Early communication

An evaluation of secondary prophylaxis for rheumatic heart disease in rural Egypt

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ABSTRACT

Background: Although essentially disappeared from the industrialized world, rheumatic heart disease (RHD) is still prevalent in developing countries, with 300,000 new cases identified each year. In Aswan, Egypt, RHD affects about 2.3% of children with over 90% of the cases being subclinical. Secondary prophylaxis has proved to be an effective method of preventing the progression of RHD. However, its efficacy is limited by low patient adherence. A systematic, generalizable tool is necessary to outline, and ultimately address these barriers.

Methods: A 43-item semi-structured questionnaire was developed based on the three domains outlined by Fishbein (capability, intention, and health care barriers). A preliminary evaluation of the barriers to RHD prophylaxis use in Aswan, Egypt was carried out as a pilot study using this tool. Participants were local school children diagnosed with RHD or flagged as high-risk (as per a set of echocardiographic criteria developed by the Aswan Heart Centre) through a previous screening program of randomly selected 3,062 school children in Aswan.

Results: 29 patients were interviewed (65.5% adherent to RHD prophylaxis). Compared to non-adherent patients, adherent patients had better understanding of the disease (68.4% versus 20% in the non-adherent group, p = 0.021), and were more aware of the consequences of missing prophylaxis doses (79% versus 40% of non-adherent patients, p = 0.005). Furthermore, 90% of non-adherent patients consciously choose to miss injection appointments (as compared to 31.6% of adherent patients, p = 0.005). Clinic wait time was the most frequently reported deterrent for both groups.

Conclusion: A standardized tool that systematically outlines barriers to prophylaxis is a necessary first step to improving adherence to penicillin. Although individually developed tools exist for specific populations, a generalizable tool that takes into account the demographic and cultural differences in the populations of interest will allow for more reliable data collection methodology. Application of this tool will be used to further explore barriers to prophylaxis adherence and inform the basis for the design of future KT interventions.

BACKGROUND

Rheumatic heat disease (RHD) is the most common cardiovascular disease in people aged 25 years and under in the developing world.[1] It occurs as a result of rheumatic fever (RF) – an autoimmune disease that follows group A β-haemolytic streptococcal (GAS) infection of the throat, which can lead to an inflammatory response targeted mainly at the tissues of the heart, joints, and the central nervous system.[1,2] Two-thirds of RF patients develop valvular heart disease which mainly manifests clinically as mitral, or aortic valve regurgitation and/or stenosis.[2] As gradual scarring of the valve leaflets occur, this can progress to severe valvular dysfunction, atrial fibrillation and heart failure.[1,2] As the cardiac valve deteriorates, valve replacement/repair surgery is often required.

Rheumatic fever and rheumatic heart disease have essentially disappeared from industrialized/high income countries. However, the same cannot be said for developing countries when the predominant risk factor for the disease is poverty. In 2005, 15.6 – 19.6 million people in low- and middle-income countries were estimated to have RHD, and close to 300,000 new cases of RHD are identified each year with 233,000 directly attributable deaths.[3]

True primary prevention of RHD means eliminating conditions such as overcrowding, and socio-economic deprivation.[2] However, in the absence of this possibility, and unavailability of a GAS vaccine, an effective primary prevention strategy against RF is the treatment of GAS pharyngitis with antibiotics - usually a single dose of intramuscular (IM) penicillin. While clinically effective, the practicality and cost-effectiveness of throat screening programs are still unclear.[1]

Recurrent attacks of RF and the progression of RHD can be prevented by prophylactic antibiotics, with IM injection of benzathine penicillin at three-week intervals being one of the most effective antibiotic regimens.[2] Patients usually remain on this prophylaxis for at least 5 years following the first attack of RF, or until they are 21 years of age. However, prolonged therapy is more effective for those with persistent evidence of carditis, with recommended prophylaxis for at least ten years after the attack, or until the patient is 40 years of age.[2]

