

Caroline Ribeiro de Borja-Oliveira

Pill organizers and pill cutters: risks and limitations

ABSTRACT

In this essay, based on documental analysis, the limitations associated with the use of pill organizers and cutters are discussed and analyzed as a matter of public health. The use of the organizers for storing and carrying tablets and capsules exposes these medications to environmental factors from which their original packaging protected them, compromising their stability and safeness. Cutters also pose the additional risk of causing loss of efficacy, adverse reactions and overdose. On the other hand, the user carrying their own medication reflects the balance between autonomy and self-care, and splitting is sometimes required to comply with certain regimens. It can be concluded that healthcare professionals should observe and guide patients and caregivers in order to avoid risks.

DESCRIPTORS: Tablets, administration & dosage. Administration, Oral. Drug Utilization. Drug Storage Drug Packaging. Drug Stability. Drugs of Continuous Use.

Escola de Artes, Ciências e Humanidades.
Universidade de São Paulo. São Paulo, SP,
Brasil

Correspondence:

Av. Arlindo Béttio, 1000 Ermelino Matarazzo
03828-000 São Paulo, SP, Brasil
E-mail: cborja@usp.br

Received: 2/21/2012
Approved: 7/18/2012

INTRODUCTION

Medication is an essential resource to prevent and cure illness, alleviate symptoms and improve quality of life. Not following treatment regimes, above all for elderly patients, is often associated with cognitive and functional decline and the complexity of dosage regimes may, however, compromise the effectiveness of the pharmacotherapy.³ Treatments involving administering multiple daily doses prescribed for patients using other medications are factors that increase the complexity of treatment, and affect adherence. The need to split pills to have the correct dose has an additional impact on adherence to treatment, particularly in the elderly.⁵

Pill organizers and pill cutters are strategies which may help patients follow their regimes. A study⁸ carried out in Nigeria in 2008, involving around 300 HIV positive patients showed that the use of pill organizers improved adherence to the anti-retroviral treatment. In this context, following the treatment is particularly important, as a fall in the level of anti-retroviral encourages the development of viral resistant strains.²

Since 2009, the *Universidade Aberta à Terceira Idade* (UnATI) of the *Universidade de São Paulo* (USP) has offered pharmaceutical workshops. In these workshops, the indiscriminate use of these tools – especially bottles to transport medicine – is observed. The elderly who frequent the UnATI – the majority of whom are independent, socially active situations with access to health services, use medication, especially continuous- use medications. In order to reconcile their day-to-day activities with the need to follow their dosage regimes, they are searching for solutions, such as carrying their medications with them. Resorting to these solutions is necessary in order to reconcile their independence, their participation in society, active old age, looking after themselves, following the prescribed treatment and other aspects which UnATI aims to encourage, stimulate and include. However, storing medications in pill organizers, out of their original packaging is a procedure which poses risks to their conservation and stability. This may result in outcomes ranging from loss of treatment efficacy to patient overdose, the latter resulting from dividing modified release tablets or cutting medications with a narrow therapeutic range, such as digoxin, into unequal parts.

This study describes the types of pill cutters and pill organizers available on the national market and discusses certain restrictions associated with their use, based on their characteristics. Through documental analysis, these characteristics were compared with the best practice, concepts and requirements established by ANVISA – (*Agência Nacional de Vigilância Sanitária* – National Agency for Health Monitoring) ordinances, resolutions and instructions. These documents were obtained through VISALEGIS (*Sistema de Legislação da Vigilância Sanitária* – Health Monitoring Legislation System) database.

LIMITATIONS IN THE USE OF PILL ORGANIZERS

Also known as “pill carriers” or “pill boxes”, pill organizers come in the shape of bottles, boxes or cases, with one or more compartments and are designed to store forms of medicine, such as capsules. The size of the compartments varies and some organizers have a compartment for every period of the seven days of the week. There are products which include an alarm which can be set to go off at the time the medicine need to be taken, products with Braille to identify the time the pills should be taken and even those which can be attached to the body. These products are sold in online and traditional shops and are not restricted to pharmacies or drug stores. There are no guidelines on restrictions to their use, nor recommendations for their user to consult a health professional on correct usage.

