

Medication adherence among heart and/or lung transplant recipients: An exploratory study

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Objectives: To investigate medication nonadherence in heart and/or lung transplant recipients; to explore patients' opinions about their medications and transplant experience; and to investigate strategies used to facilitate adherence.

Methods: A semi-structured questionnaire was developed to address the objectives of this exploratory study. Face-to-face interviews were conducted with inpatients and clinic outpatients at a large public teaching hospital.

Results: Thirty three patients consented to participate. Sixteen (48.5%) admitted to having missed a dose of their immunosuppressant medications at some time since the transplant, with five (15.2%) missing a dose in the two weeks prior to data collection. The main reasons for missing doses were 'forgetfulness' (n = 16, 48.5%) or 'being busy with other things' (9, 27.3%). Most nonadherence was unintentional, only 4 (12.1%) ever chose not to take a dose. Participants had strong opinions about their medications and condition. Most had a positive feeling towards their transplant and all had positive feelings about the team. Reported reasons for adherence included increased life span and quality of life. All but one of the participants used strategies or aids to facilitate adherence.

Conclusions: Self-reported nonadherence rates identified were low compared with literature reports for adherence in chronic disease and in other transplant populations. Participants' opinions about their medications and transplant experience may have acted as a strong motivator for adherence.

Keywords: adherence, compliance, heart and lung transplantation, pharmacist

Introduction

Goals of medication therapy are often undermined by poor patient adherence. Causes of nonadherence to a prescribed treatment regimen are variable throughout different disease states (Rovelli et al 1989). They include factors associated with the patient, such as patient beliefs (Greenstein and Siegal 1998; Horne and Weinman 1999), disease severity (Ostrop et al 2000; Dunbar-Jacob and Mortimer-Stephens 2001), difficulty remembering a dose (Greenstein and Siegal 1998; Ostrop et al 2000); the treatment regimen, including difficult (Ostrop et al 2000; Dunbar-Jacob and Mortimer-Stephens 2001) or inconvenient (Sketris et al 1994) dosage regimens, number of medications (Kiley et al 1993; Meyers et al 1996); and the patient's relationships with their family members (De Geest et al 1995) and their physicians (Kiley et al 1993; Raiz et al 1999). Factors specific to adherence to immunosuppressant therapy in heart and/or lung transplant recipients have been reported in a recent review and include socioeconomic, condition, therapy, and patient-related factors (De Geest et al 2005). Horne and Weinman (1999) found that for patients with chronic illness, beliefs about medications were a stronger predictor of adherence than clinical or sociodemographic factors.

There is evidence that adherence to medication is a critical requirement for the success of an organ transplant (Ostrop et al 2000; Kiley et al 1993;

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De Geest et al 1995; Raiz et al 1999). Though recent evidence has indicated that a successful organ transplant can occur for up to 5 years without immunosuppressive therapy (Alexander et al 2008; Kawai et al 2008; Scandling et al 2008). Frequent omission of immunosuppressant medications results in adverse clinical outcomes (Meyers et al 1996), such as rejection episodes, decreased quality of life, organ loss, and possibly death (Rovelli et al 1989; Kiley et al 1993; De Geest et al 1995; Greenstein and Siegal 1998; Dew et al 1999; Chisholm et al 2001). Increased healthcare costs are also a consequence of poor adherence (Dunbar-Jacob and Mortimer-Stephens 2001; Chisholm et al 2001) due to the costs associated with performing the transplant and dealing with the rejection episode, as well as the loss of the organ resource (Rovelli et al 1989).

Most transplant recipients take between 5 and 20 different medications, with over 50% of these dosed three to four times a day (SVH 2002). Studies have shown the prevalence of nonadherence to immunosuppressant medications to be as high as 75% (Kiley et al 1993; De Geest et al 1995; Greenstein and Siegal 1998). While the prevalence ranges from 25% (Dew et al 1996) to 36% (Dew et al 1999) in heart transplant recipients, with reports of approximately 23% (Teichman et al 2000) and 37% (Matthees et al 2001) in lung transplant recipients.

Patients who report less than perfect adherence may benefit from the use of strategies to facilitate adherence. These strategies need to be targeted at a specific cause of nonadherence within a particular patient group (Frazier et al 1994; Dunbar-Jacob and Mortimer-Stephens 2001). However, a greater understanding of factors associated with nonadherence is needed prior to the development of any interventions (Raiz et al 1999).

The majority of studies in the area of medication adherence in solid organ (SO) transplant recipients have been conducted in kidney transplant recipients with only a few studies on heart (Rovelli et al 1989; Schweizer et al 1990; Dew et al 1996, 1999) or lung (Teichman et al 2000; Matthees et al 2001) transplant recipients. This can be attributed to kidney transplants being more common than any other SO transplant (Chisholm 2002).

