Oral Solid Dosage form Modification in Community Pharmacies of Kavrepalanchok and Bhaktapur Districts of Nepal

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ABSTRACT

Background

People may modify their oral solid dosage form of medicine to deal with problem faced during medicine administration. The modification of dosage form may adversely affect the quality, safety and efficacy of the medicine.

Objective

To investigate the causes and practices of oral solid dosage form modification among the consumers going to community pharmacies.

Method

A descriptive, cross-sectional study was conducted in five community pharmacies of Kavrepalanchok and Bhaktapur districts of Nepal. The consumers visiting these pharmacies for their oral solid dosage form of medicine were invited to participate in interview using structured questionnaire.

Result

Among 419 participants,13.6% of participants reported having problem of taking intact medicine. Most of them (12.4% of total participants) experienced difficulty swallowing the medicine. The swallowing difficulty is significantly associated with age and sex ($p < 0.05$). Around one third (36.8%) of participant with medicine administration problem modified the dosage form of medicines. One quarter of medicine dosage form modifications (25.0%) were inappropriate. Medicine dosage form modification is associated with age and number of daily medicine intake ($p < 0.05$). Among participants modifying dosage form of medicines, 66.7% were advised to do so mainly by family and friends; 33.3% were modifying on their own and 76.2% were unaware of possible effects of medicine dosage form modification. About 62.3% of total participants were never asked about any problems on taking medicines by doctor/pharmacists.

Conclusion

Difficulty swallowing medicines and medicine dosage form modification were prevalent in the Nepalese population. Medicine dosage form modifications also involved inappropriate modifications due to specialized design of such dosage forms. So, it seems important to provide proper counseling while dispensing such dosage forms.

KEY WORDS

Capsules, Dosage forms, Medication error, Oral medicine, Pharmaceutical preparations, Tablets

INTRODUCTION

Oral solid dosage forms such as tablets and capsules have been the most popular and commonly used dosage form due to its ease of handling, convenience of use, physical, chemical and microbiological stability and dosing accuracy.[1] The administration of such dosage forms of medicine for some patients such as elderly, children, patients with dysphagia and patients on enteral tube feeding may be difficult due to swallowing difficulty or unavailability of proper dose.[2] As a result, the patients or the health care provider may modify their dosage form prior to administration, which include crushing or splitting the tablets, opening the capsules, mixing the dosage form in food or juice.[3-8]

Dosage form modifications for some medicines are equally safe and efficacious as that when administered intact.[9-12] However, some dosage form should not be modified resulting the possibility of harmful consequences as change in pharmacokinetics, side effects, unacceptable taste, incorrect dosage administration, medicine instability, potential risks to health care provider etc.[8,13-17] For this reason, the prevalence of oral solid dosage form modifications and inappropriate medicine administration have been studied in various countries.[3-6,18-25] These modifications may be done under the guidance of health professional. Meanwhile, in many cases, this is done by the patients themselves without knowing the possible harmful effects.[3-6] Therefore, it is important to understand the solid dosage form modification practice in the community level in order to plan any intervention required to prevent an inappropriate medicine administration problem.

In our context, no such studies have been conducted, so this study aims to investigate the causes and practices of oral solid dosage form modification among the consumers going to community pharmacies of selected regions in Nepal.

METHODS

A descriptive, cross sectional study was conducted in five conveniently selected community pharmacies. Among them, three were located in Kavrepalanchok and two were located in Bhaktapur district of Nepal. The consumers above 18 years old, visiting these pharmacies for purchasing the oral solid dosage form of medicine for themselves and were taking at least one oral solid dosage form of medicine for at least 5 days were invited to participate into the study. The sample size was calculated using the formula n= Z^2pq/d^2, assuming: (i) the prevalence (p) to be 50% in order to obtain maximum sample size (ii) q=1-p (iii) 5% margin of error (d) and (iv) Z value 1.96 at 95% confidence interval.[26] The calculated sample size was 385 to which 10% was added to accommodate the incompletely filled questionnaire and obtained the value of 424. Written consents were obtained from both the participants and the community pharmacy personnel. During March to April 2021, the data were obtained via interview using the structured questionnaire by five researchers. In order to ensure uniformity in the data collection, all of the researchers involved in the data collections were provided with training.

The structured questionnaire was developed after reviewing the related literatures.[3-6] The questionnaire consisted of basic socio-demographic information, oral solid medicine details (number, name, therapeutic class, type of dosage form, duration), details of oral solid medicine administration problem (type of problem, onset, nature, duration, causes of swallowing difficulty), communication between doctors and patients about medicine administration problem, measures patients take to comply with medicine, details of medicine dosage form modifications (name, dosage form, type of medicine modification), general practices about medicine dosage form modification and knowledge about the effect of medicine dosage form modification. The appropriateness of observed dosage form modification was determined by referring to Australian don't rush to crush handbook.[27] The questionnaire was initially drafted in English and then was translated into Nepali identifying required improvements, appropriateness, questions comprehensibility and content study. The face validity was obtained after reviewing the questionnaire by experts from Pharmacy Department, Kathmandu University and pretesting on 10 randomly selected participants and modifying the content accordingly.