When using a pill organizer, the user removes the pill or capsule from its original packaging, defined as the form of packaging which is in direct contact with the product.^a The expiry date, which is the final date by which the medication should be used, is based in tests of stability and depends upon storage and transport conditions. The expiry date may, then, be altered if the conditions referred to in the information leaflet are not adhered to.^{b,c} The stability of pharmaceutical products – and, therefore, the efficacy and safeness of medications – depend on environmental factors such as temperature, humidity and light, and on other factors associated with the product itself, such as the chemical and physical properties of the active ingredients and pharmaceutical

^a Ministério da Saúde. Agência Nacional de Vigilância Sanitária. Resolução RDC nº 157, de 31 de maio de 2002. Estabelecer os requisitos para o registro de medicamentos similares, constantes da presente Resolução e de seus anexos: Anexo I - Informações e Documentação Necessárias para a Solicitação de Registro de Medicamentos Similares. *Diário Oficial*. 7 jun 2002 [cited 2011 Jul 1]. Available from: http://www.anvisa.gov.br/legis/resol/2002/157_02rdc.htm

^b Ministério da Saúde. Agência Nacional de Vigilância Sanitária. Resolução nº 328, de 22 de julho de 1999. Dispõe sobre requisitos exigidos para a dispensação de produtos de interesse à saúde em farmácias e drogarias. *Diário Oficial*. 26 jul 1999 [cited 2011 Jul 1]. Available from: http://www.anvisa.gov.br/legis/resol/328_99.htm

^c Ministério da Saúde. Agência Nacional de Vigilância Sanitária. Resolução nº 35, de 25 de fevereiro de 2003. Dispõe sobre o Regulamento Técnico para o gerenciamento de resíduos de serviços de saúde. *Diário Oficial*. 5 mar 2003 [cited 2011 Jul 1]. Available from: http://www.anvisa.gov.br/legis/resol/2003/rdc/35_03rdc.pdf

excipients. Stability is also linked to the form of the medication and to properties of the materials in which it is packaged. In order to renew a drug's registration, the manufacturer must confirm its validity with stability studies lasting 24 months.^d However, the information leaflet does not give information on how the expiration data may be altered when medications are removed from their original packaging and so the amount of time a pill or capsule is stored in a pill organizer depends solely upon the user, placing the safety and efficacy of the treatment at risk.

Storage conditions for medications are closely linked to their characteristics. Hygroscopic medications, sensitive to humidity, can be packed in hermetically sealed bottles containing desiccant substances, such as packets of silica gel, which should not be discarded or separated from the medication.^e Photosensitive products are packaged in containers which prevent the passage of light.^d

One way of preventing the pill or capsule's exposure to these environmental factors is to cut up the blister pack which surrounds it, without opening it. For this, a pill organizer with compartments large enough to store the cut up blister pack is needed. However, this caution does not circumvent the problems of identifying the medication, as it is the external packaging which contains information including the name of the medication, the concentration, batch number and expiry date etc. Removing the pill or capsule or cutting up the blister pack increases the chance of the user taking an out of date product or of confusing it with another medicine or another dose. The user should be advised to keep the original packaging when using a pill organizer makes this necessary.

If all medications were sold in original packaging which could be easily divided – such as those developed for medicines with fractionated dosage – cutting up the blister pack would not impede the identification of the medication. In this type of original packaging each pill contains information on the reverse identifying the product, such as its commercial name – when not dealing with a generic medication –, its common name in Brazil or, if this is not available, its common name internationally, concentration of the active ingredient, manufacturer's name, expiry date and batch number.^f Although this may be a possible solution to making storing medications in pill organizers safer, the limited

space on the reverse of each unit containing a pill or capsule means that very small writing must be used, which makes this information difficult to read, especially for the elderly. Even on the outer packaging, which generally has more space, information for the user, such as expiry date, is in very small writing and is difficult to read.

