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Oral drugs at a hospital unit: adequacy for use via enteral feeding tubes

Medicamentos orais de uma unidade hospitalar: adequação ao uso por cateteres enterais

Medicamentos orales de una unidad hospitalaria: adecuación al uso utilizando sondas gástricas

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ABSTRACT

Objective: to describe the profile of standardized oral drugs at a hospital unit and assess their adequacy for use via enteral feeding tubes, according to recommendations from the literature. **Method:** descriptive study, with data on drugs collected from the Pharmacy Service Dispensing System. Specific recommendations for the use of these drugs via enteral feeding tubes were found after searches in literary databases, books, manuals, guidelines and package insert collections. **Results:** among the 236 dispensed oral drugs, 86% were in solid form; of those, 32 were "non-crushable", with the liquid form available at the institution. Twenty-eight drugs with potential interactions with enteral nutrition were identified. Sixty percent of those presented specific recommendations on their administration via enteral feeding tube. **Conclusion:** the joint participation of multidisciplinary nutritional therapy and care teams and the implementation of programs for continuous training are suggested strategies for the prevention of potential problems in the administration of drugs in the hospital setting.

Descriptors: Pharmaceutical Preparations; Catheters; Enteral Nutrition; Food-drug Interaction; Patient Safety.

RESUMO

Objetivo: descrever o perfil de medicamentos orais padronizados em uma unidade hospitalar e verificar sua adequação quanto ao uso por cateteres enterais, de acordo com recomendações da literatura. **Método:** estudo descritivo, com dados sobre medicamentos coletados do Sistema de Dispensação do Serviço de Farmácia. As recomendações específicas para uso de tais medicamentos por cateteres enterais foram obtidas após busca em bases literárias, livros, manuais, *guidelines* e bulários. **Resultados:** dos 236 medicamentos orais dispensados, 86% estavam na forma sólida; destes, 32 eram "não trituráveis", havendo disponibilidade da forma líquida na instituição. Foram identificados 28 medicamentos com potenciais interações com a nutrição enteral. Sessenta porcento deles apresentavam recomendações específicas sobre sua administração por cateter enteral. **Conclusão:** a participação conjunta das equipes multidisciplinares de terapia nutricional e de assistência e a implementação de programas para treinamento contínuo constituem estratégias sugeridas para a prevenção de potenciais problemas na administração de medicamentos no espaço hospitalar.

Descritores: Preparações Farmacêuticas; Cateteres; Nutrição Enteral; Interação Alimento-Droga; Segurança do Paciente.

RESUMEN

Objetivo: describir el perfil de medicamentos orales estandarizados en una unidad hospitalaria y verificar su adecuación respecto del uso vía sondas gástricas, según recomendaciones de la literatura. **Método**: estudio descriptivo, con datos sobre medicamentos recolectados del Sistema de Dispensación del Servicio de Farmacia. Las recomendaciones específicas de uso por sondas gástricas fueron obtenidas por búsqueda en bases de literatura, libros, manuales, *guidelines* y vademécums. **Resultados**: De los 236 medicamentos orales dispensados, 86% se presentaban en forma sólida; de ellos, 32 eran "no triturables", existiendo disponibilidad de la forma líquida en la institución. Fueron identificados 28 medicamentos con potenciales interacciones con la nutrición enteral. El 60% incluía recomendaciones específicas sobre administración por sonda gástrica. **Conclusión**: la participación conjunta de equipos multidisciplinarios de terapia nutricional y de atención y la implementación de programas de capacitación

permanente constituye estrategias sugeridas para prevenir potenciales problemas en administración de medicamentos en el ámbito hospitalario.
Descriptores: Preparaciones Farmacéuticas; Catéteres; Nutrición Enteral; Interacción Alimento-Droga; Seguridad del Paciente.