The ethical approval for the study was obtained from ethical review board of Nepal Health Research Council, Government of Nepal, Kathmandu, Nepal.

Data storage and analysis was done using Statistical Package for Social Sciences (SPSS) version 17. Descriptive data were presented using frequencies and percentages in the form of figures and tables. Categorical variables were compared using Pearson's chi-square test at 0.05 level of significance. While testing the association between the variables, the expected frequencies were below the required minimum (i.e. 5) in some cases; hence, the data from the adjacent categories were pooled to achieve the required minimum.

RESULTS

Out of recruited 424 participants, 5 were excluded due to incomplete information. A total of 419 participants were included in the study. Most of the participants (29.1%; n=122) belonged to 40-49 years age group and the least one tenth (11.7%; n=49) belonged to 60 years and above. Equal participants were found between males (49.9%; n=209) and females (50.1%; n=210). Most of the participants (34.6%; n=145) completed primary education and about three fourth (73.5%; n=308) were from Kavrepalanchok district. The participants from two districts were similar with respect to age group, gender, religion and education ($p > 0.05$) (Table 1).

Table 1. Socio-demographic characteristic of participants (n=419)

Variable	District		Total	p value
	Kavrepalanchok	Bhaktapur		
Age (years)[a]				
18-29	72 (17.2)	33 (7.9)	105 (25.1)	0.092
30-39	54 (12.9)	29 (6.9)	83 (19.8)	
40-49	98 (23.4)	24 (5.7)	122 (29.1)	
50-59	46 (11.0)	14 (3.3)	60 (14.3)	
≥ 60	38 (9.1)	11 (2.6)	49 (11.7)	
Total	308 (73.5)	111 (26.5)	419 (100.0)	
Gender[a]				
Male	152 (36.3)	57 (13.6)	209 (49.9)	0.718
Female	156 (37.2)	54 (12.9)	210 (50.1)	
Total	308 (73.5)	111 (26.5)	419 (100.0)	
Religion[a]				
Hindu	287 (68.5)	104 (24.8)	391 (93.3)	0.853
Buddhist	21 (5.0)	7 (1.7)	28 (6.7)	
Total	308 (73.5)	111 (26.5)	419 (100.0)	
Education[a]				
Graduate	55 (13.1)	13 (3.1)	68(16.2)	0.118
Secondary (9-12 grade)	93 (22.2)	28 (6.7)	121 (28.9)	
Primary (upto 8 grade)	97 (23.2)	48 (11.5)	145 (34.6)	
Illiterate	63 (15.0)	22 (5.3)	85 (20.3)	
Total	308 (73.5)	111 (26.5)	419 (100.0)	

[a]Result expressed as number of participants (percent). Percent calculated out of 419 participants.

Oral solid dosage form of medicine profile

All of the participants reported a total of 826 medicine administration. More than half of the participants (54.4%; n=228) reported of taking medicines regularly and nearly half of the participants (42.2%; n=177) took at least one medicine daily. The number of participants decreased as the number of daily medicine increased (Table 2).Out of total medicine administrations, the commonly administered categories of medicine were cardiovascular medicines (20.1%; n=166), analgesics (18.6%; n=154), medicines acting on gastrointestinal tract (15.7%; n=130) and hormones and related drugs (14.3%; n=118) (Table 3). Within the hormones and related drugs, 72.9% (n=86) accounted for oral hypoglycemic medicines and within the cardiovascular medicine, 76.5% (n=127) accounted for anti-hypertensive medicines. In terms of medicine, the top five commonly administered medicines reported were pantoprazole (8.1%; n=67), metformin (6.6%; n=55), amlodipine (5.1%; n=42), paracetamol and ibuprofen in fixed dose combination form (5.1%; n=42) and paracetamol (4.3%; n=36). Most commonly used dosage form was conventional immediate release tablets (36.3%; n=300) (Table 3). About half of the total medicines (50.8%; n=420) were administered for more than one month and the medicine administration was higher (30.6%; n=253) in 40-49 years age group (Table 2). The distribution of medicines across two districts were significantly different ($p < 0.001$). On further post hoc analysis of chi-square test, statistically different distribution of antimicrobial ($p < 0.001$), hormones and related medicine ($p < 0.001$) and other medicines ($p=0.01$) in two districts were observed.

Table 2. Regularity, number and duration of oral solid dosage form of medicine taken daily

