constitutes a significant barrier to the effective treatment of many acute and chronic diseases (7, 8). This is in part due to an increasing incidence of people taking drug therapy, the manufacture of more potent drugs, and the development of resistance to many anti-infective agents (9, 10). After decades of adherence research, very little consistent information is available, apart from the fact that people do not take their medicines as prescribed.

One of the most interesting aspects of the adherence phenomenon is how rarely patients do all that is recommended by the HCP (11–13). One reviewer of the adherence literature has estimated that on average only one-third of patients correctly follow directions from their HCP (14). The reported incidence of non-adherence to therapy ranges from 4% to 92% with an average non-adherence rate for chronic drug therapy of 50% (9, 15). The highest non-adherence rates have consistently been found in patients with chronic disorders involving long-term treatment and in whom the illness has asymptomatic periods during which the clinical consequences of non-adherence are often delayed (15), such as HIV/AIDS.

Patients may have various reasons for not adhering to their therapy and can be regarded as either intentional or unintentional non-adherers. Unintentional failure to adhere to therapy can result from a number of factors, all of which are more likely to occur with increasing complexity of the regimen (9, 10, 14–18). Forgetfulness, lack of information and/or knowledge, e.g. inadequate understanding of the disease

or condition and lack of insight into the importance of continuing with the treatment, could result in unintentional failure to adhere to therapy (9, 10, 17, 19–21).

According to Morris and Halperin (20) written medicines information, if designed appropriately, can improve adherence in short-term therapy, satisfy patient information needs and educate patients on the correct use of their medicine. It can also play an important role in making the patient more health conscious, aware of why and how to take medicines, and a more active participant in medical decisions. Written medicines information, such as PILs, with the appropriate tone, length and design can do much to aid responsible medicine taking (22, 23).

The objective of this study was to assess the impact of written medicines information on adherence to co-trimoxazole therapy in low-literate HIV/AIDS patients.

Methods

Study site and study population

The study was conducted in Grahamstown, a small town in the largely rural Eastern Cape province. It is one of the poorest of the nine South African provinces with an extremely high unemployment rate (24). The majority of the local African population (84%) belongs to the Xhosa ethnic group and have isiXhosa as their home language. Eighteen per cent of the province's population aged 20 years and over have had no schooling at all, with only 8.4% holding a tertiary education (24).

The majority of the interviews took place in five local primary health care clinics. Written permission from the relevant health authorities was obtained to conduct the research and patients signed consent forms when agreeing to participate in the study. Ethical approval for the study was obtained from the Rhodes University Ethical Standards Committee.

The study population included participants over the age of 16 from a variety of educational backgrounds, ranging from no schooling at all up to a maximum of 12 years of formal education. An inclusion criterion was the ability to read and understand either English or isiXhosa. Approximately 120 HIV-positive outpatients on chronic co-trimoxazole therapy were identified and the initial interview was conducted on site. The follow-up interview, which took place approximately 14 days later, was conducted either at the participant's home or at the clinic. Participants were randomly allocated on an alternating basis to a control group (who received no PIL), group A (who received a longer, more 'complex PIL' containing no pictograms) and group B (who received a 'simple PIL' incorporating pictograms).

Research material

Two PILs were designed for co-trimoxazole tablets. Information sources consulted included Australian consumer medicines information (CMI), USP-DI, various fact sheets, medicine information sheets,

monographs and package inserts (25–30). PILs were available in English and isiXhosa, and were printed back to back on white paper.

The 'simple PIL' was a single A4 page in a Z-fold design, written in simple language and incorporating pictograms. Souvenir (bold) size 24 font was used for the main heading, which was in capital letters, and Souvenir (bold) size 14 font was used for the subheadings. In order to highlight the subheadings, a line was ruled above and below them. The text in the PIL was typed using Souvenir size 14 font and contained 376 words. Special attention was paid to ensure the inclusion of uncomplicated words, translating medical terminology to commonly used plain language (where possible), as well as using short sentences to suit people with limited reading skills. The active voice was used and most of the information aimed at directly informing the patient about their therapy. In a previous study (31), a similar PIL that provided information about nystatin oral suspension was developed using the same format, layout, standard of text and visuals. This PIL was evaluated for readability and was shown to be well understood in a similar target population.

