Journal of Pharmacy Practice and Community Medicine.2017, 3(1):12-16 • http://dx.doi.org/10.5530/jppcm.2017.1.3 e-ISSN: 2455-3255

SHORT COMMUNICATION

OPEN ACCESS

Inattentiveness to Warnings and Precautions on Prescription Drug Labels among Malaysian Adult Patients: The Influence of Polypharmacy

Huan-Keat Chan[1]*, Siti Nadiah Abd Rahim[2], Mohd Shainol Azmar Kassim[2], Beng-Hoong Chew[2], Mohd Azri Mohd Suan[1]

[1]*Clinical Research Centre, Sultanah Bahiyah Hospital, 05460 Alor Setar, Kedah, MALAYSIA.*

[2]*Department of Pharmacy, Sultanah Bahiyah Hospital, 05460 Alor Setar, Kedah, MALAYSIA.*

Received: 21 September 2016;

Accepted: 11 November, 2016

***Correspondence to:**

Mr. Huan-Keat Chan, M.Sc,
Clinical Research Centre,
Sultanah Bahiyah Hospital,
05460 Alor Setar, Kedah, MALAYSIA.
Email: huankeat123@yahoo.com

DOI: 10.5530/jppcm.2017.1.3

Abstract

Background: Cautionary information on prescription drug labels is crucial to ensure safe administration. The current study examined patients' attentiveness to warnings and precautions on drug labels in a Malaysian public hospital. **Methods:** Five labels of the most commonly prescribed medications in the hospital were shown to 208 adult patients. Using face-to-face interviews, participants were asked to interpret the information on the labels. **Results:** The majority (78.4%) of the participants did not attempt to interpret the warnings and precautions of at least one label. Inattentiveness to such information was also found to be associated with polypharmacy, which was defined as taking five or more prescription medications (adjusted odds ratio: 8.57; 95% confidence interval: 1.44, 50.96; p=0.02). **Conclusion:** This study confirms the lack of awareness of drug safety among the Malaysian population in general, highlighting the need for improving patient education and revising the labeling format.

Key words: Drug labeling, Malaysia, Public hospitals, Polypharmacy, Prescription drugs.

INTRODUCTION

Warnings and precautions on containers or packaging, commonly designed as small colored stickers, provide additional cautionary information as to safe administration of a medication.[1] Yet, most patients, in particular those with low health literacy, did not pay attention to the auxiliary labels.[2,3] Therefore, in Malaysia, a number of public hospitals have been using the e-Hospital Information System (e-HIS) to assist in dispensing medications, with all drug-related information, including warnings and precautions, printed on a same label.[4] Although a US study also demonstrated that patients preferred having pertinent warnings and precautions presented on the main labels rather than on auxiliary labels,[5] such information could still be easily overlooked due to the lack of awareness.

The use of five or more prescription drugs, often termed polypharmacy, has been shown to increase the risk of adverse outcomes such as duplicated therapy and contraindicated drug combinations.[6] Nevertheless, the relationship between polypharmacy and patients' awareness of safety-related information on drug labels has yet to be fully investigated. Hence, this study was specifically designed to determine patients'

Publishing Partner : EManuscript [www.emanuscript.in]

attentiveness to warnings and precautions on prescription drug labels, and to subsequently identify the associations of their characteristics, particularly the number of medications taken, with their attentiveness.

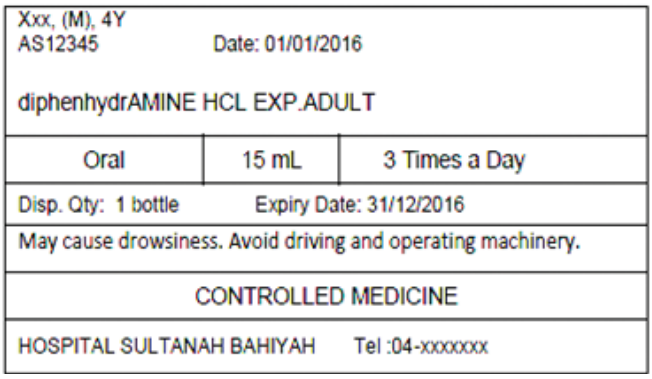
METHODS AND MATERIAL

This cross-sectional study took place in the Sultanah Bahiyah Hospital, one of the government-funded, tertiary medical centers in Northern Malaysia, over a three-month period (June to August 2015). This hospital caters to patients seeking general, specialized and subspecialized medical services from a number of departments, ranging from General Medicine, Surgery to Emergency and Trauma.

