

RESEARCH ARTICLE

Streptokinase and streptokinase card: questionnaire validation to evaluate knowledge among post-STEMI patients in a Malaysian Tertiary Hospital

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Abstract

Background: Although recombinant tissue plasminogen activator has become the first-line thrombolytic agent, streptokinase remains in use in acute ST-elevation myocardial infarction (STEMI) patients in Malaysian public hospitals. In a state hospital in Malaysia, all post-STEMI patients given streptokinase are counselled and issued with a streptokinase card by pharmacists. Due to its highly antigenic nature, patient knowledge of streptokinase and the streptokinase card serve as important alerts to healthcare providers. This study aimed to develop a validated questionnaire on evaluating knowledge of streptokinase and the streptokinase card among post-STEMI patients.

Methods: A Malay language questionnaire was developed based on literature review and a standard streptokinase counselling checklist. The questionnaire consisted of three parts: demographics, knowledge of streptokinase and understanding of streptokinase card. The content of the questionnaire was revised by eight experts (emergency specialists, physicians and pharmacists) and six patients were interviewed via telephone, 2 weeks after being issued with a streptokinase card, to test for comprehensibility. Then, a telephone survey was conducted during June-December 2017 involving another 60 patients to test for construct validity and reliability.

Results: The questionnaire was finalised by decreasing the overall number of items from 6 to 5 (Section B) and 6 to 4 (Section C). The overall measurement of sample adequacy (MSA) was 0.758. Bartlett's test was highly significant (<0.001). The Cronbach's alpha values for Sections B and C were 0.747 and 0.841, respectively.

Conclusion: Our nine-item questionnaire is a valid and reliable instrument to assess knowledge of streptokinase and the streptokinase card among Malaysian post-STEMI patients.

Keywords: streptokinase, knowledge, STEMI, surveys and questionnaires.

INTRODUCTION

Cardiovascular disease (CVD) remains the leading cause of death in Malaysia, accounting for 20–25% of all deaths in public hospitals.¹ One subgroup of CVD is acute ST-elevation myocardial infarction (STEMI).² In Malaysia, fibrinolytic therapy is more readily available and constitutes the main reperfusion strategy in the early management of acute STEMI.³ Fibrinolytic therapy has been shown to reduce mortality when given within the appropriate time frame.²⁻⁴ Streptokinase, a non-

fibrin-specific fibrinolytic agent, is the most widely used reperfusion therapy in Malaysian public hospitals for STEMI patients.¹ Although tissue plasminogen activator (t-PA) agents, such as tenecteplase have become the first-line thrombolytic agents in various guidelines, streptokinase remains in use in more than 50% of countries worldwide due to its affordability, especially in developing countries.³ In Malaysian public hospitals, tenecteplase is only reserved for recurrent STEMI patients who received streptokinase within the previous one-year period.

When streptokinase is administered to a patient, it will provoke an immune response that causes anti-streptococcal antibodies to be produced.⁵ These antibodies will eventually react to a subsequently administered

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dose of streptokinase, and therefore will stimulate either an allergic reaction or neutralise the streptokinase, rendering it ineffective.⁶⁻⁸ Due to its highly antigenic nature, studies on antibody titres post-streptokinase injection.^{9,10} recommend that streptokinase should not be readministered within a one-year period as it may cause severe allergic reaction(s) such as anaphylaxis and it may not be efficacious for subsequent STEMI event(s) within that time period.^{5,10}

In Hospital Tuanku Fauziah, our hospital setting, every STEMI patient who is administered streptokinase is counselled and issued with a streptokinase card (Figure 1) in the ward by a pharmacist. It is thought that knowledge retention about streptokinase and the streptokinase card among these patients will empower them to notify other healthcare providers that they received streptokinase as dated on the card. To the best of our knowledge, there is no validated questionnaire to assess patients' knowledge of streptokinase and their understanding of the streptokinase card. Therefore, the aim of this study was to develop a validated questionnaire evaluating knowledge of streptokinase and the role of the streptokinase card among post-STEMI patients.

METHODS

Ethics Statement

This study was registered with the National Medical Research Register, Malaysia (NMRR-17-635-35271) and was approved by the Medical Research Ethics Committee (MREC), Malaysia.

