Original Article

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# Comparison of Dosage Loss Between Medications Crushed with Two Different Methods by Two Nurses: An *In Vitro* Study

## İki Farklı Yöntemle ve İki Farklı Hemşire Tarafından Ezilen İlaçlar Arasındaki Doz Kaybının Karşılaştırılması: *İn Vitro* Çalışma

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## ABSTRACT

**Objective:** Administration of crushed medications can lead to various problems associated with use of inappropriate crushing method, such as administration of an incorrect dosage, alterations in drug bioavailability, and reduction in the effectiveness of the treatment. This experimental study aimed to compare the dosage loss of crushed metoclopramide hydrochloride (MT-HCI) 10-mg tablet using two crushing methods.

**Methods:** MT-HCI 10 mg tablets (n=80) were crushed by two nurses, and each nurse used a pill crusher and a pestle and plastic bag to crush the tablet. Dosage loss was calculated by a specialist pharmacist in a laboratory environment.

**Results:** The dosage loss was 0.515±0.299 mg (5.16%) with the pestle and self-sealing plastic bag and 0.415±0.359 mg (4.16%) with the pill crusher. No statistically significant difference was found between the two methods (p>0.05). The mean dosage loss was 0.482±0.367 mg for the first nurse and 0.449±0.298 mg for the second nurse. No statistically significant difference was noted in the mean dose between the two nurses (p>0.05).

**Conclusion:** This study found no significant difference between the nurses and the crushing methods, but the mean dosage loss with both methods was not within the limits recommended by the United States Food and Drug Administration.

**Keywords:** Medications, dosage loss, tablet crushing, tablets crushing device, nursing skills

## ÖZ

**Amaç:** İlaçların ezilerek verilmesi, ilaçların uygun olmayan yöntemlerle ezilmesi, yanlış dozda verilmesi, biyoyararlanımının değişmesi, tedavinin etkinliğinin azaltılması gibi birçok soruna yol açabilir. Bu deneysel çalışma, farklı iki hemşire tarafından, iki farklı yöntemle metoklopramid hidroklorür (MT-HCI) 10 mg tabletlerin ezildikten sonra, rezervuarda kalan doz kaybını karşılaştırmak amacıyla yapıldı.

**Yöntemler:** MT-HCI 10 mg tabletler (n=80) iki araştırmacı hemşire tarafından iki farklı yöntemle ezildi. Her hemşire ezmek için her iki yöntemi de (tablet ezici veya kilitli plastik torba içinde havaneli ile ezilerek) kullandı. Tablet ezici ve plastic torba içinden ilaç alındıktan sonra kalan doz kaybı laboratuvar ortamında uzman bir eczacı tarafından hesaplandı.

**Bulgular:** Kalan doz kaybı, kilitli plastik torbada havaneli yöntemiyle ezme yöntemiyle ortalama 0,515±0,299 mg, (%5,16) ve tablet ezici ile 0,415±0,359 mg (%4,16) olarak hesaplandı. İki yöntem arasında istatistiksel olarak anlamlı bir fark yoktu (p>0,05). Ortalama doz kaybı birinci hemşire için ortalama 0,482±0,367 mg ve ikinci hemşire için ortalama 0,449±0,298 mg idi. İki hemşire arasında kalan doz ortlamaları açısından istatistiksel olarak anlamlı bir fark yoktu (p>0,05).

**Sonuç:** Bu çalışma, ezme yöntemleri ile hemşireler arasında anlamlı bir fark olmadığını gösterdi. Ancak her iki yöntemde de ortalama doz kaybı Amerika Birleşik Devletleri Gıda ve İlaç İdaresi tarafından önerilen sınırlar içinde değildi.