Patients, who were above 18 years of age and presented to the Outpatient Pharmacy Department with a prescription for at least one oral medication, were included. Excluded patients were those who were unable to communicate in the Malay language, or had impairments with hearing or vision. Using convenient sampling, patients were approached at the waiting area of the Outpatient Pharmacy Department and screened for eligibility. Potential participants were briefed on the study information, and were required to provide informed consent prior to any data collection procedures.

A semi-structured, face-to-face interview was conducted with each participant by one of the investigators (pharmacists) in a private room affiliated with the Outpatient Pharmacy Department. First, their self-reported demographics, including gender, age, ethnicity, educational level, employment status and monthly income, were recorded. The total number of oral prescription medications taken on the day of interview was retrieved from the e-HIS. Subsequently, the samples of labels of five most commonly prescribed oral medications in the hospital, including amlodipine, amoxicillin, erythromycin succinate, frusemide, and diphenhydramine hydrochloride (liquid), were shown in the same order to all the participants for review (Figure 1). Adapting the method of Davis *et al*., the participants were then asked "what does this label mean to you?" for each label.[2] Based on the participants' responses, investigators documented whether they attempted to interpret the warnings and precautions on the labels.

Sample Size and Data Analysis: This study was powered to estimate the prevalence of inattentiveness to warnings and precautions on drug labels at the 95% confidence interval (CI) with a 5% error margin, assuming an expected prevalence of 85% based on a pilot study involving 30 participants. To account for a 20% dropout rate, the minimal sample size needed was adjusted to 245 patients.[7]


Xxx, (M), 4Y
AS12345 Date: 01/01/2016

diphenhydrAMINE HCL EXP.ADULT

Oral	15 mL	3 Times a Day

Disp. Qty: 1 bottle Expiry Date: 31/12/2016

May cause drowsiness. Avoid driving and operating machinery.

CONTROLLED MEDICINE

HOSPITAL SULTANAH BAHIYAH Tel :04-xxxxxxx

Figure 1: Sample of a drug label generated by the e-Hospital Information System (e-HIS), with warnings and precautions presented after the dosing instructions.

Statistical analyses were performed using the SPSS version 20.0 (IBM, New York). Participants' demographics, along with the rates of inattentiveness to (having no attempt to interpret) warnings and precautions on each label, were expressed as frequencies and percentages. The associations between participants' demographics and the number of medications taken were assessed using Pearson's chi-square and Fisher's exact tests, as appropriate. The backward stepwise multiple logistic regression analysis was used to determine the associations of participants' characteristics, including the number of medications taken, with the rate of inattentiveness to warnings and precautions of at least one label. All factors showing $p<0.25$ in univariable analyses were included in the final regression model,[8] and the magnitude of association of each factor was expressed as odds ratio (OR) and 95% CI. Results of all analyses were considered statistically significant if $p<0.05$.

Ethics Approval: The study protocol was registered with the National Medical Research Register, Malaysia (NMRR-15-939-26083), and was approved by the Medical Research Ethics Committee, Malaysia.

RESULTS

Of 245 patients approached, 208 consented to participate in this study (response rate: 84.9%). The majority of participants were male (57.2%) and Malay (76.4%). Nearly half (48.1%) of them were above 40 years of age, and 72.1% reported a secondary level of education or below. Approximately 70% of the participants were employed or self-employed; however, 60.6% reported a relatively low monthly income (less than MYR 2000). Twenty-seven (13%) participants received at least five medications. Polypharmacy was significantly associated with age group ($p<0.001$), ethnicity ($p=0.033$), educational level ($p<0.001$) and employment status ($p<0.001$) (Table 1).

Table 1: Participants' characteristics by the number of medications taken (n=208)

Variable	Number of medications taken		p-value
	Less than five	Five or above	
Gender, n (%)			0.85*
Male	104 (87.4)	15 (12.6)	
Female	77 (86.5)	12 (13.5)	
Age Group, years, n (%)			<0.001*
18-29	70 (95.9)	3 (4.1)	
30-39	33 (94.3)	2 (5.7)	
40-49	38 (92.7)	3 (7.3)	
50-59	32 (82.1)	7 (17.9)	
60 or above	8 (40)	12 (60)	
Ethnicity, n (%)			0.03†
Malay	143 (89.9)	16 (10.1)	
Chinese	24 (72.7)	9 (27.3)	
Indian	14 (87.5)	2 (12.5)	
Education, n (%) ‡			<0.001†
Primary	2 (13.3)	13 (86.7)	
Secondary	129 (95.6)	6 (4.4)	
Tertiary	50 (86.2)	8 (13.8)	
Employment status, n (%)			<0.001†
Employed/ self-employed	30 (83.3)	6 (16.7)	
Public service	84 (90.3)	9 (9.7)	
Private sector	15 (78.9)	4 (21.1)	
Self-employed			
Not working/ unemployed			
Student	30 (93.8)	2 (6.2)	
Unemployed	15 (83.3)	3 (16.7)	
Housewife	6 (100)	0 (0)	
Retiree	1 (25)	3 (75)	
Monthly income, MYR, n (%)			0.29†
Below 1000	30 (81.1)	7 (18.9)	
1000-1999	80 (89.9)	9 (10.1)	
2000-2999	25 (89.3)	3 (10.7)	
3000-3999	18 (78.3)	5 (21.7)	
4000-4999	2 (66.7)	1 (33.3)	
5000 or above	26 (92.8)	2 (7.2)	