	Age (years)					
	18-29	30-39	40-49	50-59	≥ 60	Total
Consumption of oral solid medicine regularly[a]						
Yes	16 (3.8)	31 (7.4)	87 (20.8)	49 (11.7)	45 (10.7)	228 (54.4)
No	89 (21.2)	52 (12.4)	35 (8.4)	11 (2.6)	4 (1.0)	191 (45.6)
Total	105 (25.1)	83 (19.8)	122 (29.1)	60 (14.3)	49 (11.7)	419 (100)
Number of oral solid medicine taken daily[a]						
One	59 (14.1)	37 (8.8)	47 (11.2)	23 (5.5)	11 (2.6)	177 (42.2)
Two	34 (8.1)	25 (6.0)	38 (9.1)	17 (4.1)	12 (2.9)	126 (30.1)
Three	8 (1.9)	19 (4.5)	18 (4.3)	14 (3.3)	9 (2.1)	68 (16.2)
Four and above	4 (1.0)	2 (0.5)	19 (4.5)	6 (1.4)	17 (4.1)	48 (11.5)
Total	105 (25.1)	83 (19.8)	122 (29.1)	60 (14.3)	49 (11.7)	419 (100)
Duration of oral solid medicine (days)[b]						
Less than 7	116 (14.0)	69 (8.4)	56 (6.8)	18 (2.2)	8 (1.0)	267 (32.3)
8-14	22 (2.7)	24 (2.9)	28 (3.4)	6 (0.7)	7 (0.8)	87 (10.5)
15-30	11 (1.3)	13 (1.6)	19 (2.3)	7 (0.8)	2 (0.2)	52 (6.3)
More than 30	19 (2.3)	46 (5.6)	150 (18.2)	93 (11.3)	112 (13.6)	420 (50.8)
Total	168 (20.3)	152 (18.4)	253 (30.6)	124 (15.0)	129 (15.6)	826 (100)

[a]Result expressed as number of participants (percent). Percent calculated out of 419 participants.
[b]Result expressed as number of medicines (percent). Percent calculated out of 826 medicines.

Oral solid dosage from of medicine administration problem and associated risk factors

A 13.6% of total participants reported altogether 8.4% (n=69) medicine administration problem (Table 4). Most of the participants (12.4%; n=52) had difficulty swallowing their medicine and rest of participants (1.2%; n=5) had not found their required dose of medicine commercially. Majority of participants with swallowing difficulty were female (73.1%; n=38); belonged to 18-29 years (44.2%; n=23) followed by 60 years and above (21.2%; n=11) and were taking one medicine daily (38.5%; n=20). A three fourth (75.0%; n=39)

Table 3. Therapeutic category and type of dosage form of administered medicines (n=826)

Variable	n (%)
Therapeutic category	
Analgesic	154 (18.6)
Antimicrobial	54 (6.5)
Drug acting on nervous system	57 (6.9)
Drug acting on cardiovascular system	166 (20.1)
Drug acting on gastrointestinal tract	130 (15.7)
Drug acting on respiratory system	24(2.9)
Nutritional supplement	82(9.9)
Hormones and related drug	118(14.3)
Other	41(5.0)
Type of dosage form	
Immediate release uncoated tablet	300 (36.3)
Film coated tablet	265 (32.1)
Enteric coated tablet	114 (13.8)
Modified release tablet	57 (6.9)
Hard gelatin capsule	53 (6.4)
Soft gelatin capsule	18(2.2)
Other	19(2.3)

had ongoing swallowing difficulties and 78.8% (n=41) were experiencing swallowing difficulty for less than one year (Table 4). About half of the participants (50.0%; n=26) with swallowing difficulty believed big tablet size or tablet stuck in throat as the cause of swallowing difficulty (Fig. 1). The prevalence of swallowing difficulty is significantly associated with age ($p < 0.001$) and gender ($p < 0.001$) but not with the number and duration of daily medicine intake ($p > 0.05$) (Table 5). In terms of medicine, 64 medicines were reported difficult to swallow with the common medicines being paracetamol and ibuprofen combination tablet (20.3%; n=13), metformin tablet (15.6%; n=10) and paracetamol tablet (12.5%; n=8).

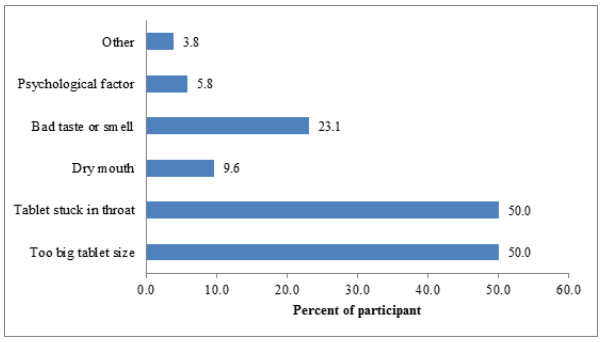

Figure 1. Possible causes for difficulty swallowing oral solid dosage form of medicine reported by participants having difficulty swallowing oral solid dosage form of medicine (n=52). Multiple responses were possible.