One factor that limits the efficacy of secondary prophylaxis programs is low patient adherence.[1] Previous studies have reported that non-adherence, most frequently defined as patients taking less than 80% of expected medication,[4] can be as high as 50%, and have outlined several possible factors for this observation.[5] Generally, low medication adherence rates are hypothesized to be linked to several factors which include older age, males, low socioeconomic status, use of traditional healers, lack of hospitalization history, lack of symptoms, short intervals between prophylaxis doses, beliefs concerning effectiveness of the drug, and lower degree of knowledge of RHD.[5–8] Studies looking at general prophylaxis adherence rates have shown that increased understanding of the risks of one's condition improves adherence to prophylaxis.[9] However, a discrepancy does appear between what patients perceive they understand and how much they truly do understand in respect to the details of their health condition, with studies showing up to a 43% difference between the two.[9] The difficulties that patients might face in reaching the clinic on regular basis, the painful nature of these injections, and a lack of awareness and understanding may form a combination of barriers that collectively lead to these low adherence rates.[9,10]

In Aswan, Egypt, RHD affects 2.3% of school children with over 90% of the cases being subclinical.[11] The high rate of asymptomatic cases reinforces the use of secondary prophylaxis as a method of controlling RHD. At the Aswan Heart Center, prophylaxis injections are given to RHD patients at the clinic at three-week intervals, with patients coming to the clinic for these injections. Physicians at the center have noted that there is low patient adherence to the prophylaxis and the clinic checkups, both of which are offered at no expense to the patients.

Some barriers to medication adherence may be common across different conditions and populations. However, many barriers are contextual in nature.[12] Sociocultural, location, and the health care system structure differences can all influence the type of barriers that affect a specific population. In order to develop future knowledge translation (KT) strategies to improve adherence to RHD prophylaxis, the contextual barriers to optimal adherence in specific populations must be better understood. This study outlines the development of a tool that will allow for a systematic measurement of these barriers, and inform the basis for the design of future KT interventions. A preliminary evaluation of the barriers to RHD prophylaxis use in Aswan, Egypt was carried out as a pilot study using this tool.

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METHODS

Questionnaire development

The questionnaire was developed using an iterative stepwise approach. A set of general questions was first developed from the literature using identified barriers and facilitators to medication adherence. These questions were then refined by an expert panel involving cardiologists, epidemiologists and knowledge translation researchers. A series of open-ended questions was included to capture barriers and facilitators not reported in the literature or hypothesized by our study group.

Questions were grouped using the three domains outlined by Fishbein; capability, intention, and health care barriers. According to this model, when one has the ability, a strong intention, and does not have environmental constraints to perform a behavior, this behavior is very likely to occur.[13] A patient was categorized as 'knowledgeable' if a minimum of two correct answers were marked for each question under the capability domain. The questionnaire was applied to the study population for further question modification.

Setting and population

The Aswan Heart Center is a cardiac center that serves the 1,499,000 inhabitants of Aswan as well as those in neighbouring Upper Egypt.[14] The majority of patients served by the RHD clinic are asymptomatic children, under the age of 18. These children were identified through cross sectional RHD screening of a cohort of randomly selected 3,062 school children between the ages of 5 and 15 years in Aswan.[11]

Patients were classified as either adherent or non-adherent. Patients who received less than twelve injections in the past year ($<75\%$) were considered to have sub-optimal adherence, and those who received over twelve injections ($>75\%$) were considered to have optimal adherence to prophylaxis.[4]

Data collection and question modification

A series of three structured interviews, using a preliminary set of questions, were carried out with both adherent and non-adherent patients. For patients under the age of 12, questions were directed at the parental guardian if present. Responses from these interviews, as well as medical information from patient files were used to form the basis of the final questionnaire. Questions were modified to reflect previously unmentioned barriers outlined by the participants.

The questionnaire was then tested for readability in a non-study group, then modified as needed. The final questionnaires (Appendix A) was distributed to the patients or parental guardian if present, during their time in the waiting room for their prophylaxis appointment. Resources were provided to patients who required assistance reading the questionnaire.

