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Quantitative analysis of drug losses administered via nasogastric tube – In vitro study

Adriana Ruzsíková [a,b], Lenka Součková [a,c], Pavel Suk [a,c], Radka Opatřilová [d], Martina Kejdušová [d], Vladimír Šrámek [a,c,*]

[a] Department of Anaesthesiology and Intensive Care, St. Anne's University Hospital Brno, Brno, Czech Republic
[b] International Clinical Research Center, St. Anne's University Hospital Brno, Brno, Czech Republic
[c] Faculty of Medicine, Masaryk University, Brno, Czech Republic
[d] Faculty of Pharmacy, University of Veterinary and Pharmaceutical Sciences Brno, Brno, Czech Republic

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ABSTRACT

Purpose: Drug administration through nasogastric tube (NGT) is a standard practice but the real amount of the delivered drug is unknown. Therefore, we designed a study to determine the losses of various dosage forms administered by different methods through NGT.
Methods: In vitro model was used. Five different administration methods (A–E) and six dosage forms (simple compressed tablets – T/S; film coated tablets – T/FC; enteric coated tablets – T/EC; capsules with powder filling – C/P; capsules containing extended release pellets – C/ER; capsules containing gastro-resistant pellets – C/GR) were investigated. Measurement was repeated six times for each drug-method combination. The overall losses were determined by gravimetry. In method A partial losses associated with each step of drug administration were also determined.
Results: Significant drug losses were measured (4–38%). Only methods A (crushing–beaker–syringe–water–NGT) and B (crushing–water–syringe–NGT) were suitable for administration of all tested dosage forms. Method B proved the most effective for all kinds of tablets and C/GR ($p < 0.05$) and tended to be more effective also for C/ER ($p = 0.052$) compared to method A. C/P showed minimal losses for both tested methods (B and E). Flushing of the drug through NGT causes major losses during drug administration compared to crushing and transfer ($p < 0.05$). All methods for intact pellets (C–E) were found inappropriate for clinical practice due to NGT clogging.
Conclusions: Choosing a suitable administration method can significantly affect the amount of drugs delivered through NGT.

1. Introduction

Enteral feeding is the preferred route of nutrition in ICU patients (Kreymann et al., 2006). The frequent inability to swallow necessitates insertion of the orogastric or more frequently nasogastric tube (NGT) into the stomach (National Collaborating Centre for Acute Care (UK), 2006). However, many obstacles can hamper adequate delivery of medications to the gastrointestinal tract and their absorption when NGT is used – e.g., crushing and dissolving of the tablets can lead to significant losses. Furthermore, not all oral dosage forms are suitable for administering via NGT (e.g., slow release tablets, enteric coated tablets and irritating drugs) (Gilbar and Pract, 1999; Zhu and Zhou, 2013). Impaired stomach emptying, gut mucosa damage, intestinal and splanchnic hypoperfusion are further factors which can reduce drug bioavailability (Clarke, 2008; Gilbar and Pract, 1999; Součková et al., 2013). In practice, all these aspects result in a limited drug administration into gastrointestinal tract (do Nascimento et al., 2012).

From the vast spectrum of drugs administered via NGT in ICU patients, only the bioavailability of proton pump inhibitors (PPI) was extensively studied comparing intravenous versus gastric routes (Olsen and Devlin, 2008; Täubel et al., 2001), administration via NGT versus *per os* (Sostek et al., 2003) and evaluating modifications of NGT administration (Freston et al., 2004; Tsai et al., 2000).

Ponrouch et al. investigated in vitro the impact of various technical parameters on availability of four PPIs in pediatric

* Corresponding author at: Department of Anaesthesiology and Intensive Care, St. Anne's University Hospital Brno, Brno, Czech Republic.
Tel.: +420 543 182 552; fax: +420 543 182 555.
E-mail address: vladimir.sramek@fnusa.cz (V. Šrámek).

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practice. They found that diameter and type of PPI but not the length of the NGT influence the recovery of the active drug at the end of NGT (Ponrouch et al., 2010).

Devlin et al. also found a big difference between various PPIs and their forms in drug effectivity. The results were not influenced by nurse experience (Devlin et al., 2006).

Data on other drugs except of PPIs are limited. In an elegant combined in vitro and clinical study, Kotake et al. found that up to 30% of amiodarone is lost during drug administration via NGT (Kotake et al., 2006).

As adequate data on drug losses during preparation for NGT administration are lacking, we designed an in vitro study assessing the impact of dosage form and way of preparation on drug losses when administered via NGT.