Table 4. Details of oral solid dosage form of medicine administration problem

	Age (years)					
	18-29	**30-39**	**40-49**	**50-59**	**≥ 60**	**Total**
Presence of oral solid medicine administration problem[a]						
Yes	24 (5.7)	5 (1.2)	5 (1.2)	10 (2.4)	13 (3.1)	57 (13.6)
No	81 (19.3)	78 (18.6)	117 (27.9)	50 (11.9)	36 (8.6)	362 (86.4)
Presence of swallowing difficulty[a]	23 (5.5)	5 (1.2)	5 (1.2)	8 (1.9)	11 (2.6)	52 (12.4)
Onset of swallowing difficulty[b]						
Ongoing swallowing difficulty	18 (34.6)	2 (3.8)	4 (7.7)	6 (11.5)	9 (17.3)	39 (75.0)
Past swallowing difficulty	5 (9.6)	3 (5.8)	1 (1.9)	2 (3.8)	2 (3.8)	13 (25.0)
Total	23 (44.2)	5 (9.6)	5 (9.6)	8 (15.4)	11 (21.2)	52 (100)
Duration of swallowing difficulty (year)[b]						
< 1	19 (36.5)	5 (9.6)	4 (7.7)	8 (15.4)	5 (9.6)	41 (78.8)
1-3	1 (1.9)	-	-	-	2 (3.8)	3 (5.8)
3-5	1 (1.9)	-	-	-	1 (1.9)	2 (3.8)
>5	2 (3.8)	-	1 (1.9)	-	3 (5.8)	6(11.5)
Gender[b]						
Male	6 (11.5)	-	1 (1.9)	4 (7.7)	3 (5.8)	14 (26.9)
Female	17 (32.7)	5 (9.6)	4 (7.7)	4 (7.7)	8 (15.4)	38 (73.1)
Number of oral solid medicine taken daily[b]						
One	16 (30.8)	-	1 (1.9)	1 (1.9)	2 (3.8)	20 (38.5)
Two	5 (9.6)	3 (5.8)	1 (1.9)	1 (1.9)	-	10 (19.2)
Three	1 (1.9)	2 (3.8)	1 (1.9)	5 (9.6)	3 (5.8)	12 (23.1)
Four and above	1 (1.9)	-	2 (3.8)	1 (1.9)	6 (11.5)	10 (19.2)

[a]Result expressed as number of participants (percent). Percent calculated out of 419 participants
[b]Result expressed as number of participants with swallowing difficulty (percent). Percent calculated out of 52 participants

Oral solid dosage form modification and associated risk factors

Among the participants with medicine administration problem, 56.1% (n=32) drank more water, 36.8% (n=21) modified medicine dosage form, 5.3% (n=3) asked for other formulation and 1.8% (n=1) did nothing as a technique to solve their problem. Most medicine dosage form modification was done by female participants (61.9%; n=13); participants taking three or more medicine (61.9%;

Table 5. Association of swallowing difficulty with different variables

Variable	Swallowing difficulty		Total	p value
	Yes	No		
Age (years)[a]				
18-29	23 (5.5)	82 (19.6)	105 (25.1)	0.000*
30-39	5 (1.2)	78 (18.6)	83 (19.8)	
40-49	5 (1.2)	117 (27.9)	122 (29.1)	
50-59	8 (1.9)	52 (12.4)	60 (14.3)	
≥ 60	11 (2.6)	38 (9.1)	49 (11.7)	
Gender[a]				
Female	38 (9.1)	172 (41.1)	210 (50.1)	0.000*
Male	14 (3.3)	195 (46.5)	209 (49.9)	
District[a]				
Kavrepalan-chowk	36 (8.6)	272 (64.9)	308 (73.5)	0.455
Bhaktapur	16 (3.8)	95 (22.7)	111 (26.5)	
Number of daily medicine intake[a]				
One	20 (4.8)	157 (37.5)	177 (42.2)	0.061
Two	10 (2.4)	116 (27.7)	126 (30.1)	
Three	12 (2.9)	56 (13.4)	68 (16.2)	
Four and above	10 (2.4)	38 (9.1)	48 (11.5)	
Duration of daily medicine intake (days)[b]				
< 7	23 (2.8)	244 (29.5)	267 (32.3)	0.650
8-30	12 (1.5)	127 (15.4)	139 (16.8)	
> 30	29 (3.5)	391 (47.3)	420 (50.8)	

[a]Result expressed as number of participants (percent). Percent calculated out of 419 participants.
[b]Result expressed as number of medicines (percent). Percent calculated out of 826 medicines.
*Statistically significant

n=13) and from the age 50 years and above (61.9%; n=13) (Table 6). Significant association is observed between the medicine dosage form modification and age (p=0.01) and number of daily medicine intake (p=0.04). Meanwhile, there was no significant association between the medicine dosage form modification and gender, education level, district and duration of medicine intake (p > 0.05) (Table 7).

Among total medicine administration, 2.9% medicines (n=24) were modified that include splitting tablets (70.8%; n=17), crushing tablets (16.7%; n=4), opening capsule (8.3%; n=2) and mixing with food and juices (4.2%; n=1). The modified dosage forms included immediate release uncoated tablets (41.7%; n=10), film coated tablets (20.8%; n=5), modified release tablets (20.8%; n=5), hard gelatin capsules (12.5%; n=3) and enteric coated tablet (4.2%; n=1) (Table 8). Most of these modifications were due to swallowing difficulty (79.2%; n=19) and rest were due to unavailability of required dose (20.8%; n=5). The three most commonly modified medicines were paracetamol and ibuprofen combination tablet (25.0%; n=6), metformin modified released tablet (20.8%; n=5) and frusemide and spironolactone combination tablet (12.5%; n=3) (Fig. 2).