Patients who did not regularly come to clinic visits were contacted by phone. Upon receiving verbal informed consent, the same questionnaire was administered over the phone. Each patient was called a maximum of three times on separate days, and was excluded from the study if no response was acquired at that point.

Statistical analysis

For specific domains, where applicable, item responses from the questionnaire were captured using a 5-point Likert scale (1 = strongly agree, 2 = agree, 3 = undecided, 4 = disagree and 5 = strongly disagree) for each domain. Percentages were reported for each item score from the total number of patients in each group. Comparisons across adherent and non-adherent groups were conducted using Fisher's Exact Test for binary responses (Yes/No) and item responses ('strongly agree' vs 'all others'). In addition, item response from 5-point Likert scale were transformed to a normalized score on a 0 to 100 scale (for statistical comparisons) where higher scores suggested improved satisfaction/knowledge. Normalized scores were compared across groups using a two-tailed Student t-test. Statistical analyses were conducted using SAS version 9.2.

RESULTS

A total of 29 patients met the inclusion criteria (Figure 1), with 65.5% adherent and 34.5% non-adherent patients. The questionnaire was successfully carried out with all patients involved, either individually or verbally with the assistance of a member of the research team. The adherent group showed a higher
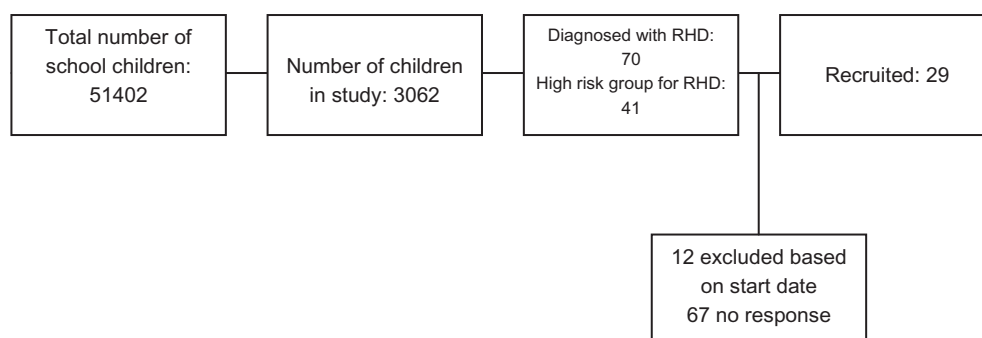
Figure 1. Study population.

overall degree of capability and intention. There was no significant difference in the results pertaining to health care barriers.

Under the capability domain, there was a statistically significant difference between adherent and non-adherent patients in the degree of understanding of the disease. 68.4% of adherent patients were knowledgeable about RHD compared to 20% of non-adherent patients (p = 0.021). Two significant barriers were also observed under the intention domain. Awareness of the consequences of missing prophylaxis doses was apparent in 79% of adherent patients as opposed to 40% of non-adherent patients (p = 0.005). Furthermore, 90% of non-adherent patients consciously choose to miss injection appointments, while only 31.6% of adherent patients choose to do so (p = 0.005) (table 1).

Table 1. Factors Associated With Adherence To Prophylaxis.

Domain	Adherent (N = 19)	Non-adherent (N = 10)	P Value
Capability, n (%)			
Knowledge of nature of disease	13 (68.4%)	2 (20%)	0.021
Intention, n (%)			
Knowledge of consequences of missing prophylaxis doses	15 (79%)	4 (40%)	0.005
Consciously choosing to miss injection appointments	6 (31.6%)	9 (90%)	0.005

There was a positive unanimous response for the role of family members in reminding patients of appointment times. Wait times as a deterrent to attending injection appointments showed a mean difference of 0.5%, with 60% of adherent and 60.5% of non-adherent patients reporting this as a barrier. 66% of patients waited in the clinic for 1−3 hours, with an average wait time of 2 hours.

DISCUSSION

The effectiveness of secondary prophylaxis is compromised by lack of adherence. Previous research in low-income countries, using self-developed tools, has shown differing factors for this low adherence.