Medication should not be stored near air conditioning units, stoves, fridges, freezers, microwaves, televisions or other devices which emit heat and/or humidity.^e It is fundamental that medication not be stored near to windows or in anywhere where they may be in direct sunlight. The user should try and avoid excessive exposure of the medications to heat, especially when the pill organizers are carried in pockets, bags or inside cars.

Pill organizers which can be fixed to the body can, by this very convenience, mean the medications inside are even more exposed to heat, from the body itself or from the atmosphere, and humidity.

In addition to avoiding exposure to these environmental factors, keeping the medications in their original packaging had the advantage of delaying handling the pill or capsule until the moment of taking it. This is important for certain types of pills, such as orodispersible tablets which melt in the mouth, which can easily dissolve on contact with the hands on being taken out of their blister pack. Using pill organizers may also encourage repeated contact with pills or capsules whose components may be absorbed by the skin. Examples of these are 5-alpha reductase inhibitors such as finasteride and dutasteride. These drugs which, if the capsules leak or the pills crumble may be absorbed by the skin during handling, are associated with inhibiting the development of the external genitalia of a male fetus, an effect due to decreased levels of dihydrotestosterone, which poses a risk to pregnant women and women of childbearing age. Abnormalities in the development of external genitalia in fetuses has been demonstrated in studies with animals exposed to finasteride.^{4,6} Although these substances are commonly prescribed for men being treated for benign prostatic hyperplasia (BPH) or androgenetic alopecia, it is not uncommon for pills or capsules to be handled by carers or family members helping in giving or organizing medicine. Patients and care givers should be warned of any necessary precautions for handling these medications when they are prescribed or dispensed.

^dMinistério da Saúde. Agência Nacional de Vigilância Sanitária. Resolução RE nº 1, de 29 de julho de 2005. Determina a publicação do Guia para a Realização de Estudos de Estabilidade. *Diário Oficial*. 1 ago 2005 [cited 2011 Jul 1]. Available from: http://www.anvisa.gov.br/medicamentos/legis/01_05_re_comentada.pdf

^eMinistério da Saúde. Secretaria de Ciência, Tecnologia e Insumos Estratégicos. Departamento de Assistência Farmacêutica e Insumos Estratégicos. Assistência farmacêutica na atenção básica: instruções técnicas para sua organização. 2. ed, Brasília (DF); 2006.

^fMinistério da Saúde. Agência Nacional de Vigilância Sanitária. Resolução RDC nº 80, de 11 de maio de 2006. Dispõe sobre o fracionamento de Medicamentos em Farmácias e Drogarias. *Diário Oficial*. 12 maio 2006 [cited 2011 Jul 1]. Available from: http://www.anvisa.gov.br/hotsite/fraciona/rdc_80.htm

RESTRICTIONS ON PILL CUTTERS

Products designed to cut pills are devices which contain a stainless steel blade in the interior, specifically designed for dividing them into two or four equal pieces. The most common model on the market is made up of an upper part connected to the base where the pill to be cut is placed. The pressure of the upper part, which contains the blade, results in the pill being divided. Pill cutters often come with a compartment in which to store pills and sometimes with a “crushing” accessory.

In addition to being subject to all of the limitations previously noted for pill organizers, pill cutters have additional limitations. The main ones are connected to the type of release of the solid oral medications available on the market. There are those which are instant release, in which the entire dosage of the active ingredient is available soon after taking it.⁸ Some forms of instant release pills have indentations, making it easier to divide the solid pill to suit the dosage. However, it is often difficult to divide a pill into equal parts, the pill may crumble, compromising the administration of the correct dose and, therefore, the efficacy and safety of the treatment. This procedure may lead to serious consequences when the drug contained in these medications has a narrow therapeutic range.⁹ Tahaineh & Gharaibeh⁷ demonstrated that cutting a digoxin tablet into two may result in halves of uneven weight, increasing the toxicity risk.

