Knowledge and Use of Sublingual Glyceryl Trinitrate: A Single Centre Experience

*Nazmi Liana Azmi, Azleen Azreen Azmi, Chua Wei Lian, Suhaini Mat Seman,
Izyani Mohd Sukri

Department of Pharmacy, Raja Perempuan Zainab II Hospital, Ministry of Health Malaysia, Kota Bharu, Kelantan, Malaysia-
15586
*Correspondence: nazmiliana@moh.gov.my

Abstract—Introduction: Angina is a common symptom of coronary heart disease which is managed with sublingual glyceryl trinitrate (SL GTN). In order to obtain the maximum benefit of the treatment, it is important that patients acquire the right knowledge and use of SL GTN. Therefore, our study aimed to assess the level of knowledge and use of SL GTN as well as their associated factors among patients in Raja Perempuan Zainab II Hospital, Kelantan, Malaysia. Methodology: A cross-sectional study utilizing validated questionnaire through guided interview was conducted from April to October 2017. The inclusion criteria were adult patients diagnosed with cardiovascular disease and prescribed with SL GTN. Those who were unable to converse in Malay or English were excluded from the study. Data were then analysed using R version 3.5.1. Results: A total of 280 patients were recruited with mean (SD) knowledge of 4.3 (1.4) and mean (SD) use of 4.4 (1.2). Among the respondents, 70.4% (n=197) had moderate knowledge and 26.8% (n=75) had poor knowledge. Only 8 patients had good knowledge (2.9%). As for the use of SL GTN; patients mostly only managed to achieve poor scores [52.9% (n=148)]. Further test showed that there was a significant fair correlation between knowledge and use of SL GTN (r=0.45, p<0.001). In the multivariable analysis, the only significant factor associated with both knowledge and use of SL GTN was gender (p=0.048 and 0.034, respectively). Conclusion: Overall, it was found that our respondents had unsatisfactory level of knowledge and use of SL GTN. Apart from that, we also noted that gender was the only factor associated with knowledge and use of SL GTN. These outcomes call for reinforcement of patient education and counselling.

Keywords— Knowledge, use, sublingual glyceryl trinitrate, cardiovascular disease, angina.

I. INTRODUCTION

Coronary artery disease (CAD) prevalently remains as one of the leading causes of death globally. The presenting complaint of patients with CAD is usually chest pain, mostly associated with angina [1], [2].

Angina is a common symptom of CAD which is managed with sublingual glyceryl trinitrate (SL GTN). Various international guidelines recommend the use of SL GTN for the acute relief of angina [3]–[5]. It is considered as a standard treatment and first line therapy for angina pain control [1]–[6]. SL GTN works within a couple of minutes, thus prominently a lifesaving agent [1].

SL GTN is an organic nitrate and vasodilating agent. It works by releasing nitric oxide that relaxes vascular smooth muscle and dilates both arterial and venous blood vessels [2]. SL GTN differs from the usual tablet form and detailed instructions must be explained to the patients to ensure proper understanding and handling of SL GTN [6], [7].

This is vital because SL GTN is prescribed on a day to day basis and is used by patients at their own discretion. Moreover, SL GTN can cause adverse effects such as headache, nausea, vomiting and hypotension [6], [8]. Patients should also be made aware of the restrictions on the number and timing of doses that can be safely used within the day [6]. Apart from that, it is important that patients are informed regarding the stability and correct storage of SL GTN [9].

Despite the wide use of SL GTN, only limited publications are available on the current knowledge and use of SL GTN among CAD patients. The report by Kimble and Kunik (2000) showed a high number of patients demonstrated lack of knowledge for safe and appropriate self-administration of SL GTN [8]. The same alarming findings were also found in small studies conducted by local healthcare practitioners in several regions in Malaysia [10]–[12]. Due to these reasons, our study aimed to assess the level of knowledge and use of SL GTN as well as their associated factors among patients in Raja Perempuan Zainab II Hospital (HRPZ II), Kelantan, Malaysia.