Although these studies are a positive step forward, a generalizable tool that takes into account the demographic and cultural differences in the populations of interest will allow for a more systematic approach in assessing these barriers and ultimately addressing them.

The tool developed and tested in this study drew upon barriers to medication outlined in previous studies pertaining to cardiovascular disease, as well as more specific studies focusing on RHD. Questions were posed using both a closed (including Likert scale, dichotomous responses) and an open ended approach. Although the purpose of the Likert scale was to allow for more insight into the degree of effect that specific barriers have, patients in this population found the scale difficult and tended to select either extremes on the scale. Cultural differences have been noted to exist in response to Likert scales, with some cultures experiencing difficulty with the ordered continuum and preferring a dichotomous response tool. Some ethnic groups also encounter "end-aversion bias" resulting in an increased likelihood of selecting midpoint responses compared to their American counterparts.[15]

These observations need to be taken into account when considering the generalizability of this questionnaire across different populations. Comparing age groups, it is worthwhile to take note that younger children tend to answer at the extremes of the response continuum on emotion-based questions, as compared to older children. Nevertheless, the Likert scale has been reported to be the optimal tool for questionnaires targeted at children as compared to other scales, such as the simple Visual Analogue Scale (VAS) and the numeric VAS. Patient reported preference, as well as less instances of missed questions adds to the feasibility of the scale.[16] In this study, questionnaires were answered by parental guardians for children under the age of 12. It may prove worthwhile to explore the difference in response, and perspective of barriers between children and their guardians.

Open-ended questions aimed to provide space for patients to express any proactive steps that they felt can be taken to eliminate barriers affecting their medication adherence, as well as highlight the main barrier encountered. This patient insight is essential and can be used to further fine-tune the close ended questions.

The pilot study allowed for a preliminary look at the barriers to RHD patients at the Aswan Heart Center. The setting for this study has not been previously explored and is unique as the health care service is free and patients are asymptomatic and under 18 years of age.

The knowledge gap between adherent and non-adherent patients was evident in this study. Fewer patients in the non-adherent group understood the nature of their disease and the consequences of missing the prophylaxis injections. Even though it was confirmed by both the physician and the patients that this information was provided to them, the gap appeared in patient retention and understanding of this information. Furthermore, concerns surrounding several misconceptions, specifically the link between prophylaxis and possible resulting paralysis, was voiced by several patients.

These two factors combined can be seen as the root of the third barrier. The lack of intention of non-adherent patients to receive their prophylaxis was most clearly outlined by the 90% of non-adherent patients who consciously choose to miss these appointments. Several patients reported frustration that they could not physically see any proof of the effectiveness of the injections.

The importance of the role of the family in the patients' health care can be seen by the number of family members that attended clinic appointments with their children, as well as the role they took in reminding patients about their appointment times. Steps taken to improve adherence should be inclusive to the family as a whole, and not solely directed towards the patient.

Although barriers under the health care domain showed no significant difference between the two groups of patients, it was the most frequently reported concern in response to the open ended-question asking patients to list barriers they felt affected their adherence rates. Dissatisfaction was expressed by patients, 66% of whom waited for 1−3 hours every three weeks in the clinic for their injections.

These conclusions are limited by the low statistical power of the study and self-reported date. The small study sample, composed of only 25% of the total population from which the sample was drawn, is non-representative of the larger population. Self-reported data by the study population, which included frequency of clinic appointments attended, could have led to recall and social desirability bias. Ensuring a system is in place to track adherence for each patient before administering the questionnaire will allow for a clearer understanding of barriers.

However, the goal of this study was not to draw solid conclusions about the barriers to RHD prophylaxis, but rather to test the tool developed in a pilot study. Conclusions can be drawn by further application of this tool. Given a more accurate picture of these barriers, future KT interventions may include schedule optimization to reduce waiting time, and interactive education workshops targeted at patients as well as their families to provide accessible knowledge about RHD.