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INTRODUCTION

Drug preparation and administration are very important daily practices in hospital institutions. Patients under enteral nutrition through enteral feeding tubes frequently receive medication via those devices, since it is a more physiological method. However, it is not free of complications. Drug administration via enteral feeding tubes often disregards the products' license terms, with implications for workers involved in the prescription, dispensation and administration of the substance, making them responsible for any adverse events that might happen. For example, when tablets are crushed before administration, the manufacturer is no longer liable for any adverse events that happen[1]. Moreover, errors in the crushing process may cause tube obstruction, drug contamination, changes or inactivation of the desired effects of the drug or nutrient, possibly compromising the enteral nutrition therapy and the effectiveness and safety of the pharmacological therapy[2].

Although literature presents evidences of benefits in the administration of oral drugs via enteral feeding tubes[3], in order to correctly conduct this process without harming patients, it is necessary that all institutions have qualified and trained multi-professional teams[4]"publisher-place":"Belo Horizonte","genre":"Monografia de especialização em farmácia clínica e serviços de saúde","event-place":"Belo Horizonte","abstract":"As diversas desvantagens da administração de medicamentos juntamente com Nutrição\nEnteral (NE for the discussion and standardization of technical and care procedures, which should be adapted to the new practices, and the adoption of new knowledge.

Critical analysis of therapy options available at Brazilian hospitals, as well as possible issues associated with administration via enteral feeding tubes, may contribute to the improvement of techniques that are adequate and safe for patients.

OBJECTIVE

This study aimed to describe the profile of oral drugs used at an infectious disease hospital unit and assess their adequacy for use via enteral feeding tubes.

METHOD

Ethical aspects

According to standards and guidelines of Resolution No. 466/12 of the Brazilian National Health Council[5], because of the adopted method, this study was exempt from appreciation by the research ethics committee of the institution.

Design, study location and period

This is a descriptive, exploratory study conducted at the Evandro Chagas National Institute of Infectious Diseases – Fiocruz, a reference hospital unit for the treatment of infectious diseases, located in the city of Rio de Janeiro. Data on drugs were collected from the Computer Dispensing System and from the Drug Storage Control of the Pharmacy Service, considering the hospital formulary oral drugs dispensed for hospitalized patients between January 211 and January 2013.

Sample and inclusion and exclusion criteria

Drugs were selected and included in the study according to the average quantity of units dispensed monthly (average monthly consumption, AMC). The authors opted to exclude oral drugs with zero dispensation in the described period. After selection, drugs were organized according to the Anatomical Therapeutic Chemical classification system of World Health Organization (ATC – WHO)[6], and each drug presentation characteristics were described, such as dosage forms and pharmaceutical formulation.

Study protocol

Based on drugs previously identified, we conducted a bibliographical review in the databases Medline, Lilacs and Scielo, using the following terms: enteral nutrition and drugs; enteral feeding tube and drug administration; drugs and enteral feeding tube. Selection criteria included articles, essays and theses published in Portuguese, English and Spanish, with abstracts available at the aforementioned databases and published between 1999 and 2013; that addressed drug preparation and administration via enteral feeding tubes in adults. Drug descriptions were analyzed through the electronic package insert collection of the National Health Surveillance Agency (ANVISA)[7], as well as dissertations available at MICROMEDEX[8], books, manuals from other health institutions[9–11] and guidelines from international societies[12-13].

Analysis of results and statistics

Drugs selected by AMC were described according to therapeutic class and dosage form. Based on a literature review, solid oral drugs that could be switched for liquid dosage forms, solid drugs that could not be crushed, drugs with potential interaction with enteral nutrition and drugs whose preparation and administration methods were different from others were identified. These data were entered in a Microsoft® Office Excel 2007 spreadsheet and descriptively analyzed.

RESULTS

A final list was obtained from the compilation that derived from the list of hospital formulary drugs. That final list contained 236 drugs dispensed to the hospital center in the two-year period. Considering level one in the ATC classification, 12 different drugs classes were found (Figure 1).