* Pearson's chi-square tests.
† Fisher's exact tests.
‡ Categorized into primary (compulsory 6-year education), secondary (5 to 7 years, including pre-university education) and tertiary (university and college education).

Overall, 163 (78.4%) participants did not attend to the warnings and precautions on at least one of the five labels. The rates of inattentiveness to the warnings and precautions of each label ranged from 59.1% to 70.7% (Table 2). In the multivariable analysis, participants taking five or more medications had 8.57 times the odds of not attending to the warnings and precautions on at least one label (95% CI: 1.44, 50.96; p=0.02). Participants, who were above 40 years of age, non-Malay, and employed or self-employed, were also more likely to overlook such information (Table 3).

DISCUSSION

Different from previous studies which focused predominantly on auxiliary labels,[1-3,9] this study investigated the patients' attentiveness to warnings and precautions which were presented, along with their particulars and dosing instructions, on the same drug label. The findings confirm that approximately 80% of patients receiving medications from public hospitals in Malaysia did not pay attention to such information. Therefore, pharmacists should not assume that patients can understand and act on all written instructions, even though the label is considered clear and simple. Given that failure to heed such instructions could potentially lead to suboptimal treatment outcomes and adverse drug events,[10] efforts to improve patients' alertness are warranted.

Besides, it is noteworthy that patients' attentiveness is not necessarily influenced by the length of the warnings and precautions on drug labels. Although Davis *et al.* suggest that lengthy, multistep instructions could be more difficult to read,[3] most patients in Malaysia tended to ignore short

Table 2: Inattentiveness to warnings and precautions on prescription drug labels (n=208)

Drug	Warnings/ precautions	Having no attempt to interpret the warnings and precautions, n (%)
Amlodipine	Take with or without food.	147 (70.7)
Amoxicillin	Finish all medications. Take with food	134 (64.4)
Erythromycin succinate	Finish all medications. Take 1 hour before meal.	142 (68.3)
Frusemide	Do not stop medication without asking your doctor.	125 (60.1)
Diphenhydramine hydrochloride	May cause drowsiness. Avoid driving and operating machinery.	123 (59.1)

Table 3: Factors associated with inattentiveness to warnings and precautions of at least one prescription drug label, simple and logistic regression models

Variable	Simple logistic regression			Multiple logistic regression *		
	b	OR (95% CI)	p-value	b	OR (95% CI)	p-value
Number of medications taken						
Less than five	0	1	0.07	0	1	0.02
Five or above	1.36	3.9 (0.89, 17.12)		2.15	8.57 (1.44, 50.96)	
Age group, years						
Below 40	0	1	<0.001	0	1	<0.001
40 or above	1.98	7.21 (3.04, 17.11)		2.54	12.61 (4.71, 33.76)	
Ethnicity						
Non-Malay	0	1	0.08	0	1	0.009
Malay	0.64	1.9 (0.92, 3.92)		1.32	3.74 (1.4, 9,99)	
Employment status						
Not working/ unemployed	0	1	<0.001	0	1	<0.001
Employed/ self-employed	1.27	3.56 (1.79, 7.10)		1.64	5.16 (2.23, 11.92)	
Gender†						
Female	0	1	<0.001	-	-	-
Male	1.26	3.53 (1.76, 7.08)				
Education†						
Tertiary	0	1	0.04	-	-	-
Non-tertiary	0.72	2.05 (1.02, 4.11)				
Income‡						
2000 and above	0	1	0.55	-	-	-
Below 2000	0.21	1.23 (0.62, 2.45)				

b, regression coefficient; OR, odds ratio; CI, confidence interval.

* Multicollinearity and interaction term were checked and not found. Hosmer-Lemeshow test (p=0.39), classification table (overall correctly classified percentage=83.2%) and area under curve (82.3%) were applied to check model fitness.