**Anahtar Sözcükler:** İlaç hazırlama, doz kaybı, tablet ezme, tablet ezici, hemşirelik uygulamaları

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## Introduction

Solid medications are administered in cut or crushed form to patients with dysphagia, patients fed through a gastric tube in critical care environments, or pediatric patients who cannot swallow such medications (1-4). Solid medications have to be cut and/or crushed under proper conditions, diluted with liquids, and administered by disposable syringes via a feeding tube or orally (3,5,6). However, when drugs are in solid form, nurses administer enteric-coated and extended release tablets to patients through a feeding tube after crushing them with inappropriate methods (7,8).

While nurses generally follow written and standardized protocols for administration of parenteral medications, they do not use standardized protocols when they crush or change the original administration form, making administration errors possible (8-10). Thus, medication preparation and administration should include cutting the medication in correct dosage under proper conditions, crushing and mixing it with liquid (drinking water, distilled water, etc.), collecting the mixture with a disposable syringe, and finally administering it orally or through a feeding tube (3,5,6).

Administration of medications after crushing or changing the original medication form can result in various problems associated with the use of inappropriate crushing methods, such as administration of incorrect dosage, alterations in drug bioavailability, and reduction of the effectiveness of the treatment (11-13). The most common problems associated with crushing medications are as follows: 1) no separate crushing apparatus for each patient; 2) hardness of the medication; 3) dosage loss or contamination due to improper crushing methods such as using an inappropriate sheet of paper as lining, crushing the medication while inside the packing of a medical equipment, or crushing by hitting the medication with a piece of wood or side of a glass intravenous fluid bottle or scissors; 4) insufficient dilution with a proper liquid; 5) reduction of the effectiveness of medication due to insufficient flushing of the enteral feeding tube and adhesion of the medication to the inner surface of the tube; 6) and drug interaction due to insufficient cleaning of the medication-crushing apparatus (3,14-17). Moreover, dosage loss may occur if a wrong solution is chosen and therefore cannot properly dissolve the medication. In this case, the feeding tube may be obstructed and lead to dosage loss, decreased effectiveness of the medication or toxicity, and consecutively decreased benefit from the treatment (11-13).

Many studies have evaluated dosage loss when tablets are crushed and transferred with syringes. In a study where a mortar and pestle was used for crushing, the dosage loss during the transfer with a syringe was 4%-38% (18). Similarly, in another study using a mortar and pill crusher, the dosage loss was 0%-4.8% (3). However, flushing the mortar, which contains the crushed medication, has been reported to decrease the dosage loss (19).

Nurses are not only licensed for medication administration but are also responsible for the administration of the prescribed medication at the prescribed dosage and route (10,11). Nurses have a key role in avoiding medication administration errors, maintaining patient safety, and ensuring an effective treatment process, as they are the patient-facing part of the treatment team, in which physicians and pharmacists are also involved (20,21). However, most nurses who encounter problems with administration of medications that need crushing or modification of the original administration form do not tend to consult a pharmacist or clinical guidelines (8,22).

The correct administration of oral medications in crushed form is a challenge for nurses (23). To our knowledge, only one descriptive study from Turkey has focused on the administration of crushed medications or medications in modified forms (24), and only a few global studies have reported on the crushing method ensuring the smallest dosage loss, but these studies have different methodological designs and do not generate evidence-based data (3,18,25).

Thus, this experimental study aimed to compare the dosage loss of crushed metoclopramide hydrochloride (MTC HCl) 10-mg tablets using two crushing methods.