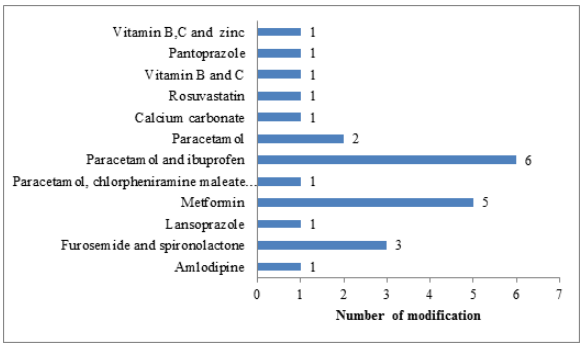

Figure 2. Oral solid medicine undergoing dosage form modification (n=24)

Table 6. Characteristic of participants modifying medicine (n=21)

	Number of participants modifying medicine (%)
Age (years)	
18-29	6 (28.6)
30-39	-
40-49	2 (9.5)
50-59	6 (28.6)
> 60	7 (33.3)
Gender	
Male	8 (38.1)
Female	13 (61.9)
Number of medicine daily	
One	4 (19.0)
Two	4 (19.0)
Three	8 (38.1)
Four and above	5 (23.8)

Among these modification, 25.0% (n=6) medicine dosage form modification were found to be inappropriate.

Practice and knowledge on oral solid dosage form modification

Overall, 6.9% of total participants (n=29) were advised to do medicine dosage form modification mainly by family and friends (62.1%; n=18) and about one fourth (26.3%; n=110) of participants advised other to make medicine modification (Table 9). Similarly, among those who modified their medicines, 66.7% (n=14) were advised to make medicine modification by family and friends (42.9 %; n=6) followed by doctors (35.7%; n=5) and pharmacists (21.4%; n=3) and 33.3 % (n=7) were doing medicine modification on their own. In addition, 28.6% of these participants (n=6) also had advised other to make medicine dosage form modification (Table 10).

More than half of the total participants (55.4%; n=232) believed that there may be harmful effects of medicine modification which most of them thought to be incorrect dose administration (56.0%; n=130) and undesirable side effect (43.5%; n=101). Among those who modified their

Table 7. Association of medicine dosage form modification among participants reporting medicine administration problem with different variables

Variable	Medicine dosage form modification		Total	p value
	Done	Not done		
Age (years)[a]				
18 - 49	8 (14.0)	26 (45.6)	34 (59.6)	0.011*
> 50	13 (22.8)	10 (17.5)	23 (40.4)	
Gender[a]				
Female	13 (22.8)	28 (49.1)	41 (71.9)	0.198
Male	8 (14.0)	8 (14.0)	16 (28.1)	
Education[a]				
Illiterate	10 (17.5)	12 (21.1)	22 (38.6)	0.549
Upto secondary	6 (10.5)	12 (21.1)	18 (31.6)	
Graduate	5 (8.8)	12 (21.1)	17 (29.8)	
District[a]				
Kavrepalanchowk	13 (22.8)	27 (47.4)	40 (70.2)	0.297
Bhaktapur	8 (14.0)	9 (15.8)	17 (29.8)	
Number of daily medicine intake[a]				
Two or less	8 (14.0)	24 (42.1)	32 (56.1)	0.036*
Three or more	13 (22.8)	12 (21.1)	25 (43.9)	
Duration of daily medicine intake (days)[b]				
30 or less	12 (17.4)	24 (34.8)	36 (52.2)	0.792
Above 30	12 (17.4)	21 (30.4)	33 (47.8)	
Knowledge of possible effects of medicine dosage form modification[a]				
Yes	5 (8.8)	20 (35.1)	25 (43.9)	0.020*
No or don't know	16 (28.1)	16 (28.1)	32 (56.1)	

[a]Result expressed as number of participants with medicine administration problem (percent). Percent calculated out of 57 participants.
[b]Result expressed as number of medicines with administration problem (percent). Percent calculated out of 69 medicines.
*Statistically significant

Table 8. Detail of medicine dosage form modification

	Type of medicine dosage form modification				
	Crush tablets	Split tablets and swallow	Open capsules	Mix with food or juices	Total
Dosage form					
Immediate release uncoated tablet	1(4.2)	9(37.5)	-	-	10(41.7)
Film coated tablet	2(8.3)	3(12.5)	-	-	5(20.8)
Enteric coated tablet	1(4.2)*	-	-	-	1(4.2)
Modified release tablet	-	5(20.8)*	-	-	5(20.8)
Hard gelatin capsule	-	-	2(8.3)	1(4.2)	3(12.5)
Total	4(16.7)	17(70.8)	2(8.3)	1(4.2)	24(100)

*Inappropriate medicine dosage form modification

Table 9. General knowledge and practices of medicine dosage form modification among participants (n=419) and their interaction with health professional.

	n (%)
Participants being advised for medicine dosage form modification[a]	
Yes	29 (6.9)
No	390 (93.1)
Person who advised for medicine dosage form modification[b]	
Family and friends	18 (62.1)
Doctors	7 (24.1)
Pharmacists	4 (13.8)
Participants advised other for medicine dosage form modification[a]	
Yes	110 (26.3)
No	309 (73.7)
Knowledge of possible effects of medicine dosage form modification[a]	
Yes	232 (55.4)
No	42 (10.0)
I don't know	145 (34.6)
Possible effects of medicine dosage form modification[c]	
Increased effect	8 (3.4)
Decreased effect	83 (35.8)
Undesirable side effects	101 (43.5)
Increased local toxicity	5 (2.2)
Unpalatable taste	17 (7.3)
Medicine instability	10 (4.3)
Incorrect dose administration	130 (56.0)
Others	4 (1.7)
Need of asking doctors/pharmacists before medicine dosage form modification[a]	
Yes	311 (74.2)
No	11 (2.6)
I don't know	97 (23.2)
Follow up of medicine administration problem by doctors/pharmacists[a]	
Yes	158 (37.7)
No	261 (62.3)
Participants ever consulted medicine administration problem with the doctors/pharmacists?[d]	
Yes	18 (31.6)
No	39 (68.4)