II. METHODOLOGY

A. Design and Study Population

A cross-sectional study was carried out from April to October 2017. The inclusion criteria were adult patients diagnosed with CAD and prescribed with SL GTN. Those who were unable to converse in Malay or English were excluded from the study.

B. Data Collection

Data were obtained from guided interview using validated questionnaire adopted from Wan Omar et al. (2014) [10]. Data collectors were adequately trained before they were able to recruit any subjects. Eligible respondents were determined through convenience sampling at outpatient pharmacy counter in HRPZ II when they came to refill their prescription. Then informed consent form was given prior to conducting the survey.

The questionnaire consisted of 2 domains; knowledge (8 items) and use of SL GTN (6 items). Each correct answer would receive 1 mark and a score of 0 was given to wrong or "do not know" response. The total score for knowledge and use ranged from 0 to 8 and 0 to 6, respectively. The

knowledge scores were further divided to 0 to 3 (poor), 4 to 6 (moderate) and 7 to 8 (high). As for the use of SL GTN, a total score of 0 to 4 was considered as poor and 5 to 6 was regarded as good use. Permission to use the research instrument was obtained from the corresponding author [10].

A sample size of minimum 264 subjects was calculated based on single proportion formula of p=0.22 for high knowledge from the same literature [10].

C. Statistical Analysis

Data were analysed using R version 3.5.1 [13]. Descriptive statistics were used to assess the levels of knowledge and use of SL GTN. Pearson's correlation was applied to test for association between variables of knowledge and use while multiple linear regression (backward) was utilized to determine the associated factors. Statistical significance was referred as p-value of less than 0.05.

D. Ethical Approval

This research was approved by the Medical Research and Ethics Committee (MREC), Ministry of Health Malaysia (NMRR-17-2469-35041) while permission to conduct the study at the site was attained from the Director of HRPZ II.

III. RESULTS

A. Demographic Characteristics

A total of 280 patients participated in the study with mean (SD) age of 57.6 (13.6) years old. Subjects were comprised of mostly male (68.9%, n=193), Malay (70.4%, n=197) with secondary education (54.6%, n=153). More than half of the patients were unemployed (52.5%, n=147), married (81.1%, n=227) and had family history of cardiovascular disease (73.2%, n=205). Majority were prescribed with SL GTN for angina (64.6%, n=181) for over 3 months (85.0%, n=238) and claimed that they used it once a month (50.7%, n=142) (Table 1).

TABLE 1. Demographic characteristics of respondents (n=280).

Demographic characteristics	n	%
Gender		
Male	193	68.9
Female	87	31.1
Age (years old)		
<49	58	20.7
50-69	126	45.0
>70	96	34.3
Ethnicity		
Malay	197	70.4
Non-Malay	83	29.6
Education level		
Primary	86	30.7
Secondary	153	54.6
Tertiary	41	14.6
Employment status		
Employed	133	47.5
Unemployed	147	52.5
Marital status		
Single	53	18.9
Married	227	81.1
Family history		
Yes	205	73.2
No	75	26.8
Diagnosis		
Angina	181	64.6
Others	99	35.4
Duration (months)		
≤ 3	42	15.0
> 3	238	85.0
Frequency		
Once a month	142	50.7
> Once a month	138	49.3

Respondents scored mean (SD) knowledge of 4.3 (1.4) and mean (SD) use of 4.4 (1.2) (Table 2). Among them, 70.4% (n=197) had moderate knowledge and 26.8% (n=75) had poor knowledge. Only 8 patients had good knowledge (2.9%). As for the use of SL GTN; patients mostly only managed to achieve poor scores [52.9% (n=148)] (Table 3).

TABLE 2. Mean (SD) for knowledge and use of SL GTN (n=280).

Variables	Mean	SD
Knowledge	4.3	1.4
Use	4.4	1.2

TABLE 3. Levels of knowledge and use of SL GTN (n=280).