## Method

This experimental study was conducted during the period from August 2018 to December 2018 in a laboratory environment. To easily detect any related difficulties in practice, MTC HCl 10-mg tablets were chosen as the active ingredient and distilled water as the dissolving solution. The dosage loss due to the undissolved MTC HCl 10-mg tablet residues in distilled water was then evaluated. A specialist pharmacist calculated the dosage loss of the medications in solid form after the tablet was crushed with a pill crusher or the pestle method before administration; the tablets were crushed by two nurse researchers in the laboratory environment. The MTC HCl 10-mg tablet was chosen as the crushable and transformable medication. A total of 80 tablets were crushed either with a pill crusher or with the pestle method by two nurse researchers, and each nurse used both crushing methods. The nurse researchers crushed the tablets at the same time, and the process took 3 h. The experiment was done in 1 day. The process involved crushing the drug, diluting and vacuuming the drug by an injector from the reservoir, diluting and vacuuming the remaining dose by an injector from the reservoir again, coding the injectors for the pharmacist with an adhesive tape, and cleaning the pill crusher to crush a new drug or preparing a new self-sealing plastic bag. One of the nurse researchers had 9 and the other had 17 years of intensive care unit and clinical care experience, and both had a PhD in the Fundamentals of Nursing.

### Medication Crushing Methods

#### Pill Crusher

A pill crusher identical to the ones used in clinical care was used by the nurse researchers. The medication in solid form was placed in the pill crusher, and the upper part was closed. To achieve complete crushing, the upper part was rotated by 360°,

the pill crusher shaken, and then rotated until the tablet was properly crushed. Twenty of the 40 MTC HCl 10-mg tablets were crushed by one of the nurse researchers, and the rest by the other nurse on different occasions (Figure 1). The crushed components were diluted with 5 mL of distilled water in the pill crusher and aspirated with a syringe. To calculate the dosage of the residues in the pill crusher, the device was rinsed with 2 ml of ethanol and the material was aspirated with a separate syringe. The pill crusher was washed under clear water, dried with a paper towel, and left open for 5 min between uses. All phases of the procedure were observed by a physician who was not otherwise associated with the study.

**Pestle Method**

Self-locking 8x10 $cm^2$ plastic bags for routine medication administration in the clinics were used in this method (Figure 1). The tablets were placed inside the plastic bag one by one and crushed by hitting them with a pestle from the outside. Twenty of the 40 MTC HCl 10-mg tablets were crushed by one of the nurse researchers, and the rest by the other nurse researcher on different occasions and a new plastic bag was used each time. The crushed medication was diluted with 5 mL of distilled water in the plastic bag and aspirated with a syringe. To calculate the quantity of the residues, the plastic bag was rinsed with 2 mL of ethanol and the mixture was aspirated with a separate syringe.

During the crushing with the pestle, some of the plastic bags were damaged or punctured. The procedure was stopped in that case, and the process was repeated with a new medication in a new plastic bag. All phases of the procedure were observed by a physician who was otherwise not associated with the study.

The syringes in which medication residues were transferred to analyze the dosage loss were labeled under the supervision of the physician, acting as the external observer, so as to identify the research nurse and the method. The research pharmacist analyzed the dosage loss under the supervision of a pharmacist acting as an external observer.

**Determination of Dosage Loss**

Medications crushed with both methods were diluted with distilled water and collected with a disposable syringe. The reservoir was then rinsed with 2 mL of ethanol, and the remaining medication solution was collected with another disposable syringe to determine dosage loss. The high-pressure liquid chromatography (HPLC) method was used with the Agilent Model 1100 series. According to developed HPLC method, the non-crushed 10-mg MTC tablet was 10.08 mg, and the detection limit of the developed HPLC method was within the acceptable limits given by the pharmacopeia. Chromatographic separations were performed using an ACE 5 Phenyl (4.6x150 $mm^2$) column as the stationary phase. The injection volume was 20 µL, and flow rate was 1 mL/min. An ultraviolet diode array detector was adjusted to 308 nm. MTC HCl was dissolved by the mobile phase, and all stock solutions were stored at +4 °C. The calibration equation was obtained by serial dilution of five points from a concentration of 100 µg/mL to 5 µg/mL with the mobile phase.

**Sample Size of the Study**

The sample size of the study was calculated using the Power Analysis and Sample Size Software, Version 11.0 (PASS V. 11.0), based on similar published studies (3,18,25). Using a confidence interval (CI) of 95%, power of 80%, and interclass correlation coefficient (ICC) of 0.75-0.90 between the amounts to be prepared by the two nurses, it would be enough to crush 40 tablets. Each nurse researcher therefore crushed 20 tablets with each method for a total of 40 tablets, and a grand total of 80 tablets were crushed (Figure 2).