The 'complex PIL' was printed on A4 paper and consisted of three columns, with a 1-cm gap between the columns. Helvetica (bold) size 26 font was used for the main heading, which was in capital letters, and Helvetica (bold) size 12 font was used for the subheadings. Again, in order to highlight the subheadings a line was ruled above and below them. The text in the PIL was typed using Arial size 10 font and contained 643 words. The Australian CMI design and structure was used as a guide to devise this PIL (32). No pictograms were included and the PIL complied with all the specifications as stated in the South African legislation (33), resulting in a longer, more complicated PIL than the 'simple PIL'.

Interview process and data collection

Nursing sisters at the five clinics were notified about the study and were asked to recruit all HIV-positive patients currently taking co-trimoxazole tablets chronically. This was done using a standard approach, in which the nursing sister was instructed to explain the details of the study to the patient and ask if the patient would like to participate. On agreeing, permission to disclose the HIV-positive status to the interviewers was obtained. The patient was assured that all information would remain strictly confidential and was asked to read and sign a consent form. The nursing sister then notified us of a potential participant to interview. The co-trimoxazole tablets were dispensed according to normal clinic protocol, with a conventional medicine label.

A standard approach was used for all interviews, which were conducted with the help of an interpreter. The date of the initial interview and the interview site was noted. The participant's name, address and contact number (if available) was recorded, as well as the current stage of HIV, which was obtained from the health passports.

In the first interview demographic data such as gender, age, home language, current employment and educational level was collected. The time, date and day that the participant would take his/her first tablet of the month's course was documented. At the end of the first interview, all participants were asked to keep their tablet packets in a safe place and not to throw them away once finished. If the participant was

allocated to either group A or B he/she was given the appropriate PIL and was instructed to read it carefully and to keep it in a safe place. To conclude this initial interview, participants were thanked for their time and given a reminder note stating the date, time and place of the follow-up interview, which took place approximately 14 days later, either at the participant's home or at the clinic.

During the follow-up interview participant adherence with the co-trimoxazole tablets was assessed using two measures; self-report adherence and tablet count. The self-report assessment comprised a set of six questions that required the participants to explain how they were using their medicine. For example, 'How many tablets are you taking each time?' and 'How many times a day are you taking your tablets?' For the tablet count, permission was obtained from the participants to count the number of tablets that were still remaining in their tablet packet. Participants were offered a small honorarium at the conclusion of the interview and were thanked for their time.

Data analysis

For the self-report assessment of adherence, responses to questions asked about their therapy were marked as being either correct or incorrect and an adherence score was allocated. For the tablet count, the number of extra doses remaining in the medicine packet was calculated and a tablet count, the number of extra doses remaining in the medicine packet was calculated and a second adherence score was allocated. The overall percentage for participant adherence was calculated using the following formula:

$$\begin{aligned} & (\text{Self-report} \times 0.2) + (\text{Tablet count} \times 0.8) \\ & = \text{Overall \% adherence.} \end{aligned}$$

This equation was formulated based on the heavily weighted objective assessment of the tablet count but also taking cognizance of the more subjective self-report measure.#10;

Results

Demographic characteristics

A total of 138 participants were approached to participate in the study; 11 participants refused for various reasons and a further seven were lost to follow-up. A final total of 120 participants were recruited and interviewed, and their demographic characteristics are presented in [Table 1](#). Participants were all Black, isiXhosa-speaking and HIV-positive patients, with co-trimoxazole tablets being part of their current drug regimen.