Therefore, the aims of this study were to: investigate medication nonadherence in lung and/or heart transplant (LHTX) recipients; explore patients' opinions about their immunosuppressant (IS) medications, condition and transplant experience; and investigate strategies used by patients to facilitate adherence.

Methods

An exploratory study was designed and conducted at a large public teaching hospital in Sydney, which has one of the largest heart and lung transplant programs in the world (SVH 2002). St Vincent's Hospital is one of the two heart/lung transplant centers in South-Eastern Australia. Approximately 45–50 transplants are performed each year. All patients (hospital in-patients post transplant and patients attending routine ambulatory clinic visits) who had undergone a LHTX and were being treated at the hospital during the study period were eligible. Patients who could not speak English and who were physically unable to participate were excluded. Written consent was obtained from all participants who were willing to take part in the study. Approval for the conduct of the study was obtained from the institution's Human Research Ethics Committee.

As the primary study aim was exploratory, no sample size calculation was performed; patients were recruited until "saturation" in the data was reached, that is, until no new themes or information were identified from the interview data (Quine 1998). Each eligible patient attending the hospital or clinic in the five-week study period was approached and invited to participate. In-patients were approached on the ward. Out-patients were approached in the waiting room of the heart and lung transplant clinic while they waited for a scheduled appointment. It is routine for all in-patients (even from day one when extubated) to keep and be responsible for taking their own medications. This is to ensure that they are able to manage their medications when discharged.

Instrument

Nonadherence, patient opinions and strategies used were assessed using a questionnaire delivered by an independent researcher, during a 20 minute face-to-face interview. An interview can be a reliable method for nonadherence assessment as long as the questions are asked in a nonthreatening and supportive manner by an independent investigator. The questionnaire's face and content validity were assessed using four researchers with a healthcare background and a small group of patients.

The questionnaire, consisting of open and closed questions, was developed, by adapting relevant questions from validated questionnaires (Frazier et al 1994; Greenstein and Siegal 1998; Horne and Weinman 1999; Kory 1999; Svarstad et al 1999; Bultman and Svarstad 2000; Ostrop et al 2000). It was designed for verbal responses using printed answer cards for the closed questions with multiple responses to

facilitate understanding and easier responding (Kiley et al 1993; Horne and Weinman 1999).

Patients were questioned about their adherence to medications since their transplant, and in the two weeks prior to the interview. This shorter recall period is thought to reduce reporting error (Svarstad et al 1999). Patients were questioned about their opinions towards their IS medications, their condition, their feelings towards the transplant process, team (surgeons, doctors, pharmacists, and nurses) and experience, as possible factors affecting medication adherence (Kiley et al 1993; Horne and Weinman 1999; Raiz et al 1999; Chisholm et al 2001); and devices or strategies used to aid adherence. For the purposes of this study adherence was defined as an 'all or nothing' principle a practice supported by previous research (Greenstein and Siegal 1998).

Data analysis

Data were entered into SPSS (Statistical Package for the Social Sciences; SPSS Inc., Chicago, IL, USA) for Windows, Version 10, and analyzed descriptively. Open questions were content-analyzed thematically (Weber 1990). The responses were first numerically coded into categories, which were assessed for themes or patterns. Those categories with similar themes were linked together, and the responses interpreted.

Nonparametric Mann-Whitney U test for two independent samples was used to test for differences between the in-patient and out-patient groups. For the purposes of this study, responses from all subjects were grouped together, irrespective of their transplant, as the study was exploratory in nature and did not set out to test hypotheses based on the organ transplanted.

Results

Patient characteristics

Thirty-three out of the 34 patients approached agreed to participate. Twenty-two (66.7%) were out-patients. The average age of the sample was 45 years (range: 16–71). Twenty-one (63.6%) were male and 29 (87.9%) were Caucasian. Twelve (36.4%) patients were employed, 11 (33.3%) were not working, and 10 (30.3%) were retired. Over half (54.5%) had reached year 10 or less at school, with 27.2% having completed tertiary education.

The majority of patients ($n = 21$, 63.6%) had received a single or double lung transplant, with 10 and 2 receiving a heart, and heart and lung transplant, respectively. The average time since transplant was 51.5 months (range: 0.8–142); and since any alteration had been made to

Table 1 Number of medications, and medication doses per day, in medication regimen for the subjects

	Self-reported	
	Mean number of medications	Mean number of doses per day
Total medications	10.8 (SD = 3.71)	16.1 (SD = 6.59)
Immunosuppressant Medications	2.9 (SD = 0.13)	4.7 (SD = 0.89)

the medication regimen was 53.5 days (range: 0–330). The number of medications taken is shown in Table 1.