**Ethical Statements**

This study did not collect or use physiological specimens. This study was not conducted on humans or any living subjects, but in a laboratory environment. Thus, a board approval in accordance with the journal policy is not necessary. The institution provided approval for the use of the laboratory for the application and evaluation phase of the research.

**Statistical and Analytical Methods**

The Statistical Package for Social Sciences for Windows Version 22.0 (SPSS Inc., Chicago, IL, USA) was used to analyze the

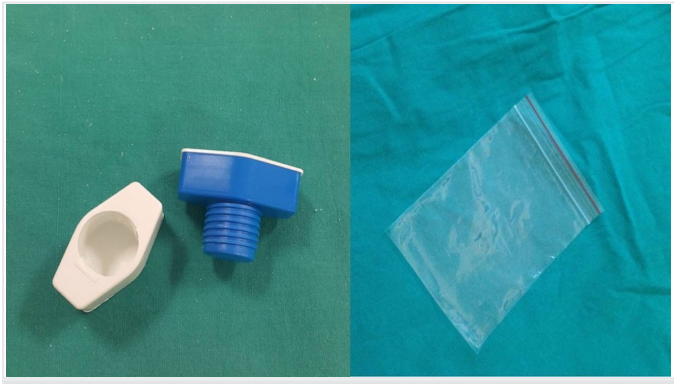

**Figure 1.** Pill crusher and plastic bag

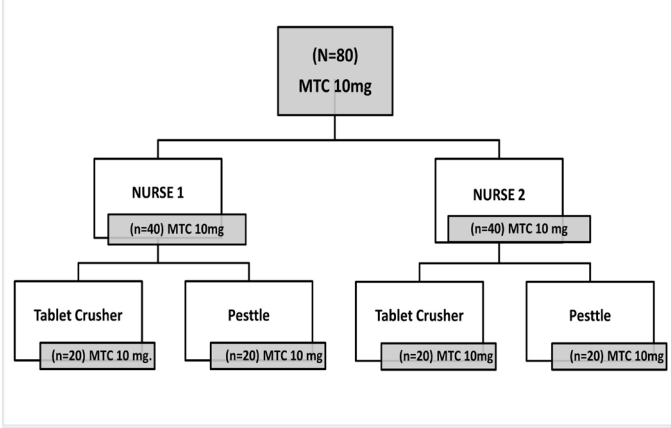


**Figure 2.** Study flow chart

collected data. Normality tests of the variables were conducted by the Shapiro-Wilk test and graphical methods. For descriptive statistics, mean ± standard deviation was used to present continuous variables, while number and percentage were used for categorical variables. Student's t-test and two-way analysis of variance were used when comparing the dosage loss between the two nurse researchers and the two crushing methods; $p<0.05$ was accepted as statistically significant.

## Results

Both nurse researchers stated that crushing the tablets was easier with the pill crusher than with the pestle method and preferred the pill crusher. In the pestle method, seven self-locking plastic bags were damaged and lost, so new tablets were crushed again using new self-sealing plastic bags (nurse 1 damaged 3 plastic bags; nurse 2 damaged 4 plastic bags). The procedure was stopped in these cases, and the procedure was repeated with a new medication in a new plastic bag. The dosage loss was 0.415±0.359 mg [minimum-maximum (min-max): 0.07-1.58 mg] with the pill crusher and 0.515±0.299 mg (min-max: 0.15-1.39 mg) with the pestle method in a self-sealing plastic bag. The dosage loss rates were 4.16% and 5.16% with the pill crusher and pestle method, respectively. The ICC between nurses was 0.78 (0.58-0.88 with 95% CI). When the remaining doses of the crushed tablets in the reservoir were measured, the dosage loss was more than 3% in 57.8% (n=47) of the tablets.