For Verrue et al,⁹ when it is necessary or unavoidable to cut a pill, as occurs when the dose prescribed is not commercially available or when there is no alternative formulation (e.g. in liquid form), the use of pill cutters is recommended. These authors showed that the variation in weight obtained using a pill cutter is lower than that when a knife is used. Auricchio et al¹ evaluated the atenolol content in grooved pills divided using a pill cutter and a kitchen knife and did not find significant differences in the levels of active ingredients in the parts obtained after cutting the pills using a kitchen knife or a pill cutter, although cutting the pill in half produced less dispersion of content in the fragments than cutting into quarters. However, both the pill cutter and the kitchen knife resulted in fragments with levels of active ingredient above the limit of variation recommended by the Brazilian Pharmacopeia – meaning that one cannot be sure of the dose received every time one takes the medication, when compared with content obtained in the whole pills. This indicates that when the pill is divided the patient will receive a dose of medication

outside the acceptable limit, posing a risk of compromising the efficacy of the treatment.

Modified methods of release are designed to gradually be released into the body, or at a different time when compared with instant release medications, even after being taken. Gastro-resistant medications, i.e., those with delayed release, were developed to resist digestive fluids and release the medication in the intestine.⁸ They have an enteric coating to protect acid-labile medicines from the action of digestive fluids or isolate those which irritate the digestive tract. Cutting this type of medication may mean it loses efficacy or may increase the risk of adverse effects.

Modified release methods, designed to gradually release the drug into the body are often represented by abbreviations accompanying the trade name of products in packaging, such as ER, XR, XL (= Extended Release), CD (= Controlled Delivery), LA (= Long Action); PA (= Prolonged Action) and SR (= Slow Release). Taking this type of medicine with a cracked or destroyed casing will mean the active ingredient is released rapidly and consequently the absorption of a higher dose than that desired or prescribed, exposing the user to the risk of overdose which could, depending on the medication and on the characteristics of the patient, prove fatal. For this reason, medications with modified release systems should not be divided, crushed, ground, dissolved or chewed. The coating of such products prevents dissolution in the upper digestive tract, delaying it until the still intact pill reaches the alkaline medium of the small intestine. An exception to the rule is Donaren® Retard,^b a slow release pill which contains the anti-depressant trazodone and has fold allowing it to be divided into three. Even in this case, the user should be advised not to crush the pill.

In the face of the above-mentioned restrictions, the indiscriminate and growing use of pill organizers and pill cutters takes on a worrying character, especially when it is considered that this study does not entirely cover – but simply casts a critical eye on – the limitations associated with the use of these tools. These devices, unregulated and commercially available, should be accompanied with instructions which encourage correct use, such as recommending that a health care professional be consulted with regard to the safe use of these devices according to the individual's treatment. For these recommendations to be successful, it would be important for health care professionals to be aware and conscious of the restrictions on the use of these devices in order to guide users correctly.

⁸Ministério da Saúde. Agência Nacional de Vigilância Sanitária. Resolução RDC nº 31, de 11 de agosto de 2010. Dispõe sobre a realização dos Estudos de Equivalência Farmacêutica e de Perfil de Dissolução Comparativo. *Diário Oficial*. 12 Aug 2010 [cited 2011 Jul 1]:36-8. Available from: http://portal.anvisa.gov.br/wps/wcm/connect/89d63480474597439fb9df3fbc4c6735/RDC_31_2010_Disp%C3%B5e+sobre+a+realiza%C3%A7%C3%A3o+dos+Estudos+de+Equival%C3%Aancia+Farmac%C3%Aautica+e+de+Perfil+de+Dissolu%C3%A7%C3%A3o+Comparativo.pdf?MOD=AJPERES

^bDonaren [Information leaflet]. São Paulo: Apfen.