No statistically significant differences were found between the in-patient and out-patient groups when comparing patient characteristics or adherence. Therefore, the responses from the two groups were combined.

Adherence to immunosuppressant medication

Sixteen (48.5%) participants admitted to having missed one dose of their medications at some stage since receiving their transplant: one subject admitted that this occurred once a week; three reported missing one dose once a month, with the remainder missing one dose less than once every 6 months. Over the two weeks prior to data collection, 15.2% of participants admitted missing one dose, but the majority of this was unintentional.

'*Forgetfulness*' (48.5%) or '*being busy with other things*' (27.3%) were the common causes of missed dose (Table 2). No respondent indicated that they had ever missed

Table 2 Reasons for missed doses ($n = 16$)*

Reason for missed dose	Frequency (n)	Relative frequency (%)
Forget medication	16	100.0
Busy with other things	9	56.3
Running out of medication	5	31.3
Away from home	4	25.0
Difficult scheduling medication taking around food	4	25.0
Choose not to take it	4	25.0
Too many medications to take	3	18.8
Misplaced medication	2	12.5
Belief that medication is not working	2	12.5
Sick of taking medications	2	12.5
Due to side effects caused	2	12.5

Notes: *The responses are not mutually exclusive. The data presented are the frequency and relative frequency (%); calculation based on $n = 16$ (total number of respondents who admitted to missing a dose).

Table 3 Patients' opinions towards their medications and condition (n = 33)

Statement	Strongly disagree Frequency (n) Relative frequency (%)	Disagree Frequency (n) Relative frequency (%)	Neutral Frequency (n) Relative frequency (%)	Agree Frequency (n) Relative frequency (%)	Strongly Agree Frequency (n) Relative frequency (%)
The medications I take for my organ should never be delayed or missed.	0 0	0 0	0 0	6 18.2	27 81.8
I will only be able to keep my organ if I take my medications.	0 0	0 0	0 0	5 15.2	28 84.8
If I don't take my medications correctly my condition will get worse.	0 0	0 0	2 6.1	9 27.3	22 66.7
Taking my medications correctly will prolong my life.	0 0	0 0	1 3	8 24.2	24 72.7
I need to take my medications for the rest of my life.	0 0	0 0	0 0	7 21.2	26 78.8
I believe that my condition is serious.	0 0	4 12.1	2 6.1	5 15.2	22 66.7

Notes: The data presented are the frequency and relative frequency (%); calculation based on n = 33 (total number of respondents).

a dose because they felt healthy. Of the 24 recipients who indicated that at least one of their medications bothered them in some way, only 2 had ever missed a dose as a result.

Patient opinions

All participants agreed or strongly agreed that they would only be able to keep their transplanted organ if they took their medications and that they should never delay or miss their medications (Table 3).

All participants had positive feelings towards the transplant team, while 31 (93.9%) had a positive feeling towards their transplant, with the reasons given falling into three broad categories. Firstly, the majority reported that their positive attitude

could be attributed to their increased life span, due to the success of the transplant. Patients felt that they had a 'second chance' at life because they were 'still alive'. An increased quality of life also contributed to their positive feelings, as the participants 'felt better' and could literally 'breathe easier' after receiving their transplant. A small number indicated that their transplant gave them the chance to spend more time with family and friends and see 'children and grandchildren grow up'.

Strategies to facilitate adherence

Nearly all (32) of the participants used at least one device or strategy to facilitate adherence (Table 4). Fifty-eight percent of the sample had a family member or friend helping them with their medications, either by reminding them to take them, or helping 'organize' their medications (ie, 'setting up the pill box', 'getting medications ready', or obtaining repeat prescriptions).

Table 4 Strategies or devices used to facilitate adherence (n = 33)*

Strategy/device	Frequency (n)	Relative frequency (%)
Obvious placement of medication(s)	30	90.9
Dosette box	14	42.4
Webster pack	2	6.1
Written list	14	42.4
The blue book	16	48.5
Messages/Post it notes	2	6.1
Alarm	9	27.3
Family member/friend	19	57.6

Notes: *The responses are not mutually exclusive. The data presented are the frequency and relative frequency (%); calculation based on n = 33 (total number of respondents).

Discussion

This study described medication adherence and opinions about immunosuppressant medications, condition and the transplant experience in lung and/or heart transplant recipients, and investigated strategies used by patients to facilitate adherence.