No statistically significant difference was found between the mean dosage loss rates between the two methods (mean (pill crusher) =0.415±0.359 mg, mean (pestle) =0.515±0.299 mg, t=1.350, p=0.181). The mean dosage loss was 0.482±0.367 mg for nurse 1 (40 tablets crushed with both methods) and 0.449±0.298 mg for nurse 2 (40 tablets crushed with both methods) with no statistically significant difference (t=0.443, p=0.659). Two-way variance analysis of the mean dosage loss by two nurse researchers with the two methods (2 nurses x 2 methods) and the post hoc Sidak's multiple comparisons test revealed no statistically significant difference between the groups (*F* (nurse) =0.201, p=0.665; *F* (method) =1.815, p=0.182; *F*(nurse*method) =0.739, p=0.392) (Figure 3). However, in some calculations, the dosage loss was not compatible with the limitations of the United States Pharmacopeia that states "the dosage delivered to the patient should not be less than 90% or more than 110% of the prescribed dosage".

## Discussion

This study compared the dosage loss when crushing solid medications with two different methods by two nurse researchers and the efficiency of the two methods. No statistically significant difference was found between the nurse researchers and the crushing methods, but the mean dosage loss rates with the pill crusher and pestle method were 4% and 5%, respectively.

The manuals published by the United States Food and Drug Administration (FDA) (26) and Green et al. (27) recommend that the dosage loss for enteral medications should be less than 3%.

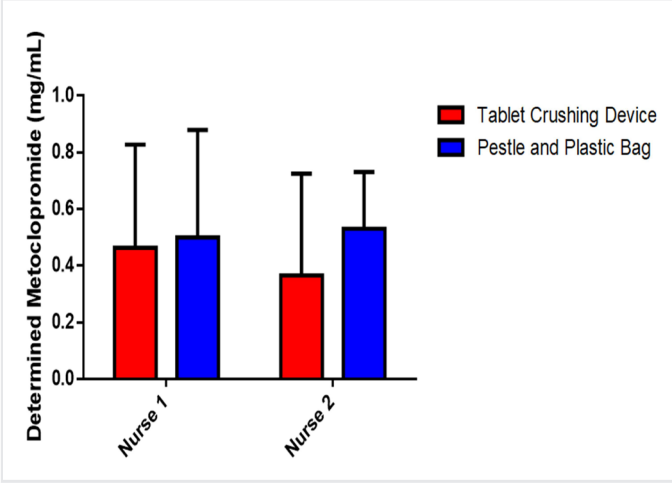


**Figure 3.** Comparison of the dosage loss between the two research nurses and two crushing methods

Methods to minimize the dosage loss and the use of pill crushers are evaluated in several studies (27). Ruzsíková et al. (18) have studied 18 different combinations of methods and tablets and found a dosage loss range of 4%-38%. Thong et al. (25) found a dosage loss of 4.2%-24.2% with various pill crushers and crushing methods and indicated that the dosage loss was higher with the use of disposable plastic bags and pill crushers with a reservoir. According to them, many pill crushers in the market were not suitable in the context of dosage loss. Several studies have recommended to rinse the reservoir of the pill crusher, not once but several times, to help minimize dosage loss (9,19,25). Many studies have reported dosage loss higher than the suggested limits, regardless of the crushing method, similar to our results (9,18,25). In this study, the mean dosage loss was higher with the pestle method using a plastic bag, similar to the findings of Thong et al. (25). We believe that medication residues collected by the second rinsing should be administered to the patients to minimize dosage loss, as suggested in various studies (9,19,25).

This study was conducted in a laboratory environment without any time restrictions, with minimal external stimulants, an easily crushable medication, under the supervision of an external observer, and the nurse researchers had sufficient experience in crushing medications in solid form. Given these conditions, it is possible that we found no statistically significant difference between the two nurse researchers and the two different methods due. However, the results in clinical practice may be quite different considering the workload of the nurses, medication type, ease of crushing the medication, time limitations, and inadequate or improper equipment or devices (3-5,12,16,17,24,28).