A cross-sectional study was conducted among post-STEMI patients who had been counselled and issued with a streptokinase card in one of the public hospitals

in Malaysia. The details and contact information of the subjects were obtained from the streptokinase card database. The exclusion criteria were patients with no contact information in the streptokinase card database and patients with any previous allergy to streptokinase.

The questionnaire was developed by the principal investigator who was an emergency clinical pharmacist, based on thematic elements from a previous study¹⁰ and our pharmacist standard counselling checklist for streptokinase and the streptokinase card. The questionnaire was constructed in the national language of using short sentences, simple and generic words that suited subjects with basic Malay literacy skills. The questionnaire was divided into three main sections: (A) sociodemographics; (B) knowledge of streptokinase, and (C) understanding of the streptokinase card. For (A) sociodemographic data, age, gender and ethnicity were taken from the streptokinase card database, while information on the primary caretaker, marital status and highest educational level were obtained during the survey. For knowledge assessment in sections B and C, respondents were required to answer whether each statement was 'true' or 'false'.

The questionnaire was distributed independently to subject matter experts in our hospital: two emergency specialists, three physicians and three ward pharmacists to provide their feedback on the content of the questionnaire. This content validation process using Delphi method¹¹ identified objectives such as patients' education level and language. It was hypothesised that the intended respondents who had no formal education could understand each question. The experts were asked both to rate the item with Likert-scale and to write free-text comments to explain their rating and/or express agreement/disagreement with the statement's

<p>A</p> <p style="text-align: right;">Serial No. :</p> <p style="text-align: center;">PHARMACY DEPT, HOSPITAL TUANKU FAUZIAH</p> <div style="border: 1px solid black; padding: 5px; text-align: center; margin: 10px auto; width: 80%;"> <p>STREPTOKINASE CARD</p> </div> <p>Name :</p> <p>IC No. :</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="width: 33%;">Date of Injection</th> <th style="width: 33%;">Dose</th> <th style="width: 33%;">Name of Medical Officer</th> </tr> </thead> <tbody> <tr> <td style="height: 30px;"></td> <td></td> <td></td> </tr> </tbody> </table> <p style="font-size: small;">The next injection can be given after one year from the date stated.</p>	Date of Injection	Dose	Name of Medical Officer				<p>B</p> <div style="text-align: center; margin-bottom: 10px;"> <div style="background-color: black; color: white; padding: 2px 10px; display: inline-block;">WARNING</div> </div> <p style="font-size: x-small; text-align: center;">Please bring and show this card when seeing doctor / pharmacist / dentist / other healthcare professionals when receiving treatment.</p> <p>Issued by:</p>
Date of Injection	Dose	Name of Medical Officer					

Figure 1 The English translation of the (a) front and (b) back of streptokinase card issued by our facility.

relevance, independently. After feedback from the experts was collected, researchers made necessary corrections according to the suggestions provided. The corrected questionnaire was sent again to the experts. A mock telephone survey was administered to the experts individually. Then, all experts were invited to a focus group discussion, to talk together about further improvement of the questionnaire to the point that all experts agreed on the finalised questionnaire. To confirm face validity, two respondents in the 30-59 age group, and four respondents aged 60 years old and above: all with different educational backgrounds were interviewed via telephone 2 weeks after being issued with the streptokinase card, to test for comprehensibility. The duration of 2 weeks was chosen based on a previous study with the same study procedure.¹² The telephone conversation began with the entry-level question in the Malay language "Did you receive a streptokinase card 2 weeks ago?". If the response was yes, the study was briefly explained and the patient was asked for consent and time to answer the questionnaire. After the respondents had given their informed consent, the questions were read out word-for-word and respondents answers were recorded. Any comments from the subjects were taken into consideration for further modification of the questionnaire.