A low level of self-reported nonadherence was seen in this study, as over half of the participants had 'never' missed a dose of their IS medications since receiving their transplant. The level of nonadherence seen in the two weeks prior to

the study interview was lower than levels reported in the literature for heart transplant recipients, where nonadherence has been reported to range from 25% (Dew et al 1996; Kory 1999) to 36% (Dew et al 1999). Caution must be used when comparing levels of adherence between studies, as any differences in results may be due to the differing definitions of, or methods used to measure adherence rather than any true difference in adherence itself (Gao and Nau 2000; Ostrop et al 2000). This study defined adherence as an 'all or nothing' principle which could lead to an inflation of nonadherence levels compared to other studies that classify taking less than 80% of medications as nonadherence (Gao and Nau 2000; Ostrop et al 2000; Chisholm et al 2001).

The high level of self-reported adherence identified in this study could also possibly be described by the Health Belief Model (Kiley et al 1993; Gao et al 2000; Poss 2001) which proposes that a patient's adherence behaviour is dependent on their perceptions regarding their susceptibility to the disease, disease severity, benefits of treating the disease, and barriers to following the required regimen. The participants had strong opinions about their IS medications and condition, with the majority strongly agreeing that their IS medications were essential to the survival of their transplanted organ and future health. This is important, as a patient's beliefs about their medication (Greenstein and Siegal 1998; Horne and Weinman 1999) and their condition (Poss 2001) have been shown to play an important role in adherence to chronic therapy. The more the patient believes their condition would deteriorate as a result of not taking their medications as prescribed, the more likely they would be adherent (Horne and Weinman 1999; Gao et al 2000).

Encouraging results were found with 94% of the study sample displaying positive feelings towards their transplant and all participants having a positive feeling towards the transplant team. The literature shows that positive feelings to the transplant in general (Evenson and Fleury 2000) and positive relationships with physicians (Kiley et al 1993; Raiz et al 1999) have been shown to have a positive impact on adherence, a possible factor contributing to the high adherence levels observed in this study.

The level of adherence reported in this study could also be reflective of the use of a self-reported questionnaire to measure adherence. Studies show that patients tend to overestimate their own adherence (Svarstad et al 1999; Gao and Nau 2000; Ostrop et al 2000) in an attempt to please their doctors (Horne and Weinman 1999). Self-reported measures of adherence are also subject to recall bias (Horne and Weinman 1999; Gao and Nau 2000), selective reporting

(Rovelli et al 1989; Horne and Weinman 1999), and social desirability bias (Gao and Nau 2000).

Frazier and colleagues (1994) found that the most commonly cited reason for missing a medication by renal transplant recipients was forgetting, followed by being busy with other things. These findings were mirrored in this study, which suggests that there are indeed similarities between the different solid organ transplant groups regarding factors affecting medication adherence.

Previous studies have found that the potential for, or actual occurrence of, adverse effects can lead to under-adherence to a treatment regimen (Haynes et al 1979; Rovelli et al 1989; Gao et al 2000; Ostrop et al 2000). This study however showed that only 2 or 6.1% of the participants who admitted to being bothered by a medication missed a dose as a result. This may be a consequence of the understanding, exhibited by the participants, as to the potential consequences associated with not taking their IS medications.

Kory (1999) reported that most patients used at least one strategy or device to facilitate adherence, with the most common method being to place medications in a noticeable position. This study demonstrated similar findings.

No differences were found between the patient characteristics, or adherence levels, of in-patients compared to out-patients in this study. This could possibly be due to the small sample size, rather than consistency between the two groups. There is no research in the literature discriminating between these two patient groups. Factors affecting adherence may be different for these two groups.

Limitations

There are specific limitations associated with the study instrument. Assessment of adherence is difficult because there is no gold standard for measurement (Raiz et al 1999). Self-reported measures, including questionnaires, overestimate the patient's adherence (Kiley et al 1993; Horne and Weinman 1999; Ostrop et al 2000) and are subject to recall bias (Horne and Weinman 1999; Poss 2001) and selective reporting (Greenstein and Siegal 1998; Horne and Weinman 1999). Direct measures of adherence are more reliable (Osterberg and Blaschke 2005), which was not possible in this study.

Conclusion

The level of nonadherence reported in this study was low, with the main contributor reported to be 'forgetfulness' and 'being busy with other things'. The low level of nonadherence seen could possibly be explained by the participants' strong opinions about their IS medications and condition.

Participants commonly used strategies to facilitate adherence, in particular, placing medications in an obvious place to act as a reminder to medication taking.

Patients' opinions about their immunosuppressant medications, their condition and transplant experience may strongly influence adherence. Health professionals should be cognizant of not only the barriers but also the facilitators or motivators which can influence adherence, and which can be targeted to enhance patient adherence to therapy. The findings of this study have been used in educating pharmacists and other clinicians in this area to better care for their patients, in particular, in optimizing adherence to therapy.

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Disclosure

The authors have no known or suspected conflicts of interest.

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