[a]Result expressed as number of participants (percent). Percent calculated out of 419 participants
[b]Result expressed as number of participants being advised to modify medicine dosage form (percent). Percent calculated out of 29 participants
[c]Result expressed as number of participants with knowledge of effect of medicine dosage form modification (percent). Percent calculated out of 232 participants
[d]Result expressed as number of participants with medicine administration problem (percent). Percent calculated out of 57 participants

Table 10. General knowledge and practices of medicine dosage form modification among participants doing medicine dosage form modification (n=21)

	n (%)
Participants being advised for medicine dosage form modification	
Yes	14 (66.7)
No	7 (33.3)
Person who advised for medicine dosage form modification	
Family and friends	6 (42.9)
Doctors	5 (35.7)
Pharmacists	3 (21.4)
Participants advised other for medicine dosage form modification	
Yes	6 (28.6)
No	15 (71.4)
Knowledge of possible effects of medicine dosage form modification	
Yes	5 (23.8)
No	3 (14.3)
I don't know	13 (61.9)

medicines, 76.2% participants (n=16) were unaware of possible harmful effects of medicine modifications (Table 10) that can be explained by the significant association between this knowledge and prevalence of medicine dosage form modification (p=0.02) (Table 7). Also the knowledge is significantly associated with the educational level of the participants (p < 0.001). Around 74.2% of total participants (n=311) thought that they should consult doctors or pharmacists before doing medicine dosage form modification (Table 9).

Doctors/Pharmacists awareness regarding patient's oral solid dosage form of medicine administration problem

One third (31.6%; n=18) of the participants with problem taking the medicines had consulted about their problems with their doctors or pharmacists. Around 62.3% of total participants (n=261) were never asked about any difficulties taking medicines by doctors or pharmacists while prescribing or dispensing the medicines (Table 9).

DISCUSSION

For the therapeutic benefit, it is crucial to understand the practice of oral solid dosage form modifications including its determinants, types of involved medicine, communication between patient and health professional regarding this issue. This study had been of the profound importance in context of Nepal due to unavailability of any previous studies in this area.

Overall 12.4% of participants experienced difficulty swallowing their oral medicines. This result is comparable to the results of other studies. In Australia, 14.1% of consumers visiting community pharmacies; in Switzerland 22.4% of polypharmacy patient going to community pharmacies; in Jordan, 10.4% of patients visiting outpatient pharmacies and in Germany, 37.4% reported to have trouble swallowing their medicines.[3-6] In a systematic review, it was reported that approximately 14.0% of older patients residing in community experienced difficulty swallowing medicines.[28] Swallowing difficulty was observed to be more in female; younger (18-29) and older participants (60 years and above) that was found to be consistent with previous studies.[3,5] It was argued that the difference in anatomical and physiological processes with respect to size and function of mouth, pharynx, upper esophageal spincter, esophagus and women being more prone to mental illness (depression and anxiety disorder) which is related to swallowing difficulty is responsible for such observation. However in older people, swallowing difficulty is expected to be more frequent due to factors such as impaired control over ingestion of bolus, pharyngeal and laryngeal event initiation delay and cricopharyngeal muscle dysfunction.[5]

It was observed that the number of daily medicine intake and duration is not associated with the swallowing difficulty. This is similar to previous study conducted in Switzerland where for majority of participants experienced difficulties at single dose (83.7%) with single medication (59.8%).[4] In the present study, difficulty swallowing the medicines appeared to have due to large tablet size as the common medicines (paracetamol and ibuprofen in combination, metformin and paracetamol tablets) that were reported difficult to swallow had large dosage and it was reported in the literature that people with swallowing difficulty were more likely to have problem in swallowing tablets of size 11 mm or more.[29,30] This is further supported by our finding that, big tablet size or tablet stuck in throat were reported to be the most common causes of swallowing difficulty.

In concordance to previous studies, most of the participants deal with their medicine administration problem by drinking more water and by modifying their medicine commonly by splitting or crushing tablets.[4,6] The present study reported the medicine dosage form modification to be done by 5.0% of overall participants and 36.8% of the participants with problems taking the medicine which is lower than previous studies. The prevalence of medicine modification was reported to be 10.6% of overall participants in Australia; about two third of studied population with swallowing difficulty in Jordan; 58.8% of the patients with swallowing difficulty in Germany.[3,5,6] Such discrepancies might have been observed due to the differences in the sociodemographic characteristic of participants and the inclusion of only two study regions. More regions of Nepal should be studied in order to obtain the representative data.