2. Materials and methods

The whole experiment was performed by one investigator (1st author of the manuscript) using an in vitro model. All medications passed through 14F (i.e., 4.7 mm outer and 3.0 mm inner diameters, respectively) feeding tube (Medicoplast, Germany) mounted to a ring stand in 30° angle to mimic the most often ICU patient position. Measurement was repeated six times for each combination of drug and method. During drug administration to the tube, the mixture of water and the drug in the syringe was constantly shaken to prevent sticking of the drug particles to the inner walls of the syringe as much as possible. The flushed mixture of the drug and water was collected in an evaporating basin at the end of NGT and evaporated to dryness. The losses were determined by gravimetry (difference between the initial drug weight and the weight of drug following passing the NGT and evaporation). Ohaus Explorer E12145 analytical scales with accuracy of four decimal positions were used for gravimetric measurements.

Six different dosage forms were tested:

- T/S – simple compressed tablet (sotalol, Sotahexal®, Hexal AG, Germany).
- T/EC – tablet with enteric coating (pantoprazole, Controloc®, Takeda, Germany).
- T/FC – simple film-coated tablet (clopidogrel, Trombex®, Zentiva, Czech Republic).
- C/P – capsule with powder filling (lactobacilles, Lacidofil®, Institut Rosell, France).
- C/ER – capsule containing extended-release pellets (theophylline, Euphyllin CR N 300®, Nycomed, Germany).
- C/GR – capsule with gastro-resistant pellets (omeprazole, Helicid®, Zentiva, Czech Republic).

Following administration techniques were used: methods A and B were used for tablets (T/S, T/EC, T/ES), methods B and E were used for capsules with powder filling (C/P), and all methods for capsules with pellets (C/ER and C/GR).

2.1. Method A (crushing–beaker–syringe–water–NGT)

Technique consisted of further steps: crushing the tablets or pellets in a mortar, transferring the crushed powder into a beaker, transferring crushed powder from the beaker to a syringe, adding water (15 ml) into the syringe, mixing the solution in the syringe, injecting the mixture into NGT and flushing the tube with water (5 ml). This method was not used for capsules with powder filling (C/P). For this method, drugs were weighted after each step of administration to define its specific contribution to the overall loss.

2.2. Method B (crushing–water–syringe–NGT)

Tablets and pellets were crushed in a mortar, in case of the capsules containing powder, the powder was poured out into the mortar. Water (10 ml) was added to the mortar and the crushed powder was mixed with water, the mixture was drawn into a syringe, then it was injected into NGT. After injection, additional 10 ml of water were poured into the mortar, the solution was drawn in the syringe and the tube was flushed with the solution.

2.3. Method C (pellets–beaker–NGT–water)

Pellets were poured from the capsule into a small beaker with a spout. The pellets were then slowly poured from the beaker to NGT. After that, the tube was flushed with 20 ml of water.

2.4. Method D (pellets–NGT–water)

Pellets were poured from the capsule right into NGT. The tube was flushed with 20 ml of water.

2.5. Method E (pellets–syringe–water–NGT)

Pellets were poured into a syringe, water added, mixture was shaken and injected into NGT.

2.6. Statistical analysis

The statistical analysis was carried out using Statistica 11 software (StatSoft Inc., USA). Data are presented as mean and 95% confidence interval. Unpaired *t*-test was used to compare differences between groups, $p < 0.05$ was considered significant.

3. Results

Eighteen combinations of drug and method have been studied. Average losses for methods A and B are shown in Fig. 1. Method B has proven as the most effective for all kinds of tablets (T/S, T/EC, T/FC) and capsules with gastro-resistant pellets (C/GR). Similarly, capsules containing extended-release pellets (C/ER) tended to be more

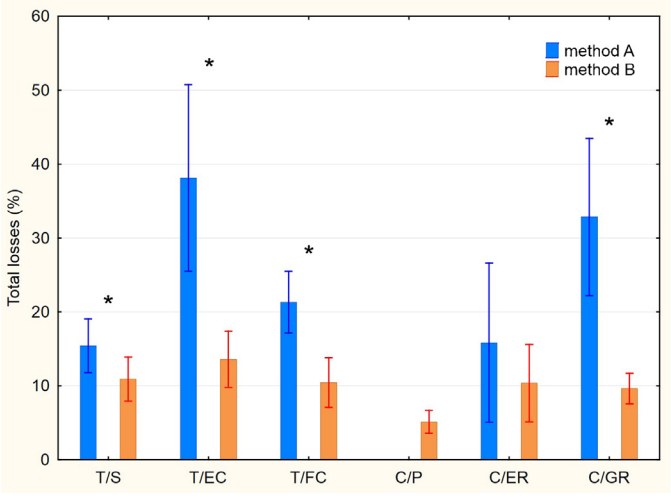

Fig. 1. Total losses (mean and 95% confidence interval) according to dosage form and administration technique by method A (crushing–beaker–syringe–water–NGT) and method B (crushing–water–syringe–NGT). Types of dosage forms: T/S – simple compressed tablet, T/EC – enteric coated tablet, T/FC – simple film coated tablet, C/P – capsule with powder filling (method B only), C/ER – capsule containing extended release pellets, C/GR – capsule containing gastro-resistant pellets. * means $p < 0001$ between methods A and B.