† Not significant in multiple logistic regression analysis (p>0.05)

‡ Not included in multiple logistic regression analysis (p>0.25).

and seemingly simple instructions, such as "take with or without food", most likely because of the use of a small font size (8-point). Hence, there is an urgent need to revise the format of drug labels generated by the e-HIS in Malaysia, particularly to enlarge the font sizes used for warnings and precautions.

The existing literature has also consistently related the lack of awareness about such information to limited health literacy.[1-3,11] Nonetheless, it is difficult to assess health literacy of all patients during the clinical encounter, especially in a busy health setting.[12] Rather, this study found a positive relationship between polypharmacy and

patients' attentiveness to warnings and precautions on labels, with all the possible confounders, including age, ethnicity and employment status, adjusted. Therefore, the number of medications, which can be easily retrieved from the electronic information system, is potentially useful for pharmacists to quickly identify those who are having difficulties in managing complex regimens and assist them by providing further counseling.

However, the generalizability of this study is mainly limited by its single-center design. Aside from that, information on the use of over-the-counter medications, supplements and medications received from other health facilities was not captured. Besides, this study focused merely on patients' attempt to interpret the warnings and precautions, which may not reflect their actual comprehension. Future studies should therefore include patients from more diverse environments, examine the effects of non-prescription medications, and assess patients' understanding of such information.

CONCLUSION

This study confirms that a vast majority of patients in Malaysia overlooked the warnings and precautions placed on the prescription drug labels, pointing to the lack of awareness of drug safety in general. Apart from that, the number of medications received was shown to be a significant predictor, and thus can be used to identify those who are most likely unaware of such information in the future. While medication safety has long been identified as a major concern in the Malaysian public hospitals, this study highlights the need for further patient education and revising the existing labeling format.

ACKNOWLEDGEMENT

We would like to thank the Director General of Health, Malaysia, for his permission to publish the findings from this study. We also acknowledge the assistance from the Pharmacy Department of the Sultanah Bahiyah Hospital in acquiring the data.

REFERENCES

1. Shiyanbola OO, Meyer BA, Locke MR, Wettergreen S. Perceptions of prescription warning labels within an underserved population. Pharm Pract (Granada) 2014;12(1):387.
2. Davis TC, Wolf MS, Bass PF 3rd, Middlebrooks M, Kennen E, Baker DW, *et al*. Low literacy impairs comprehension of prescription drug warning labels. J Gen Intern Med 2006;21(8):847-51.
3. Davis TC, Wolf MS, Bass PF 3rd, Thompson JA, Tilson HH, Neuberger M, *et al*. Literacy and misunderstanding prescription drug labels. Ann Intern Med 2006;145(12):887-94.
4. Chan HK, Hassali MA, Lim. CJ, Saleem F, Ghani NA. Improving pediatric liquid medication labeling of the hospital information system in Malaysia: qualitative analysis of pharmacists' perceptions. Pharm Pract (Granada) 2016;14(2):699.
5. Mohan A, Riley MB, Boyington D, Johnston P, Trochez K, Jennings C, *et al*. Development of a patient-centered bilingual prescription drug label. J Health Commun. 2013;18(1):49-61.
6. Golchin N, Frank SH, Vince A, Isham L, Meropol SB. Polypharmacy in the elderly. J Res Pharm Pract 2015;4(2):85-8.
7. Naing NN. Determination of sample size. Malays J Med Sci 2003;10(2):84-6.
8. Bursac Z, Gauss CH, Williams DK, Hosmer DW. Purposeful selection of variables in logistic regression. Source Code Biol Med 2008;3:17.
9. Wolf MS, Davis TC, Bass PF, Curtis LM, Lindquist LA, Webb JA, *et al*. Improving prescription drug warnings to promote patient comprehension. Arch Intern Med 2010;170(1):50-6.
10. Culbertson A, Fiszman M, Shin D, Rindflesch TC. Semantic processing to identify adverse drug event information from black box warnings. AMIA Annu Symp Proc 2014;2014:442-8.
11. Bailey SC, Sarkar U, Chen AH, Schillinger D, Wolf MS. Evaluation of language concordant, patient-centered drug label instructions. J Gen Intern Med 2012; 27(12): 1707-13.
12. Schwartz KL, Bartoces M, Campbell-Voytal K, West P, Monsur J, Sartor A, *et al*. Estimating health literacy in family medicine clinics in metropolitan Detroit: a MetroNet study. J the Ame Boar Fami Med. 2013;26(5):566-70.

Cite this article as: Chan H, Rahim SNA, Kassim MSA, Chew B, Suan MAM. Inattentiveness to Warnings and Precautions on Prescription Drug Labels among Malaysian Adult Patients: The Influence of Polypharmacy. J Pharm Pract Community Med. 2017;3(1):12-16.