After content and face validation, the revised questionnaire was tested for construct validity and reliability. The corrected questionnaire (12 questions) was administered using the same procedure as the face validation phase, to another 60 respondents by applying 1:5 as the item-to-respondent ratio to calculate the sample size to produce good reliability and valid factor solution.^{13,14} Statistical analyses were performed using IBM SPSS Statistics for Windows (Ver. 20.0, IBM Corp., Armonk, NY, USA). Principal component analysis (PCA) was conducted in order to ascertain the construct validity of the proposed questionnaire by using varimax rotation.¹⁵ The Kaiser-Meyer-Olkin (KMO) and Bartlett's test of the sphericity (BTS) were done to measure the sampling adequacy. The sample was considered adequate if the KMO value was higher than 0.5 and BTS was significant ($P < 0.05$). The factor analysis required the correlation matrix to be more than 0.3 and anti-image correlation Measure of Sampling Adequacy (MSA) to be more than 0.5 between the variables included in the analysis. Communalities represent the proportion of the variance in the original variables that is accounted for the factor solution.¹⁶ Community values for each variable should be more than 0.50.

The reliability of the questionnaire was tested using Cronbach's alpha (CA). Cronbach's alpha is a measure of internal consistency reliability, that is, how closely

related a set of items are as a domain. Since there are two domains in the survey, two values of CA were obtained for the knowledge domain of streptokinase and the domain in assessing the understanding of streptokinase card. CA of 0.70 or higher is considered acceptable in most social science research.¹⁶ A high value of CA exhibits good item inter-relatedness, which describes the degree to which all the items in a test measure the same concept or construct.¹⁶

RESULTS

The first draft of the questionnaire consists of six questions regarding knowledge of streptokinase (Section B) and six questions regarding knowledge of the streptokinase card (Section C). After content validation, one question was added, and one question was deleted, in the respective sections.

No changes were made in the face validation process. All the subjects claimed to understand the language used in the questionnaire. A telephone survey took approximately 10-15 min to complete and was generally well-received by the respondents.

In construct validity, out of the 60 respondents, most of them were aged between 40 to 59 years old (63.3%), male (81.7%), Malay (88.3%), married (80.0%), spouse as primary caretaker (70.0%) and secondary school leavers (33.3%), as in Table 1. For validity testing, principal component analyses on three individual variables, namely Section B (Questions 1 and 2), and Section C (Question 4), had zero variance. Correlation coefficients could not be computed for these pairs of variables. No further statistics were computed for items B1, B2 and C4. The overall KMO MSA for the set of variables included in the analysis was 0.758, while Bartlett's test of sphericity was highly significant ($P < 0.001$). This was considered adequate for the factor analysis. Using the correlation matrix between individual variables, there were 61 correlations for this set of variables in the matrix greater than 0.30, satisfying this requirement. Using anti-image correlation, the KMO MSA for all of the individual variables included in the analysis was greater than 0.50, ranged from 0.704 (C5) to 0.852 (C3), supporting their retention in the analysis. Community values for all variables ranged from 0.774 (B4) to 0.966 (C5).

For reliability testing, the overall CA coefficient was computed. For Section B, the overall CA value was increased from 0.697 to 0.747 after questions B1 and B2 were deleted (Table 2). For Section C, the overall CA was increased from 0.788 to 0.841 after question C4 was deleted.

Table 1 Sociodemographics of respondents ($n = 60$)

Characteristics	n (%)
Age group	
30–39	2 (3.3)
40–59	38 (63.3)
60–79	18 (30.0)
>80	2 (3.3)
Gender	
Male	49 (81.7)
Female	11 (18.3)
Ethnicity	
Malay	53 (88.3)
Non-Malay	7 (11.7)
Primary caretaker	
Spouse	42 (70.0)
Children	15 (25.0)
Close relatives	2 (3.3)
Parents	1 (1.7)
Marital status	
Married	48 (80.0)
Widowed	10 (16.7)
Single	1 (1.7)
Divorced	1 (1.7)
Highest education level	
No formal education	13 (21.7)
Primary school	14 (23.3)
Secondary school	20 (33.3)
Diploma/pre-university	8 (13.3)
Degree and above	5 (8.3)

For Section B, only 39 (65.0%) respondents answered question B6 correctly, followed closely by B5 ($n = 40$, 66.7%) and then B4 ($n = 44$, 73.3%); Meanwhile for Section C, only 48 (80.0%) answered C3 correctly, followed by C2 ($n = 54$, 90.0%), as shown in Table 2. Scores below the median scores of four for both sections were considered to have poor knowledge while scores of four and above were considered to have good knowledge. For Section B and C respectively, 33.3% and 21.7% of the respondents had knowledge scores of 0–3 (Table 3).