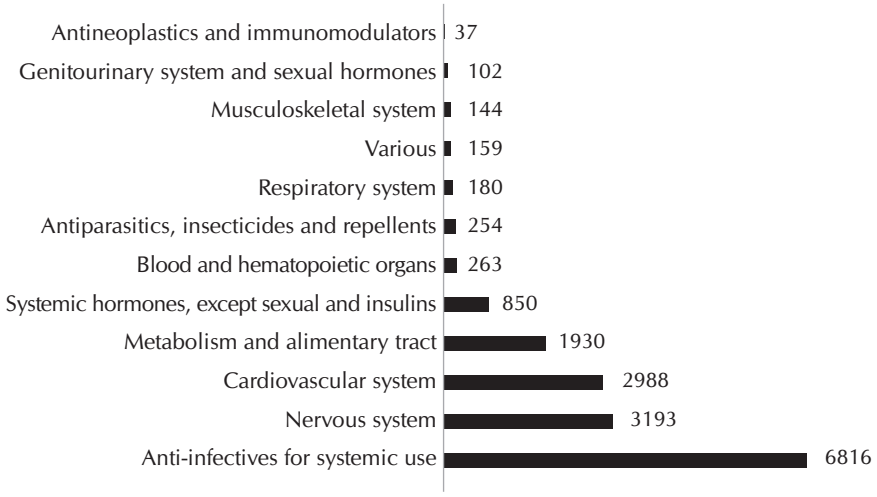

Figure 1 – Average monthly consumption of oral drugs used at the hospital center of Evandro Chagas National Institute of Infectious Diseases, classified according to the 1st level of the Anatomical Therapeutic Chemical classification, Rio de Janeiro, Brazil, January 2011 – January 2013

Anti-infective drugs for systemic use, drugs that act on the nervous system, on the cardiovascular system and on metabolism and alimentary tract were the classes with the highest AMC, encompassing 88% of total dispensed units. Anti-infective drugs for systemic use was the most frequent class and, within that class, antiretrovirals can be highlighted, with approximately 60% of AMC. Tuberculosis drugs also stood out, such as isoniazid pyrazinamide and ethambutol, comprising 15.2% of the anti-infectives for systemic use class.

The class of drugs that act on the nervous system was responsible for approximately 19% of total dispensed units and, inside that class, antiepileptics (37.4%) and anxiolytics (27.3%) stood out. Drugs that act on the cardiovascular system had 18% of AMC; of those, 59% were inhibitors for angiotensin converting enzyme.

Regarding dosage forms, 86% (204) of dispensed drugs were solid. Of those, 17% were available in liquid form at the institution, 11% were available in Brazil's pharmaceutical market, with the remaining 147 solid drugs with no liquid form version. Ten drugs in liquid pharmaceutical form or in powder for oral suspension had AMC equal to zero.

According to the researched literature, 15% (31) of dispensed drugs were classified as "non-crushable", therefore, they should not be administered via enteral feeding tubes (Table 1)

Twenty-eight drugs were found to have a potential interaction with enteral feeding (Table 2).

Table 1 – Solid non-crushable drugs dispensed to the hospital center of Evandro Chagas National Institute of Infectious Diseases, Rio de Janeiro, Brazil, January 2011 – January 2013

Solid drugs	Concentration	Dosage form
Albendazole	400 mg	Chewable tablet
Bisacodyl	5 mg	Dragee
Scopolamine butylbromide	10 mg	Dragee
Cephalexin	500 mg	Dragee
Potassium chloride	600 mg	Dragee
Bupropion hydrochloride	150 mg	Sustained release tablet
Socycycline hydrochloride	100 mg	Dragee
Hydralazine hydrochloride	25 mg	Dragee
Hydralazine hydrochloride	50 mg	Dragee
Imipramine hydrochloride	25 mg	Dragee
Ondansetron hydrochloride	4 mg	Orally disintegrating tablet
Paroxetine hydrochloride	20 mg	Coated tablet
Tramadol hydrochloride	100 mg	Sustained release tablet
Diclofenac potassium	50 mg	Dragee
Didanosine	250 mg	Capsule with sustained release granules
Didanosine	400 mg	Capsule with sustained release granules
Efavirenz	600 mg	Coated tablet
Isosorbide dinitrate	10 mg	Tablet
Isosorbide dinitrate	5 mg	Sublingual tablete
Itraconazole	100 mg	Capsule
Ivermectin	6 mg	Tablet