The higher prevalence of medicine modification in polypharmacy patient (taking three or more medicines) and above 50 years was found to be in accordance with the previous studies.[3,4] The most prevalent form of medicine modification is splitting the tablet which is similar to previous studies.[5,6] The reason may be because tablets form

of dosage form was frequently prescribed in this study and it is more convenient to break the tablets into two by hand or knife. It was observed that the one fourth of medicine modifications included modified release tablets that are not supposed to crushed or cut leading to inappropriate modification. This observation is in accordance with the previous studies where inappropriate modification ranged from 4.5% to 32% in hospital and aged care facility.[19,21,24]

Most of the participants (66.7%) modifying their medicine were advised to do so mainly by family and friends (42.9%) and one third were doing medicine modification on their own. Family and friends more often advised to medicine modification because most of the participants (68.4%) did not discuss their problems with doctors/pharmacists. The finding is supported by previous studies where 63.0% and 85.4% of participants with swallowing difficulty did not discuss their problems with their physician or pharmacist in the study conducted in Switzerland and Jordan respectively.[4,6] Moreover, health professional were also failing to ask the participant about the presence of any difficulties taking the medicine which is found in some previous studies as well.[4-6]

There are some limitations in this study. First, the study was conducted in five conveniently selected pharmacies located in two districts of Nepal. So it may not be extrapolated to represent the data for whole nations. However, it does provide some indication of the prevalence and views of participants about the solid dosage form modification in the selected regions. Second, the study was focused toward the community pharmacies, so there is a possibility that those higher age group people who are not able to go the pharmacy to collect their medicines are being excluded in the study. So, this study may be reinforced by including the participant from hospitals and aged care facility. Lastly, this type of studies has not yet been conducted in Nepal and its neighboring region. So, there is requirement of more in-depth studies that include more participants of different facilities of different regions to have overall estimate. Furthermore, due to limited literature in the south Asian region, the comparison was limited to include developed counties only.

CONCLUSION

In the present study, swallowing difficulty and medicine dosage form modification were observed in the Nepalese population. Inappropriate medicine modifications were found that may compromise the therapeutic benefit to patient. So,there is a need of more detailed study covering the older cohort for deeper understanding of the scenario in the Nepalese population. In addition, there seemed lack of communication between the health care provider such as doctors or pharmacist regarding the issues of swallowing difficulty and medicine dosage form modification especially of the modified release type. This is a high time that the doctors should ask about the presence of swallowing difficulty and pharmacist to give enough information and counseling to patient about medicine dosage form modification especially for modified release type of dosage form.

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REFERENCES

1. Aulton ME, Taylor KMG, editors. Aulton'spharmaceutics: the design and manufacture of medicine. 5th ed. Elsevier; 2018.
2. Northern Ireland (NI) Regional Medicines and Poisons Information Service. Choosing medicines for patients unable to take solid oral dosage form [internet]. [place unknown]:[publisher unknown]; 2018 [cited 2021 May 26]. Available from:http://niformulary.hscni.net/download/91/swallowing-difficulties/3332/hsc-guideline-swallowing-difficulties
3. Lau ETL. Steadman KJ, Mak M, Cichero JAY, Nissen LM. Prevalence of swallowing difficulties and medication modification in customers of community pharmacists. *J Pharm Pract Res*. 2015;45(1):18-23. https://doi.org/10.1002/jppr.1052
4. Marquis J, Schneider MP, Payot V, Cordonier AC, Bugnon O, Hersberger KE, et al. Swallowing difficulties with oral drugs among polypharmacy patients attending community pharmacies. *Int J Clin Pharm.* 2013; 35:1130-6. https://doi.org/10.1007/s11096-013-9836-2
5. Schiele JT, Quinzler R, Klimm HD, Pruszydlo MG, Haefeli WE. Difficulties swallowing solid oral dosage forms in a general practice population: prevalence, causes, and relationship to dosage forms. *Eur J Clin Pharmacol.* 2013; 69 (4):937-48. https://doi.org/10.1007/s00228-012-1417-0
6. Tahaineh L, Wazaify M. Difficulties in swallowing oral medications in Jordan. *Int J Clin Pharm*. 2017; 39: 373-9. https://doi.org/10.1007/s11096-017-0449-z
7. Clauson H, Rull F, Thibault M, Ordekyan A, Tavernier J. Crushing oral solid drugs: assessment of nursing practices in health-care facilities in Auvergne, France. *Int J Nurs Pract*. 2016; 22 (4): 384-90. https://doi.org/10.1111/ijn.12446
8. Royal Pharmaceutical Association, Pharmaceutical issues when crushing, opening or splitting oral dosage forms [internet]. [place unknown]:[publisher unknown]; 2011 [cited 2021 May 26]. Available from https://www.rpharms.com/Portals/0/RPS%20document%20library/Open%20access/Support/toolkit/pharmaceuticalissuesdosageforms-%282%29.pdf
9. Lippert C, Gbenado S, Qiu C, Lavin B, Kovacs SJ. The bioequivalence of telithromycin administered orally as crushed tablets versus tablets swallowed whole. *J Clin Pharmacol*. 2005; 45 (9): 1025-31.https://doi.org/10.1177/0091270005279273
10. Argenti D, Ireland D, Heald DL. A pharmacokinetic and pharmacodymanic comparison of desmopressin administered as a whole, chewed and crushed tablets, and as an oral solution. *J Urol*. 2001; 165 (5): 1446-51. PMID: 11342894.