Variables	n	%
Knowledge		
Poor	75	26.8
Moderate	197	70.4
Good	8	2.9
Use		
Poor	148	52.9
Good	132	47.1

In terms of response to knowledge of SL GTN, 6 out of 8 items had the most correct answers. Many were still unsure about its mechanism of action, use of SL GTN as prevention and the potential adverse effects [74.6% (n=209), 84.6% (n=237) and 76.1% (n=213), respectively) (Table 4). As for the use of SL GTN, majority of respondents gained correct answers for all 6 items (Table 5).

TABLE 4. Response to knowledge of SL GTN (n=280).

Items	Correct n (%)	Incorrect n (%)
Indication for SL GTN	229 (81.8)	51 (18.2)
Mechanism of action of SL GTN	71 (25.4)	209 (74.6)
Proper storage of SL GTN	241 (86.1)	39 (13.9)
Max no. of tablet per episode	211 (75.4)	69 (24.6)
Time sequencing of SL GTN	196 (70.0)	84 (30.0)
Stability of SL GTN	144 (51.4)	136 (48.6)
Use of SL GTN as prevention	43 (15.4)	237 (84.6)
Potential adverse effects	67 (23.9)	213 (76.1)

TABLE 5. Response to use of SL GTN (n=280).

Items	Correct n (%)	Incorrect n (%)
Do you carry the SL GTN at all times?	217 (77.5)	63 (22.5)
How do you carry your SL GTN?	187 (66.8)	93 (33.2)
What container do you use to carry SL GTN?	205 (73.2)	75 (26.8)
What is the recommended body position before taking the medication?	204 (72.9)	76 (27.1)
Describe how would you use the medication during an angina attack?	189 (67.5)	91 (32.5)
Apart from getting a prescription or refill medication, when do you need to see your Doctor about your angina?	220 (78.6)	60 (21.4)

Further analysis also showed that there was a significant fair correlation between knowledge and use of SL GTN ($r=0.45$, $p<0.001$) (Table 6). When tested using multiple linear regression (backward), the only significant factor associated with both knowledge and use of SL GTN was gender ($p=0.048$ and 0.034, respectively) (Table 7 and Table 8).

TABLE 6. Correlation between level of knowledge and level of use (n=280).

Variables	Knowledge	Use
Knowledge	1.4[a]	<0.001[c]
Use	0.45[c]	1.2[a]

[a]SD, [b]p-value, [c]correlation coefficient (r)

IV. DISCUSSION

It was found that our demographic characteristics shared the same resemblance as the local report by Wan Omar et al. (2014) at Taiping Hospital, Perak. Most of their respondents were also male, Malay, aged between 50 to 69 years old with secondary education and had been prescribed with SL GTN for more than 3 months [10].

Most of our patients had poor to moderate knowledge and use of SL GTN which were supported by previous local and abroad studies [6], [8], [10]–[12]. Wan Omar et al. (2014) as well as Kimble and Kunik (2000) noted that their respondents had moderate knowledge of SL GTN with mean (SD) score of 5.04 (1.7) and 5.1 (1.7), respectively [10]. Sa'ad et al. (2016) observed that only one-third of their respondents in Melaka Hospital (30.0%) had high knowledge of SL GTN while Nasira et al. (2016) found that 70.3% of their subjects in Balik Pulau Hospital, Penang had poor knowledge score [11], [12]. High percentages of our patients scored wrong answer for the mechanism of action, use of SL GTN as prevention and its potential adverse effects which were in-lined with Wan Omar et al. (2014) [74.6 vs. 76%, 84.6% vs. 88% and 76.1% vs. 72%, respectively] [10]

Consistent findings were found for the use of SL GTN. Both Wan Omar et al. (2014) as well as Sa'ad et al. (2016) reported poor use of SL GTN among their study population (54.2% and 67.0%, respectively). Alford et al. (2001) revealed that the management of angina was inexorably poor due to the low knowledge of SL GTN [14]. Our results bore a striking similarity with Wan Omar et al. whereby majority of patients brought along their SL GTN at all times in the appropriate manner using the original container or amber glass bottle [10].