The majority (69.2%) of the participants were in stage 4 (asymptomatic stage) of their disease, with 31% being in stage 5 (AIDS-related complex). During stage 4 no signs or symptoms are visible and the patient is prescribed co-trimoxazole tablets prophylactically to prevent opportunistic infections such as PCP.

Most (60.8%) of the participants were between the ages of 26 and 40 years and more than two-thirds (73.3%) were female. Just under half (44.2%) had between 8 and 12 years of formal education, 44

(36.7%) participants had been to school for between 5 and 7 years, and seven (5.8%) participants had no formal education. All participants interviewed were from a socioeconomically disadvantaged background and this was clearly demonstrated by the fact that only 11 (9.2%) participants were employed at the time of the study. Only five (4.2%) participants were unable to tell the time from a clock face, but all could interpret a digital face.

Assessment of participant adherence

For the self-report assessment, when the participants were asked 'Have you been taking your tablets as directed?' only one participant acknowledged that she was not doing so. However, [Table 2](#) clearly illustrates the unreliability of this as a sole measure of adherence as only 28 (70.0%) participants in the control group knew how many tablets to take and when to take them. This improved to 78% in group A (complex PIL) and 92.5% in group B (simple PIL). This suggests that the PIL, together with the information on the medicine label was useful in promoting understanding of how to take the medicine correctly. The other questions were all answered relatively well, indicating that overall 80% of the participants were apparently 100% adherent with their medicine.

When comparing adherence (self-report) between groups ([Table 2](#)), significantly more participants in group B (92.5%) obtained 100% adherence when compared with those participants in the control group (70.0%). This indicates that the presence of pictograms may have a positive influence on adherence to short-term therapy. One hundred per cent adherence was also achieved by 31 (78%) participants in group A (complex PIL).

The results from the tablet count concurred with the self-report assessment and showed that the mean percentage adherence was significantly higher in those participants who received the 'simple PIL' (86.5%) when compared with the control group (65.1%) or group A (70.1%). A significant difference was observed between the number of participants who achieved 100% adherence in the group who received the 'simple PIL' (35%) compared with the other two groups (2.5% in each group).

When combining results from the self-report and tablet count using the above-mentioned formula, it was found that the overall mean percentage adherence of the participants in group B (88.3%) was significantly higher than those in group A (73.6%), as well as in the control group (67.7%).

Discussion

In the past few decades, hundreds of research articles have been published on non-adherence, and dozens of devices and programmes have been developed to assess and attempt to resolve adherence-related problems. Yet, despite the tremendous efforts of pharmacists and other HCPs, non-adherence to prescribed therapy remains a significant health problem resulting in poor patient outcomes and increased healthcare use ([8](#), [12](#), [13](#)). In people with limited literacy, lack of cognitive skills is undoubtedly a contributing factor to non-adherence. This research has illustrated the positive influence of improved

understanding of medicines information on patient adherence to short-term therapy and highlighted the need for simple, understandable text and visual aids such as pictograms in medicines information material.

The problem of non-adherence affects all populations, however some are more vulnerable than others. High-risk populations such as those with low literacy skills, or people with disease states such as HIV/AIDS, who require complex drug regimens, should be identified and targeted for intervention studies (8). Poirier and NicholsEnglish (34) have recommended that HCPs should strive to provide medicines information materials that are written at a low-literacy level in order to help improve patient adherence to therapy in these high-risk populations. They suggest that medicines information materials should be short, simple and contain culturally sensitive pictograms, and be used in combination with verbal instructions. This was the approach adopted in this study where PILs were designed in collaboration with the target population and were provided to the low-literate Xhosa participants in their home language. The results of this intervention showed that significantly higher adherence to short-term therapy was noted for those participants who received the PIL incorporating simple text and pictograms. These findings support those of Dowse and Ehlers (35), as well as Ngoh and Shepherd (36) who reported significantly higher comprehension and adherence measures in the patient group that received visual aids.