DISCUSSION

The final validated questionnaire developed consisted of three sections: six items on sociodemographics; five items on knowledge of streptokinase and four items on the understanding of the streptokinase card.

In the questionnaire development phase, the knowledge of streptokinase domain consisted of six questions which included: knowledge of the indication, route of administration, the interval of readministration, ineffectiveness of readministration, the risk of readministration

within a one-year period and the importance of preventing readministration if the patient has a history of allergic reaction with streptokinase. During content validation, the suggestion of adding a new question “family member or caretaker should know that you had been given streptokinase” was accepted and was agreed unanimously by the panel of experts, which increased the number of questions to seven. We considered the question important as family members also play a vital role in providing accurate and reliable information on the patient’s past medical and medication history to healthcare providers. This was in concordance with a study done by Mitnick *et al.*,¹⁷ which described that a patient’s health status information provided by the caregiver may be as relevant and reliable as information on medical records.

The domain for the streptokinase card was made up of six questions, including knowing the date of administration on the card, who to present the card to, where to present the card, to take the card everywhere, family member or caretaker knows the location of the card and how to replace a lost card. The question “The streptokinase card should be brought with you at all times” with the theme of “to bring the card anywhere” was deleted due to the possibility of repetitious theme and ambiguous interpretation of that question during the content validation process. The existing question of “This card should only be carried when you get treatment at Hospital Tuanku Fauziah only” should cover the objective of the deleted question, although this question was the least correctly answered question during the construct validation phase. It might be a tricky question as the patients may assume that they’re only required to show the streptokinase card in the hospital where it was originally issued. Our hospital is the only hospital in the state of Perlis which borders Thailand in the north that serves a population of 252,200 and also serves the northern region of the neighbouring state of Kedah.

In the construct validation phase, items B1 (indication), B2 (route of administration) and C4 (to bring the card anywhere) could not be analysed as these questions were answered correctly by all respondents involved in the study, and therefore show no variance regarding the response to the questions. Information on these deleted items could be included in the introductory part of the telephone call as an extra reminder to the respondents. CA values for both sections increased as well after the deletion of these items. Overall, the questionnaire has good psychometric properties: the presence of substantial correlations (correlation matrix), high sampling adequacy of both individual variables (KMO MSA in anti-image correlation) and set of variables (overall KMO MSA) and highly significant result

Table 2 All questions analysed in construct validation phase ($n = 60$)

Item	n (%) answered correctly	Corrected item-total correlation	Cronbach's alpha if item deleted
Section B			
B1. This drug aims to treat heart attack. ^a	60 (100.0)	0.000	0.717 ^b
B2. This drug had been given by putting it under the tongue.	60 (100.0)	0.000	0.717 ^b
B3. This drug can be given more than once in a year.	50 (83.3)	0.489	0.639
B4. This drug is still effective if given again within a year.	44 (73.3)	0.606	0.597
B5. You are at risk of getting allergic reaction or allergy if repeated within a year. ^a	40 (66.7)	0.566	0.614
B6. If you have allergic reaction or allergy to this drug, you may still be given this medication for the second time	39 (65.0)	0.582	0.608
B7. Family member or caretaker should know that you had been given streptokinase. ^a	58 (96.7)	0.399	0.678
Section C			
C1. The streptokinase card states the date the drug was given. ^a	57 (95.0)	0.716	0.714
C2. The streptokinase card should be shown to medical staff when you get treatment. ^a	54 (90.0)	0.820	0.652
C3. This card should only be carried when you get treatment at Hospital Tuanku Fauziah only.	48 (80.0)	0.519	0.811
C4. Family member or caretaker do not need to know where you store the streptokinase card	60 (100.0)	0.000	0.841 ^b
C5. If you lose your streptokinase card, you can get a new card at the hospital's pharmacy department. ^a	55 (91.7)	0.802	0.606

^aTrue response as the correct answer.
^bItem deleted in the final validated questionnaire.