To be continued

Table 1 (concluded)

Solid drugs	Concentration	Dosage form
Dexchlorpheniramine maleate	2 mg	Tablet
Nifedipine	10 mg	Capsule
Nifedipine	20 mg (retard)	Sustained release tablet
Omeprazole	20 mg	Capsule with gastro-resistant granules
Pentoxifylline	400 mg	Sustained release tablet
Rifampicin	300 mg	Capsule
Sulfamethoxazole + Trimethoprim	400 + 80 mg	Tablet
Sulfamethoxazole + Trimethoprim	800 + 160 mg	Tablet
Tenoxicam	20 mg	Coated tablet
Theophylline	200 mg	Capsule with sustained release granules
Vitamin B12 + vit B6 + vit B2 + vit B1	5.000 mcg + 100 mg + 100 mg	Dragee

Note: vit = vitamin.

Table 2 – Drugs with a potential interaction with enteral nutrition dispensed to the hospital center of Evandro Chagas National Institute of Infectious Diseases, Rio de Janeiro, Brazil, January 2011 – January 2013

Drugs	Interaction type
Atenolol Captopril Carbamazepine Cephalexin Metoclopramide hydrochloride Efavirenz Flunitrazepam Furosemide Isosorbide Levodopa + cabidopa Levofloxacin Levothyroxine Norfloxacin Ritonavir	Absorption diminishing or augmentation
Isoniazid Isoniazid + rifampicin Isoniazid + rifampicin + pyrazinamide + ethambutol chloride Itraconazole Metronidazole Pyridoxine (vitamin B6) Rifampicin Saquinavir Atazanavir Sulfate Warfarin	Bioavailability diminishing or augmentation
Digoxin Phenytoin Posaconazole	Serum concentration diminishing or augmentation
Chlorpromazine	Precipitation by incompatibility

Variations in preparation techniques and drug administration via enteral feeding tubes were observed for 16 drugs (Table 3).

Table 3 – Drugs with variations in preparation techniques and administration via enteral feeding tubes dispensed to the hospital center of Evandro Chagas National Institute of Infectious Diseases, Rio de Janeiro, Brazil, January 2011 – January 2013

Drugs	Variations in preparation and administration via enteral feeding tube
Valproic acid Allopurinol Lactulose Lopinavir + ritonavir Dexchlorpheniramine maleate Nitrofurantoin Calcium polystyrene sulfonate	Increase in water volume for dilution and irrigation of tube after administration
Clarithromycin Tizanidine hydrochloride Fluoxetine Rifabutin	Immediate administration to avoid drug degradation
Captopril Ciprofloxacin Aluminium hydroxide Levodopa + carbidopa Levofloxacin Metronidazole Rifampicin Saquinavir	Prolonged pause of enteral nutrition before and/or after drug administration

DISCUSSION

In this study, anti-infective drugs for systemic use was the most dispensed class and, within that class, antiretrovirals such as lamivudine, tenofovir and lopinavir + ritonavir. The type of

institution where the research took place may have influenced this predominance, since the majority of patients was HIV-positive and under treatment with multiple drugs. Drugs used in the treatment of coinfections in HIV-positive patients also had a high level of consumption, such as isoniazid, pyrazinamide and ethambutol, for prophylaxis and treatment of tuberculosis. This reflects the patients' epidemiological profile, in which tuberculosis is an important and frequent coinfection[14].

The considerable dispensation of drugs that act on the central nervous system is possibly justified by the direct action of HIV, opportunistic manifestations that affect the central nervous system, chronicity and severity of the disease, anatomical effects caused by treatment (such as lypodistrophia) and social and emotional limitations[14].