CONCLUSION

A generalizable tool that systematically outlines barriers to prophylaxis is a necessary first step to improving adherence to penicillin. Although some tools do exist for specific populations, a standardized tool will allow for a more reliable data collection methodology. The tool developed in this study can be used to further explore barriers to adherence. Initial findings showed that barriers to penicillin prophylaxis adherence in the Aswan Heart Center are closely tied to an underlying knowledge

gap between adherent and non-adherent patients. Further research and solutions directly targeting these barriers can improve patient adherence and decrease their overall risk of RHD.

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Appendix A

Gender: Male/Female   Age:

Do you attend clinic appointments: Alone / With a family member

If with a family member, what is the relationship to the patient? [parent, sibling, other relative, friend, other]

What is your diagnosis? [Free text]

Rheumatic Heart disease (check all that apply):

    [ ] can cause cancer

    [ ] can cause weakness to the valves of the heart

    [ ] can cause High blood pressure

    [ ] can sometimes not show any symptoms

    [ ] can cause palpitations

    [ ] If not treated can lead to serious complications

    [ ] Unsure

When did you start prophylaxis? [free text]

How many appointments have you missed in the past year? [free text]

Does anyone in your immediate family had RHD? Yes/No

If I do not take these injections what can happen:

    [ ] my heart condition will get worse/symptoms will start to appear

    [ ] it's ok to miss a few doses, nothing will happen

Are you aware of the side effects of the injections? Yes/No

What symptoms will you get if you do not take your penicillin? [free text]

Are you aware that you might need heart surgery if you do not remain on prophylaxis? Yes/No

If you miss an appointment what do you do?

    [ ] wait until my next appointment

    [ ] go a few days later

How long do you usually wait at the clinic? ($<$1 hour, 1–3 hours, 3–5, $>$5)

I will need to continue these injections for about 20 years: True/False

I am aware that these injections can stop the progression of Rheumatic heart disease: Yes/No

Do you believe that there is a more effective traditional method (homeopathic medicine-or local term in Egypt) to treat RHD? Yes/No

Have you ever been hospitalized because of your condition? Yes/No

Have you ever had a bad reaction (more than local swelling and tenderness) following a previous penicillin injection? Yes/No

How long does it take you to get to the clinic? [< 20 min, 20 – 40 min, 40 – 60 min, 1 – 2 hours, > 2 hours]

What mode of transportation do you use to get to the clinic? [Bus, car, Train, walking]

When you miss an appointment, it is because:

[ ] you forgot

[ ] you consciously choose to/ were unable to make it

What would most help you attend your clinic appointments? [free text]

What is the most prominent barrier that prevents you from regularly attending your scheduled clinic appointments for your prophylaxis? [free text]

	Strongly agree	Agree	Undecided	Disagree	Strongly disagree
My doctor has explained what Rheumatic heart disease is.	1	2	3	4	5
My doctor clarified why the injections are important.	1	2	3	4	5
I believe that this medication is effective.	1	2	3	4	5
I need to take this medication even if you do not feel any symptoms.	1	2	3	4	5
Taking the injections will make me better.	1	2	3	4	5
Members of my family remind me to go for my appointment.	1	2	3	4	5
I trust the information the doctors provide.	1	2	3	4	5
I want to come to the clinic on a regular basis but am unable to.	1	2	3	4	5
I will be able to continue your clinic visits until the end of the treatment regimen.	1	2	3	4	5
Coming to these clinic visits is worth your time and effort.	1	2	3	4	5
My number one priority is making it to my scheduled clinic appointments.	1	2	3	4	5
Taking the injections make me feel unwell.	1	2	3	4	5
Taking the injections is painful.	1	2	3	4	5
The painful nature of the injection deter me from taking the injections.	1	2	3	4	5
The distance to the clinic is a deterrent to attend appointments.	1	2	3	4	5
Costs associated to coming to the clinic (days off work, transportation, etc) prevent me from coming.	1	2	3	4	5
It is difficult to keep track of appointment times.	1	2	3	4	5
Long wait times at the clinic are a deterrent to come to my appointment.	1	2	3	4	5