Although the MTC HCl 10-mg tablets had no reported health-threatening major adverse effects in healthy adults, a major concern is the transfer of medication dust through the skin or respiratory system of individuals who have crushed them. Aerosolization during crushing and preparation of the solution via the enteral route is therefore a risk for healthcare professionals, particularly for nurses. Secondary intake of the medication through the respiratory system is possible when the crushing is unintentional,

especially with chemotherapeutics and antibiotic agents, leading to allergic reactions and even toxicity (25,29). Thong et al. (25) reported that the dosage loss by aerosolization is 1.1% during the crushing process while tapping the remnant dust of the crushed tablet and 0.2% when it is collected by rinsing the reservoir with water. It is therefore recommended to crush the medication in a sealed plastic bag or a closed pill crushers and to dilute it in the reservoir where it was crushed, as we performed in this study; dosage loss by aerosolization is important.

### Study Limitations

This study had some limitations. First, a medication that can be easily crushed was selected. Medications that are hard to crush or break may lead to different results. Second, this study was conducted under controlled conditions in a laboratory environment with experienced nurse researchers. However, dosage loss is affected not only by the crushing method or device but also by many factors including, but not limited, to stressors in clinical care, experience of the nurse, workload of the nurse, time limitation, availability and convenience of the pill crusher, and the cost effectiveness of the method.

Treatment and administration of medication is a complex process, which involves physicians, pharmacist, and nurses. In this process, the nurse is responsible for the proper preparation and administration of medication and the post-administration observation of possible intended or adverse effects of the medication (2,24,28). Risk of dosage loss at every phase of the treatment should be taken into account by the physician who prescribes and decides on the administration method of the medication, by the pharmacist who supplies it in the prescribed form, and by the nurse who modifies it into the administration form or who trains the patients and their relatives on how to alter the medication in solid form into solutions to be administered through an enteral feeding tube (1,4,25). In this scientifically and technologically advanced new era, it is recommended to prefer medications in liquid form instead of changing medications in solid form into solutions by crushing.

However, if crushing solid medications is inevitable, using a closed reservoir such as a pill crusher or a self-sealing plastic bag, ensuring minimal residues in the reservoir, and avoiding dosage loss in other phases of medication administration are recommended.

Further clinical studies and publishing evidence-based guidelines on safe and secure medication administration through an enteral feeding tube without dosage loss may contribute to better clinical practice and improve patient outcomes.

## Conclusion

In this study, no significant difference was found between the research nurses and the crushing methods, but the mean dosage loss with both methods were not within the limits recommended by the United States FDA, 2013 (30) on the dosage loss for enteral medications. As a standard protocol in the literature, during the transfer of the drug from the pill crusher or from the single-use medication-crushing bag, the whole reservoir must be washed twice and kept. Moreover, to the best of our knowledge, no guideline has been established on the use of pill crusher in any country. However, more research is needed to determine whether device performance varies between tablet types and users and to what extent laboratory research reflects the drug loss during clinical use. Indeed, more clinical studies are needed to obtain new evidence, and guidelines should be published in the light of this evidence.

### Ethics

**Ethics Committee Approval:** The institution provided approval for the use of the laboratory for the application and evaluation phase of the research.

**Peer-review:** Externally peer reviewed.

### Authorship Contributions

Surgical and Medical Practices: B.T., N.Ü., N.Ö., Concept: B.T., N.Ü., N.Ö., Design: B.T., N.Ü., N.Ö., Data Collection or Processing: B.T., N.Ü., N.Ö., F.A., Analysis or Interpretation: B.T., N.Ü., N.Ö., F.A., Literature Search: B.T., N.Ü., N.Ö., F.A., Writing: B.T.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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