Drugs that act on the cardiovascular system came in third in number of dispensed units, which is consistent with the institution's profile, since patients may develop metabolic disturbances due to antiretroviral drugs use[14], in addition to the use of these drugs in the treatment of Chagas disease carriers, who frequently seek care in the institution.

Concerning identified dosage forms, 86% of dispensed drugs were solid. Similar results were found in a large general hospital in the state of Minas Gerais, where 95% of available oral drugs at the hospital pharmacy were solid[3]. Studies that analyzed patterns in drugs prescriptions for patients with enteral feeding tubes demonstrated a trend of prescribing solid drugs in the dosage form of simple tablets for administration via enteral feeding tubes[15-16]. It is important to emphasize that a large part of simple tablets can be administered via enteral feeding tubes if they are prepared correctly because, when it comes to administering tablets by this via, not only the dosage form should be observed, but also the physical-chemical characteristics of the drugs' active principle.

The small quantity of drugs in liquid dosage form is a complicating factor for drug preparation and administration via tubes, since this is the dosage form indicated in literature as the most adequate in drug therapy for patients[12].

A higher availability of liquid dosage form at the institution could benefit not only patients under enteral nutrition therapy but also those who complain of dysphagia, odynophagia and patients with megaesophagus, which are common conditions in that hospital.

Findings related to solid drugs available in liquid dosage form at the institution or in the Brazilian pharmaceutical market and that, therefore, represented a better option for patients with enteral feeding tubes, in addition to the observation that there were 10 drugs in liquid or powder dosage forms for oral suspension that had AMC equal to zero which were dispensed in solid dosage form may demonstrate lack of knowledge from prescribers regarding availability of these drugs at the institution's pharmacy or communication problems among sectors. Participation of a multidisciplinary team for nutritional therapy is crucial for analyzing prescriptions, which would enable interventions from medical, nursing, pharmacy and nutrition teams.

The literature shows that problems when choosing the best dosage form for patients under enteral nutrition therapy are frequent. A study conducted in the intensive care unit of a university hospital in Puerto Rico[17] showed that, among 115 drugs administered via enteral feeding tubes, 43.5% were considered wrongly administered. The study included, among other errors, the administration of solid drugs also available in liquid dosage form. In Brazil, a study in intensive care units of seven university hospitals identified potential drug-nutrient interactions in 6.3% (20) to 7.7% (39) of patients under enteral feeding tube nutrition, at 24 hours and 120 hours of hospitalization, respectively. The drugs that were most frequently involved in interactions were hydralazine, phenytoin, Levothyroxine and warfarin. The last three have narrow therapy indexes, which shows the clinical relevance of their monitoring[18].

Studies show that approximately 25% of educational interventions about the best therapeutic choice for patients under enteral nutrition, instruct the medical team about the availability of liquid dosage forms of prescribed drugs[4,17]"publisher-place":"Belo Horizonte","genre":"Monografia de especialização em farmácia clínica e serviços de saúde","event-place":"Belo Horizonte","abstract":"As diversas desvantagens da administração de medicamentos juntamente com Nutrição\nEnteral (NE. Nurses take on the fundamental role of planning drugs scheduling and diet; thus, becoming crucial in the prevention of potential interactions. However, errors might occur at all stages, from prescription until drug administration to the patient, which demands actions based on a multidisciplinary perspective[18].

In this study, 60% of drugs with higher AMC had specific documented recommendations regarding their administration via enteral feeding tubes. However, a bibliographical review showed that there are still gaps in national recommendations about drug preparation and administration via enteral feeding tubes, even on their prescription package inserts. Important information such as osmolality of liquid drugs was also observed. Most of the information available comes from research conducted in other countries.

Use of non-crushable drugs via enteral feeding tubes is also described in other studies[19]. Contraindications for crushing take into consideration dosage form (oral dispersion tablets, dragees, sustained release tablets and effervescent) and the specific characteristics of each drug (i.e., paroxetine hydrochloride and efavirenz, whose coating can obstruct the tube)[1]. Some, despite not having specific information, such as "do not open" or "do not crush", are used via enteral feeding tubes based on evidence; such as the case of acetylsalicylic acid in the treatment of acute myocardial infarction[3].