To conclude, users carrying their medicines around cannot be regarded as an inappropriate practice; this behavior, which begins the moment the medications are dispensed, is a reflection of the reconciliation between independence, being active and looking after oneself which we seek so much to promote. Nor can the practice of dividing pills be halted, although it is undesirable, inappropriate and often resisted, it is a

necessary practice if some dosage regimes are to be followed. It is, however, possible to observe, monitor, study and intervene with both users and professionals to make these behaviors more appropriate and avoid the risks related to them. If the aging population and increased life expectancy leads to increased use of health services and medicines, these are the challenges which will increasingly have to be confronted.

REFERENCES

1. Auricchio MT, Yano HM, Santos AP, Bugno A. Avaliação do teor de Atenolol em comprimidos divididos com faca caseira e aparelho cortador. *Acta Paul Enferm.* 2011;24(1):74-9. DOI: <http://dx.doi.org/10.1590/S0103-21002011000100011>
2. Bangsberg DR, Deeks SG. Is average adherence to HIV antiretroviral therapy enough? *J Gen Intern Med.* 2002;17(10):812-3. DOI: <http://dx.doi.org/10.1046/j.1525-1497.2002.20812.x>
3. Borja-Oliveira CR. Atenção ao idoso no domicílio: o enfoque da farmácia. In: Domingues MA, Lemos NR, editores. *Gerontologia: os desafios nos diversos cenários de atenção.* São Paulo: Manole; 2010.
4. Clark RL, Antonello JM, Grossman SJ, Wise LD, Anderson C, Bagdon WJ, et al. External genitalia abnormalities in male rats exposed in utero to finasteride, a 5 alpha-reductase inhibitor. *Teratology.* 1990;42(1):91-100. DOI: <http://dx.doi.org/10.1002/tera.1420420111>
5. Corsonello A, Pedone C, Lattanzio F, Lucchetti M, Garasto S, Carbone C, et al. Regimen complexity and medication nonadherence in elderly patients. *Ther Clin Risk Manag.* 2009;5(1):209-16. DOI: <http://dx.doi.org/10.2147/TCRM.S4870>
6. Prahalada S, Tarantal AF, Harris GS, Ellsworth KP, Clarke AP, Skiles GL, et al. Effects of finasteride, a type 2 5-alpha reductase inhibitor, on fetal development in the rhesus monkey (*Macaca mulatta*). *Teratology.* 1997;55(2):119-31. DOI: [http://dx.doi.org/10.1002/\(SICI\)1096-9926\(199702\)55:2<119::AID-TERA1>3.0.CO;2-Z](http://dx.doi.org/10.1002/(SICI)1096-9926(199702)55:2<119::AID-TERA1>3.0.CO;2-Z)
7. Tahaine LM, Gharaibeh SF. Tablet splitting and weight uniformity of half-tablets of 4 medications in pharmacy practice. *J Pharm Pract.* 2012;25(4):471-6. DOI: [10.1177/0897190012442716](http://dx.doi.org/10.1177/0897190012442716)
8. Ukwe CV, Ekwunife OI, Udeogaranya OP, Iwuamadi UI. Self-reported adherence to HAART in South-Eastern Nigeria is related to patients' use of pill box. *SAHARA J.* 2010;7(1):10-5. DOI: <http://dx.doi.org/10.1080/17290376.2010.9724950>
9. Verrue C, Mehuys E, Boussey K, Remon JP, Petrovic M. Tablet-splitting: a common yet not so innocent practice. *J Adv Nurs.* 2011;67(1):26-32. DOI: <http://dx.doi.org/10.1111/j.1365-2648.2010.05477.x>

The author declares that there are no conflicts of interests.