Fan et al. (2009) also noted a positive relationship between knowledge and use scores which indicated both variables moved in tandem [9]. Kimble and Kunik (2000) however, noted a different finding from us. They found that the correlation coefficient was small and not significant ($r=0.18$, $p=0.10$). Nonetheless, there were some comparable findings with regards to predictors of knowledge and use of SL GTN. They reported gender as one of the significant predictors for knowledge and the only independent predictor for the use of SL GTN [8]. Another study by Gallagher et al. (2010) also reported gender among other significant factors for knowledge of SL GTN. Interestingly, they found that male gender was associated with less knowledge of SL GTN [6]. As for Fan et al. (2009), their study found that patient characteristics did not influence the level of knowledge and use of SL GTN [9].

The findings of this study support the need to strengthen our patient education, especially when it comes to its mechanism of action, use of SL GTN as prevention and the potential adverse effects. This may be due to the fact that patients do not always receive counseling regarding proper use of SL GTN. It is recommended that pharmacist should engage in a concise and directed conversations to empower patients about their treatment [7].

Several limitations of our study should be mentioned. We only recruited subjects from a single center using non-probability sampling. Therefore, the results might not represent the whole population of CAD patients in Malaysia. Despite these limitations, the outcomes of this research can be used as a reference to the current insights of knowledge and use of SL GTN.

V. CONCLUSION

Overall, it was found that the respondents in our setting had unsatisfactory level of knowledge and use of SL GTN. Apart from that, we also noted that gender was the only factor associated with knowledge and use of SL GTN. These outcomes signified an urgent need for reinforcement of patient education and counselling. Further researches are warranted to identify other possible predictors.

TABLE 7. Factors associated with knowledge of SL GTN (n=280).

Factors	SLR[a]		MLR[b]	
	b (95% CI)	p-value	Adjusted b (95% CI)	p-value
Gender				
Male[c]				
Female	-0.392 (-0.737, -0.046)	0.026	-0.350 (-0.697, -0.003)	0.048
Age (years)				
Younger	0.240 (-0.157, 0.636)	0.236	-	-
Older	-0.351 (-0.688, -0.013)	0.042	-0.305 (-0.644, 0.033)	0.077
Ethnicity				
Malay[c]				
Non-Malay	-0.040 (-0.392, 0.313)	0.826	-	-
Education				

	b (95% CI)	p-value		
Lower	-0.188 (-0.536, 0.161)	0.290	-	-
Higher	<0.001 (-0.456, 0.456)	0.999	-	-
Employment status				
Employed[c]				
Unemployed	0.157 (-0.165, 0.479)	0.339	-	-
Marital status				
Single[c]				
Married	0.361 (-0.048, 0.771)	0.083	-	-
Family history				
Yes[c]				
No	-0.327 (-0.689, 0.035)	0.076	-	-
Diagnosis				
Angina[c]				
Others	0.078 (-0.259, 0.415)	0.648	-	-
Duration (months)				
< 3[c]				
≥ 3	-0.104 (-0.555, 0.348)	0.652	-	-
Frequency				
Once a month[c]				
> once a month	0.037 (-0.285, 0.359)	0.822	-	-

[a]Simple linear regression, [b]Multiple linear regression (backward) ($R^2 = 0.019$), [c]Reference group
The model reasonably fits well. Model assumptions are met. There are no interaction and multicollinearity problem

TABLE 8. Factors associated with use of SL GTN (n=280).

Factors	SLR[a]		MLR[b]	
	b (95% CI)	p-value	Adjusted b (95% CI)	p-value
Gender				
Male[c]				
Female	-0.212 (-0.514, 0.090)	0.169	-0.377 (-0.725, -0.029)	0.034
Age (years)				
Younger	-0.068 (-0.414, 0.278)	0.699	-	-
Older	0.016 (-0.279, 0.312)	0.914	-	-
Ethnicity				
Malay[c]				
Non-Malay	-0.107 (-0.414, 0.200)	0.494	-	-
Education				
Lower	-0173 (-0.477, 0.130)	0.261	-	-
Higher	0.116 (-0.280, 0.512)	0.565	-	-
Employment status				
Employed[c]				
Unemployed	0.250 (-0.029, 0.529)	0.079	0.115 (-0.207, 0.438))	0.482
Marital status				
Single[c]				
Married	0.100 (-0.257, 0.458)	0.582	-	-
Family history				
Yes[c]				
No	-0.115 (-0.431, 0.201)	0.474	-	-
Diagnosis				
Angina[c]				
Others	-0.032 (-0.325, 0.261)	0.829	-	-
Duration (months)				
< 3[c]				
≥ 3	-0.104 (-0.496, 0.289)	0.604	-	-
Frequency				
Once a month[c]				
> once a month	0.232 (-0.512, 0.047)	0.102	-	-