Measures that prevent these types of errors include verification of availability of liquid dosage forms, administration route swap, temporary suspension of drugs and even their substitution[3,17]. Some authors suggest labeling the packaging of non-crushable drugs with figures expressing the prohibition of crushing and the message "DO NOT CRUSH" as preventive measures[19-20].

Another relevant study result was the finding that approximately 12% (28) of dispensed oral drugs had a potential interaction with enteral nutrition. Drugs with a possible interaction with enteral nutrition were also detected in other studies conducted in Brazilian general hospitals, however, varying from 12.5% (6) to 47.7% (62) of assessed drugs[4]"publisher-place":"Belo Horizonte","genre":"Monografia de especialização

em farmácia clínica e serviços de saúde",",event-place":"Belo Horizonte",",abstract":"As diversas desvantagens da administração de medicamentos juntamente com Nutrição\nEnteral (NE.

Drug-nutrient interactions can compromise therapeutic effects and impact patients' nutritional status; therefore, as soon as they are identified, feasible strategies must be considered to avoid them.

Necessary adjustments in preparation techniques and administration of 16 drugs included: increase in water volume for dilution and irrigation of the tube after drug administration, immediate administration and longer periods of pause of enteral nutrition, with the aim of, according to the active principle, maintain its stability, guarantee effectiveness and the correct dilution to avoid occlusion of tube and interaction with enteral nutrition. Solid drugs that have low water solubility or liquid drugs with high osmolality require higher water volume for uniform dilution; the stability of these drugs after preparation for administration via tubes is seldom discussed in literature.

Increase in the pause period is not always possible in clinical practice due to factors such as high number of prescribed drugs at different times and patients' nutritional status. At the institution under study, for example, patients under enteral nutrition therapy generally presented a compromised clinical and nutritional status, and enteral nutrition was administered via infusion pump for periods of 20 to 24 hours, since patients do not tolerate infusion rates above 85 mL/h. Therefore, participation of a multidisciplinary team for nutritional therapy is crucial for decision-making, seeking the best harmonization between nutritional and pharmacological therapies.

Study limitations

One could assume as a limitation of this study that the drugs data were obtained from information of the dispensation pharmacy service makes it impossible to know which proportion of these drugs were effectively administered via enteral feeding tubes.

It is also worth emphasizing that since it is a public institution, where drugs are purchased via government procurement, and these do not always result in purchases of the same brands of drugs, there might be possible variations on dosage forms and, consequently, on preparation and administration.

Contributions for the health field

The authors of this study hope it can contribute to the Brazilian scientific production concerning the safety of drug therapy, providing a data compilation that is critically assessed for use by health workers, especially for nursing workers, who are an active part of this process, in clinical practice, in the design of institutional protocols, as well as in fostering new research in the area.

CONCLUSION

In this study, conducted at a hospital unit for infectious diseases in Rio de Janeiro, anti-infectives for systemic use was the most dispensed drug class, followed by those that act on the nervous and cardiovascular systems. Taking into consideration dosage form, solid drugs were the most dispensed, although approximately 30% of them were available in liquid form, considered the most adequate for use via enteral feeding tubes.

Through critical analysis of these drugs, from the perspective of their administration via enteral feeding tubes and with scientific evidence available in literature, it was possible to observe that many dispensed drugs require a specific technique for preparation and administration, depending on the drugs' characteristics, such as their dosage forms, possibility or lack of possibility of crushing and possible incompatibilities when administered simultaneously with an enteral diet. The non-observance of these characteristics can harm pharmacological and nutritional therapy.

Thus, the importance of multi-professional groups such as multi-disciplinary teams for nutritional therapy is emphasized at all stages of the process of administering drugs via enteral feeding tubes. In this perspective, it is also worth emphasizing the need for a continuous training program with the goal of offering workers knowledge that enable a safe and rational practice, consistent with good practices for drugs preparation and administration.

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