11. Ashley ESD, Zaas AK, Fang AF, Damle B, Perfect JR. Comparative pharmacokinetics of voriconazole administered orally as either crushed or whole tablets. *Antimicrob Agents Chemother*. 2007; 51(3):877-80. https://doi.org/10.1128/AAC.01263-06
12. Volpe DA, Gupta A, Ciavarella AB, Faustino PJ, Sayeed VA, Khan MA. Comparison of the stability of split and intact gabapentin tablets. *Int J Pharm*. 2008; 350(1-2):65-9. https://doi.org/10.1016/j.ijpharm.2007.08.041
13. Clearly JD, Evans PC, Hikal AH, Chapman SW. Administration of crushed extended-release pentoxifylline tablets: bioavailability and adverse effects. *Am J Health Syst Pharm*. 1999;56(15):1529-34. https://doi.org/10.1093/ajhp/56.15.1529
14. Mandal TK. Effect of tablet integrity on the dissolution rate of sustained-release preparations. *J Clin Pharm Ther*. 1996;21(3):155-7. https://doi.org/10.1111/j.1365-2710.1996.tb00015.x
15. Hider JD, Shehab Z, Courteney-Harris R. Effectiveness of modified release isosorbidemononitrate affected by incorrect use. *BMJ*. 2000; 320(7233): 483. PMID: 10678861.
16. Cornish P. "Avoid the crush": hazards of medication administration in patients with dysphagia or a feeding tube. *CMAJ*. 2005; 172 (7):871-2. https://doi.org/10.1503/cmaj.050176
17. Schier JG, Howland MA, Hoffman RS, Nelson LS.Fatality from administration of labetalol and crushed extended-release nifedipine. *Ann Pharmacother*. 2003; 37(10): 1420-3. https://doi.org/10.1345/aph.1D091
18. Mc. Gillicuddy A, Kelly M, Sweeney C, Carmichael A, Crean AM, Sahm LJ. Modification of oral dosage forms for the older adult: an irish prevalence study. *Int J Pharm*. 2016; 510 (1): 386-93. https://doi.org/10.1016/j.ijpharm.2016.06.056
19. Mercovich N, Kyle GJ, Naunton M. Safe to Crush? A pilot study into solid dosage form modification in aged care. *Australas J Ageing*. 2014; 33 (3): 180-84.https://doi.org/10.1111/ajag.12037
20. Nissen LM, Haywood A, Steadman KJ. Solid medication dosage form modification at the bedside and in the pharmacy of Queensland hospitals. *J Pharm Pract Res*. 2009; 39 (2): 129-34. https://doi.org/10.1002/j.2055-2335.2009.tb00436.x
21. Stubbs J, Haw C, Dickens G. Dose form modification- a common but potentially hazardous practice. A literature review and study of medication administration to older psychiatric inpatients. *Int Psychogeriatr*. 2008; 20(3): 616-27.https://doi.org/10.1017/S1041610207006047
22. Ingram V, Gaunt MJ, Grissinger M. The Breakup: errors when altering oral solid dosage forms. *Pa Patient Saf Advis*. 2018;15(3):15-35.
23. Nyborg Gunhild, Brekke M, Straand J, Gjelstad S, Romoren M. Potentially inappropriate medication use in nursing homes: an observational study using the NORGEP-NH criteria. *BMC Geriatrics*. 2017; 17, 220. https://doi.org/10.1186/s12877-017-0608-z
24. Sefidani Forough A, Lau ETL, Steadman KJ, Kyle GJ, CicheroJAY, Serrano Santos JM, et al. Appropriateness of oral dosage form modification for aged care residents: a video-recorded observational study. *Int J Clin Pharm*. 2020; 42(3):938-47. https://doi.org/10.1007/s11096-020-01036-x
25. Chen LL, Tangiisuran B, Shafie AA, Hassali MAA. Evaluation of potentially inappropriate medications among older residents of Malaysian nursing homes. *Int J Clin Pharm*. 2012;34:596-603. https://doi.org/10.1007/s11096-012-9651-1
26. Daniel WW, Cross CL. Biostatistics: a foundation for analysis in the health sciences. 10ed. John Wiley and Sons; 2013.
27. Burridge N, Symons K, editors. Australian don't rush to crush handbook. 3rd ed. Collingwood, Vic, Australia: Society of Hospital Pharmacists of Australia; 2018.
28. McGillicuddy M, CreanAM, Sahm LJ. Older adults with difficulty swallowing oral medicines: a systematic review of the literature. *Eur J Clin Pharmacol*. 2016; 72: 141-51. https://doi.org/10.1007/s00228-015-1979-8
29. Katzung BG, Trevor AJ, editors. Basic and Clinical Pharmacology.13th ed. McGraw-Hill Education; 2015.
30. Liu F, Ghaffur A, Bains J, Hamdy S. Acceptability of oral solid medicines in older adults with and without dysphagia: a nested pilot validation questionnaire based observational study. *Int J Pharm*. 2016; 512 (2): 374-81. https://doi.org/10.1016/j.ijpharm.2016.03.007