

**Evaluation of Weight Uniformity of Splitting Tablet**

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ABSTRACT

Tablet-splitting is a widespread practice among all sectors of health care for different reasons: it increases dose flexibility, makes tablet parts easier to swallow and allows cost savings for both patients and healthcare providers. However, the tablet parts obtained are often not equal in size, and a substantial amount of tablet can be lost during splitting. This paper is a report of a study conducted to quantify the mean deviation from theoretical weight and the mean weight loss, of three different tablet preparations commonly used to manage hypertension. The tablets were Verapamil Hydrochloride 80mg, Metoprolol Tartrate 50mg and Atenolol 50mg. A volunteer was used in the study to split 30 randomly selected tablet of each of the preparation using two different routine methods; manual splitting and with a kitchen knife. Before and after splitting, tablets and tablet parts were weighed using an analytical balance. All the methods showed significant deviation of weight than the theoretical. Large dose deviations or weight losses can occur while splitting tablets which could have serious clinical consequences for medications with a narrow therapeutic-toxic range. On the basis of the results in this report, we recommend use of a splitting device when splitting cannot be avoided.

Key words: Tablet-splitting, Weight deviations, Therapeutic-toxic range.

INTRODUCTION

Tablet splitting has become increasingly common especially within the generic and psychiatric communities, as a means of reducing medication dose and/or cost. Physicians frequently write prescriptions for half-tablet in order to achieve doses less than the smallest available manufactured strength. Prescribers also write for half and quarter-tablets. Dose adjustment is important in case of some patients. Some patients need full dose initially and need half dose latterly depending on the condition of disease. Sometimes physician prescribe half tablet because of inavailability of smaller dose or depending on extent of disease. (Fischbach *et al.*, 2001; Biron *et al.*, 1999; Van *et al.*, 2002; Polli *et al.* 2003).

There are many kinds of split-tablets commonly used to treat cardio-vascular diseases, hypertension, diabetic and pediatric complications. Because of different cases of patient and individual variations, with an effort to achieve better clinical effect, tablet splitting is in the service of better matching drug dose to patient's tolerance and in the service of avoiding dose related adverse effects and of improving safety of medications and adherence of patients. In developed country health care provider provide tablet splitting device to split tablet. Inaccurate splitting constitutes both a wrong technique when it is performed without the correct device and a dosing error, and could potentially result in harm for patients. Various methods are used to split tablets: (i) a splitting device (e.g. Pilomat®), (ii) splitting by hand (for scored tablets) or with scissors (for unscored tablets), or (iii) with a kitchen knife. There has been previous research on the impact of tablet splitting on dose accuracy. Reports published so far have concerned splitting devices (Peek *et al.*, 2002; Cook *et al.*, 2003; Boggie *et al.*, 2004), kitchen knives (Cook *et al.*, 2003) and splitting by hand (Babington, 1997; Boggie *et al.* 2004). In our country patients are not using splitting

device due to unfamiliarity and cost. So patients split tablet manually by hand or by knife. As a result there are great chances of variation. This may cause serious harm for the patients. The aim of the study was to quantify the mean deviation from theoretical weight and the mean weight loss, after tablet-splitting with two different, commonly used splitting methods.

MATERIALS AND METHODS

An experimental design was adopted and the data were collected in July 2010 to September 2010. Three commercially available brands of three different tablets of different sizes and shapes, and which are commonly splitted in homes, were selected for the experiment. Table 1 gives an overview of the characteristics of these tablets.

Table 1: Characteristics of tablets under investigation.

Drug name	Tablet description
Verapamil hydrochloride	Circular shape; White and film coated
Metoprolol tartrate	Heart shape; Film coated
Atenolol	Circular shape; White color

Nevertheless, these tablets are often prescribed in halves or quarters. Two different routine splitting methods were assessed: (i) hand-splitting and (ii) a kitchen knife. No specific splitting guidelines or instructions were given. Per volunteer and per method, the initial weight of ten tablets of each formulation was assessed using an electronic analytical balance (Shimadzu Corporation, Japan), and the mass of each tablet was recorded with an accuracy of 0.1 mg. After splitting, each half was individually weighed. For each tablet part, the deviation from the theoretical weight and the weight loss were calculated as follows:

Theoretical weight = weight of the tablet before splitting;

Deviation (%) from theoretical weight = (weight of the tablet fragment – theoretical weight) /theoretical weight X 100;

Weight loss = weight of the tablet before splitting – sum of all tablet fragments.

Ethical considerations

The study did not require approval from an ethics committee since we did not collect patient data.

Data analysis

Percent variation and percent weight loss among the two splitting methods were compared with a one-way ANOVA test.

RESULTS

Table 2 displays the mean deviation from the theoretical weight for the different tablet parts of each product and the comparison between the two different methods, using a one-way ANOVA test. Overall results are also given. Overall, method 1 provides a significantly lower mean deviation from theoretical weight. The difference between method 1 and method 2 is not statistically significant.