Table 3 Median score and knowledge level of respondents ($n = 60$) based on the final validated questionnaire

Domain	Median score (Interquartile range)	Knowledge level, n (%)	
		Poor	Good
Streptokinase (total score of 5)	4 (3.0–5.0)	20 (33.3)	40 (66.7)
Streptokinase card (total score of 4)	4 (4.0–4.0)	13 (21.7)	47 (78.3)

for Bartlett's test. The factor solution could explain 77.4% to 96.6% of each original variable's variance.

Most respondents had a higher knowledge score for the streptokinase card domain than the streptokinase domain. For score characterisation, the respondents must be able to answer all four questions correctly on the streptokinase card, for them to be classified as having a good understanding, while respondents can provide at most one incorrect answer (out of the five questions in Section B) to be categorised as having good knowledge of streptokinase.

Domain for streptokinase was meant for patients to show their knowledge of the drug itself while domain for streptokinase card was meant for patients to show their understanding of where and when to alert health-care providers by showing the card. Some of the

information on streptokinase for Section B was printed on the streptokinase card itself (Figure 1). Although they have been counselled, patients may forget the reasons to prevent readministration. This was true of most respondents in this study who did not answer questions B5 (the risk of readministration) and B6 (not to readminister if experience allergic reactions) correctly, followed by B4 (ineffectiveness of readministration). Respondents may have had a poor baseline knowledge of allergy. In this study, we acknowledge that our patient cohort has a relatively low level of formal education. It may be argued that all the patients need to know that they should not receive streptokinase again for a year, without having to understand the dual reasons for this. However, it remains a patient's right to be informed about the substantial reasons for preventing

readministration of streptokinase within a year, as quoted “this person shall beforehand be given appropriate information as to the purpose and nature of the intervention as well as on its consequences and risks”¹⁸ According to the Elaboration Likelihood Model of persuasion by central route, patients need to appreciate the true merits of the information presented to support an advocacy or warning.¹⁹

This validated questionnaire will be useful clinically and we plan to implement it as part of a routine assessment of knowledge among patients in our setting, and for on-the-spot re-counselling for any questions that the patients answered incorrectly. The telephone survey method was preferred due to its minimal cost, and its brevity, making it less time-consuming for both patients and pharmacists. Patients do not need to travel to the hospital for the re-counselling.

To our knowledge, this is the first questionnaire developed in Malaysia to assess patient knowledge of streptokinase and the streptokinase card among post-STEMI patients. The strengths of this study are that it involved respondents from various sociodemographics and the survey was answered by the patients themselves. There are some limitations that we acknowledge in this study. Despite using a high (1:5) item to respondent ratio and having a high MSO value, the sample size for PCA could be considered small at $n = 60$. For PCA or FA, Gorsuch (1983)²⁰ suggested a minimum of 100 samples while Hutcheson and Sofroniou (1999)²¹ recommended a sample size of 150 or more for highly correlated data. However, our sample size ($n = 60$) meets the minimum number of respondents as suggested by Mac Callum, Widaman, Zhang, & Hong (1999) which should be five times or more larger than the number of variables. Confirmatory factor analysis (CFA) can be conducted further to validate the constructs of the two domains using convergent (constructs that are supposed to be related, are in fact related) and discriminant (constructs that are supposed to be unrelated, are in fact unrelated) validity.^{22,23}

There was no standardisation of the issuance of the streptokinase card among pharmacy departments of public hospitals in Malaysia, compared to the issuance of drug allergy cards (DACs) which is under the purview of the Pharmaceutical Services Programme, Ministry of Health Malaysia. We will proceed with the local proposal to the Pharmaceutical Services Programme on the potential for the standardisation of the streptokinase card across pharmacy departments of public hospitals in Malaysia, and the implementation of indirect re-counselling especially for patients with poor knowledge during the telephone survey.

In conclusion, this study had led to the development of a valid and reliable Malay language questionnaire to

assess knowledge retention about streptokinase among post-STEMI patients. It will be beneficial in helping pharmacists to assess knowledge among Malaysian post-STEMI patients about streptokinase. Intervention to improve knowledge retention, by using a complementary counselling tool (which can be as simple as the provision of a brochure) can be implemented to emphasise areas that respondents score low on, such as possible risks and the ineffectiveness of readministration.

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CONFLICTS OF INTEREST STATEMENT

The authors declare that they have no conflicts of interest to disclose.

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