[a]Simple linear regression, [b]Multiple linear regression (backward) ($R^2 = 0.029$), [c]Reference group
The model reasonably fits well. Model assumptions are met. There are no interaction and multicollinearity problem

REFERENCES

[1] J. Abrams, "Chronic stable angina," *N. Engl. J. Med.*, vol. 352, no. 24, pp. 2524–2533, 2005.
[2] Y. Wee, K. Burns, and N. Bett, "Medical management of chronic stable angina clinical evaluation," *Aust. Prescr.*, vol. 38, pp. 131–136, 2015.
[3] S. Antoniou and P. Wright, "Stable angina management," 2012.
[4] National Institute for Health and Care Excellence (NICE), "Stable angina: management," 2011.
[5] W. E. Boden, S. K. Padala, K. P. Cabral, I. R. Buschmann, and M. S. Sidhu, "Role of short-acting nitroglycerin in the management of ischemic heart disease.," *Drug Des. Devel. Ther.*, vol. 9, pp. 4793–805, 2015.
[6] R. Gallagher, J. Belshaw, A. Kirkness, K. Roach, L. Sadler, and D. Warrington, "Sublingual nitroglycerin practices in patients with coronary artery disease in Australia," *J. Cardiovasc. Nurs.*, vol. 25,

no. 6, pp. 480–486, Nov. 2010.

[7] Arbor Pharmaceuticals, "Considerations for the management of angina pectoris with nitroglycerin," *Pharmacy Times*, 2013. [Online]. Available: www.PharmacyTimes.com.

[8] L. P. Kimble and C. L. Kunik, "Knowledge and use of sublingual nitroglycerin and cardiac-related quality of life in patients with chronic stable angina," *J. Pain Symptom Manage.*, vol. 19, no. 2, pp. 109–117, 2000.

[9] M. I. Fan, M. Mitchell, G. Highered, and M. Cooke, "Cardiac patients' knowledge and use of sublingual glyceryl trinitrate (SLGTN)," *Aust. J. Adv. Nurs.*, vol. 26, no. 3, 2009.

[10] W. A. Wan Omar, S. R. J. Jasudass, and S. R. Md Saad, "Patient's knowledge and use of sublingual glyceryl trinitrate therapy in Taiping Hospital, Hospital," *Int. J. Pharmacol. Pharm. Sci.*, vol. 8, no. 10, pp. 758–761, 2014.

[11] U. Sa'ad, L. Cheong, S. Sapiyan, and W. Wan Ismail, "Evaluation of adherence among acute coronary syndrome (ACS) patients and assessment of knowledge and use of sublingual glyceryl trinitrate (GTN) in Melaka Hospital," *Malaysian J. Pharm.*, vol. 2, no. 2, p. 38, 2016.

[12] A. Nasira, A. Nurul, and S. Lee, "SL GTN: Assessment of cardiac patients' knowledge and use at Balik Pulau Hospital," *Malaysian J. Pharm.*, vol. 2, no. 2, 2016.

[13] R Core Team, "R: A language and environment for statistical computing," *R Foundation for Statistical Computing, Vienna, Austria*, 2013. [Online]. Available: https://www.r-project.org/. [Accessed: 21-Apr-2019].

[14] C. Alford, E. M. Grant, C. Johnston, and P. McIntyre, "The use of sublingual glyceryl trinitrate and aspirin in angina patients and enhancement of coronary heart disease databases," *Int. J. Pharm. Pract.*, vol. 9, no. S1, pp. 59–59, Feb. 2011.