Table 2: Mean and maximum deviation from theoretical weight (%) for the two evaluated methods (N = 30)

Sample	Method 1			Method 2			P value Method 1 vs Method 2
	Mean	SD	Max	Mean	SD	Max	
Verapamil hydrochloride	18.94	13.01	51.07	17.52	14.38	68.01	0.819
Metoprolol tartrate	11.44	9.77	35.29	12.54	11.53	53.17	0.859
Atenolol	14.58	12.51	48.00	16.02	12.99	53.83	0.840

Method 1: by hand; Method 2: with a kitchen knife.

Table 3 displays the number of tablet parts that deviate between 15% and 25% from theoretical weight, and the number of tablet parts that deviate more than 25% from the theoretical weight. While splitting the tablets, some tablet fragments fell on to the floor. These fragments were no longer included in the data processing. As the results show, both methods produced the significant number of tablet parts deviating between 15% and 25% from theoretical weight and deviating more than 25% from theoretical weight.

Table 3: Number of tablet fragments deviating more than 15% and more than 25% from the theoretical weight

Sample	Method 1		Method 2	
	Deviation 15–25%	Deviation >25%	Deviation 15–25%	Deviation >25%
Verapamil hydrochloride	6/60	12/60	4/60	1/60
Metoprolol tartrate	18/60	10/60	13/60*	9/60
Atenolol	11/60	12/60	10/60	20/60*

Method 1: by hand; Method 2: with a kitchen knife.

*Tablet fragments that fell on the floor during splitting were not included.

Not only weight deviations from theoretical weight, but also weight losses were recorded. These results are summarized in Table 4. Method 1 gave the lowest weight loss compared to method 2; the difference between methods 1 and 2 was not statistically significant. However, when pooling the results for the different tablets, method 1 induced statistically significantly less weight loss than the other method.

Table 4: Weight-loss after tablet-splitting (%), with comparison between the three methods evaluated (N = 30).

Sample	Method 1			Method 2			P value Method 1 vs Method 2
	Mean	SD	Max	Mean	SD	Max	
Verapamil hydrochloride	-0.10	0.32	-1.55	-2.25	4.74	-27.40	<0.001
Metoprolol tartrate	-4.80	3.34	-16.11	-3.40	2.76	-11.91	0.030
Atenolol	-1.49	0.97	-5.11	-4.07	2.98	-11.87	<0.001

Method 1: by hand; Method 2: with a kitchen knife.

DISCUSSION

Study limitations

This study had some limitations. It could be argued that we did not compare two distinct methods. However, we wanted to compare two routine methods in order to identify the best possible splitting guidelines for daily practice. Another criticism might be that one volunteer was included. However, we tried to find the splitting variations present even in a single individual. Moreover, we did not investigate the clinical effect of the weight deviations. It seems logical that clinical consequences are small in long-term therapies with agents with long half-lives or high therapeutic indexes. However, there might be some serious clinical consequences when a splitting method is used that produces important dose deviations, for acute therapies, or for drugs with short half-lives or low therapeutic indexes.

Effects of tablet-splitting

Splitting tablets leads to high variability in both fragment weights and weight losses. This study was undertaken to evaluate the best method for daily tablet-splitting at home. Although some literature is available on this topic, authors have reported their findings in different ways, making comparison difficult (Cook *et al.*, 2003; Mcdevitt *et al.*, 1998; Boggie *et al.*, 2004; Biron *et al.*, 1999; Peek *et al.*, 2002; Teng *et al.*, 2002; Polli *et al.*, 2003; Kayumba *et al.*, 2006). The majority of this literature is a few years old now, whereas the practice remains very alive and still problematic. We

aimed at providing patients and health care providers with advice for the best splitting technique in daily practice. This means that we needed to search for a technique that is applicable and reliable regardless of the dexterity or training level of the person performing the splitting, and regardless of the tablet's characteristics. We selected tablets with different characteristics to be included in the study. In this way, the findings can be generalized, regardless of the tablet or its brand. The results showed a high variability in weight deviation and weight loss between the two methods. Probably use of a splitting device appeared to be the best method for splitting tablets, since it may be yielded smaller weight deviations and smaller weight losses than using hand or using a kitchen knife.

CONCLUSION

Tablet-splitting is daily practice in our society. However, not all formulations are suitable for splitting, and even when they are, large dose deviations or weight losses can occur. This could have serious clinical consequences for medications with a narrow therapeutic-toxic range. On the basis of our results, we can warn the people to avoid splitting of tablets and use splitting device when splitting cannot be avoided (i.e. for example when the prescribed dose is not commercially available, or when there is no alternative formulation). As for policy implications, we recommend that manufacturers make it possible to avoid splitting, by introducing a wider range of tablet doses or liquid formulations.

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