Kitching (37) stated that 'Lack of information has been identified as a major factor among 250 reasons why patients do not take their medicines as the prescriber intends', a statement supported by the results of this study in which the highest percentage adherence was associated with receipt of a PIL containing simple text and pictograms. Adherence in these cases was found to be significantly higher than in cases where no written information at all was provided. These results clearly show the positive influence of receiving medicines information on the ability to achieve a high level of adherence to therapy and were in accordance with the findings of Regner *et al.* (38), who suggested that written materials such as PILs are essential for enabling patients to make appropriate decisions about their medicine taking.

Research has shown that drug information should be written in the simplest manner possible so that it is understood and judged as understandable by patients (39, 40). Previous research conducted by Mansoor and Dowse (31) showed that the presence of pictograms and simple text on medicines information materials significantly improved the understanding of instructions. Participants in this study also expressed an overwhelmingly positive desire for pictograms in their drug information. Materials written at a higher level may serve to depress understanding and clarity (40), preventing the patients from becoming active, responsible partners and informed decision makers in their health care (41). In fact, complex medicines information may adversely affect understanding, lead to unnecessary confusion which, in turn, may negatively affect adherence to therapy. Although this overtly negative effect was not apparent in this study, it was observed that only a non-significant increase in adherence was associated with the availability of the more complex information, whereas a significant increase in adherence was measured in the participants who received the simply written information illustrated with pictograms.

The relationship between improved understanding and adherence is generally a contentious issue; however, in this low-literate population with poor reading skills, a direct relationship was observed between understanding of the information received and adherence to therapy. Understanding of the PILs was assessed using the same methodology as described by Mansoor and Dowse (31), with the mean percentage understanding of the 'simple PIL' being significantly higher (90.8%) than that of the 'complex

PIL' (62.7%). The participants regarded the 'complex PIL' as too long and complicated, with unnecessary information, therefore the PIL incorporating simple text and pictograms was considered to be more desirable. Availability of this more complicated PIL had no significant effect on either understanding or adherence to therapy.

Measuring adherence is well known to be problematic, however before effective strategies can be devised to improve adherence, HCPs need to assess adherence and identify risk factors that may predispose the individual to non-adherence. Both direct and indirect methods are available to assess adherence. The available information suggests that self-report and tablet count would constitute the most adequate methods for measuring adherence in developing countries (16). The self-report assessment method is inexpensive and allows the HCP to interact empathetically with the patient and provide immediate feedback. However, accuracy of reporting depends on the cognitive abilities and honesty of the patient, as well as the correct interpretation of these reports by the HCP (42, 43).

Self-report has been criticized on the grounds that participants are unlikely to 'tell the truth', although some researchers (44, 45) have shown the self-report method to be acceptable. These researchers also agreed that patients generally tended to over-estimate their adherence with the important exception of those who acknowledged their non-adherence, where the reports were accurate. Our results showed similar findings especially when participants were asked for a direct global self-opinion of their adherence; however, the more in-depth, penetrating questions were answered more honestly.

Haynes *et al.* (44) commented that tablet count might be an awkward method of assessing adherence, although it may be accurate if the patient is unaware of the purpose of the assessment. Tablet counts provide an objective measure of the quantity of drug taken over a given time period, but this method is time consuming and assumes that medicine not in the container was consumed (42, 43, 45). Despite these shortcomings, our results from the self-report assessment agreed with the tablet count, therefore indicating reasonable consistency in these two different methods of assessing adherence.

In conclusion, successful therapy depends not only on taking the appropriate drug, but also on taking it in the appropriate way. This can only be achieved if the patient can access and understand the information and then act upon it. A more informed patient enables greater participation in the decision-making process, resulting in a positive impact on medicine-taking behaviour and health outcomes. Knowledge of interventions shown to improve adherence provides the HCP with tools with which to improve medicine adherence. Persistent and consistent monitoring and reassessment leads to positive rewards of improved medicine adherence and patient health.

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