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# Comparative study and optimisation of the administration mode of three proton pump inhibitors by nasogastric tube

D. Messaouik [a], V. Sautou-Miranda [a,b,*], S. Bagel-Boithias [a], J. Chopineau [a,b]

[a] *Service Pharmacie, Hôpital G. Montpied, Rue Montalembert, BP69, 63003 Clermont-Ferrand, France*
[b] *Laboratoire de Pharmacie Clinique et Biotechnique, UFR Pharmacie, Place Henri Dunant, BP38, 63001 Clermont-Ferrand, France*

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**Abstract**

Patients in intensive care often develop stress-induced ulcers. As a preventive measure, proton pump inhibitors (PPIs) are administered by nasogastric tube. However, some PPIs can block the tube. The aim of this study was to compare the behaviour of three PPIs (omeprazole, lanzoprazole and esomeprazole) during the transit of the granules through the tube and to optimise their modes of administration. For each IPP, the experiment was designed to study the influence of four variables: the tube material (silicone or polyurethane), the solvent used to dilute the granules (water or apple juice), the mode of administration (in two or three doses) and the rinse volume (10 or 20 ml). We counted the granules before transit and at the tube outlet, and assayed the active drug ingredient by UV spectrometry. The assay showed complete transit of esomeprazole through the tube, but average losses of omeprazole and lanzoprazole of 39 and 33%, respectively, were observed. No significant improvement was obtained by the variables 'diluent' and 'mode of administration'. The variable 'rinse' had a significant influence. For lanzoprazole, a polyurethane tube allowed recovery of on average 86% of the active ingredient. Esomeprazole is thus the choice PPI for the treatment of patients by nasogastric tube. Using a polyurethane tube and a rinse volume of 20 ml, the administration of lanzoprazole by tube can be considered. Use of omeprazole is not recommended because none of the modes of administration tested ensured that a sufficient concentration of active ingredient reached the stomach.


*Keywords:* Omeprazole; Lansoprazole; Esomeprazole; Nasogastric tube; Granule

## 1. Introduction

Stress-induced gastrointestinal tract bleeding (SGIB) is common in intensive care patients. In such patients, the preventive use of proton pump inhibitors (PPIs) decreases the occurrence of stress-induced ulcers, and reduces the associated mortality. The PPIs, which are sensitive to gastric acid, are formulated to resist breakdown in the stomach and favour intestinal absorption. In general, pharmaceutical suppliers advise against chewing or crushing solid drug forms. However, most patients in intensive care are unable to

* Corresponding author. Tel.: +33 4 73 75 17 63; fax: +33 4 73 75 17 57.
*E-mail address:* vmiranda@chu-clermontferrand.fr (V. Sautou-Miranda).

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swallow. For this reason, PPIs have to be administered by gastric tube after dissolution of tablets or dispersion of granules in water, or in some other solvent, such as fruit juice or sodium bicarbonate solution. PPI formulations supplied in gelatine capsules or in tablets containing stomach acid resistant granules may obstruct tubes.

A number of studies have already been conducted on the administration of omeprazole (Dunn et al., 1999; Larson et al., 1996; McAndrews and Eastham, 1999; Sharma et al., 2000), lansoprazole (Chun et al., 1996; Doan et al., 2001; Dunn et al., 1999; Freston et al., 2001; McAndrews and Eastham, 1999; Sharma et al., 2000) and esomeprazole (Sostek et al., 2003; White et al., 2002) through nasogastric tubes, but none of them sought to evaluate the impact of the different variables involved in the administration of these PPIs (tube material, dilution solvent, administration pattern, rinse volume, etc.). In addition, much published work has been carried out in conditions that are not always applicable in clinical practice. Also, the administration of these three PPIs through nasogastric tubes has never been compared in the same experimental conditions.

We thus set out first to compare the behaviour of these three PPIs when administered through nasogastric tubes in experimental conditions as close as possible to clinical practice. Second, we evaluated the influence of different variables on this behaviour, in order to optimise the mode of administration.

## 2. Materials and methods

### 2.1. Drugs and medical materials

Omeprazole (Mopral®) and esomeprazole (Inexium®) were supplied by AstraZeneca and lansoprazole (Ogast®) by Takeda. The omeprazole and lansoprazole were formulated in gelatine capsules containing gastroresistant granules. The esomeprazole was formulated in tablets of gastroresistant granules. The granules were dispersed in apple juice or natural mineral water, and injected into the nasogastric tube using a 60 ml blunt cannula syringe (Becton Dickinson).

Two types of 16 French gauge gastroduodenal tubes were used: polyurethane tubes (Salem type, length 120 cm, internal diameter 3.8 mm, Rüsch-Pilling) and silicone tubes (Levin type, length 125 cm, internal diameter 3 mm, Vygon).

The solvents and tubes used in our experiments were chosen to correspond as closely as possible to those commonly used in intensive care for the administration of medication by nasogastric tube. Apple juice is used less often than water, but much published work (Freston et al., 2001; Chun et al., 1996; Phillips et al., 1996; Tsai et al., 2000) has made use of it for studying the bioequivalence or efficacy of PPIs administered by nasogastric tube.

### 2.2. Study design

We administered the PPI granules through the nasogastric tube positioned, as it would be in a reclining patient. For each PPI a study plan was drawn up to assess the influence of four variables: the 16 French gauge tube material (silicone or polyurethane), the nature of the solvent (water or apple juice), the rinse volume (10 or 20 ml) and the administration pattern ($1\times$ 30 ml or $3\times$ 10 ml). We thus carried out 16 separate experiments (Table 1), each repeated three times.

Before each administration, the tubes were rinsed with the solvent chosen to carry the granules. The granules were then dispersed in the solvent (water or apple juice): for omeprazole and lansoprazole, the contents of each capsule were dispersed in the solvent using a beaker, and the resulting mixture was drawn through a syringe (60 ml blunt cannula syringe); for esomeprazole, the capsule contents were placed in the syringe, the solvent was drawn in, and dispersion was performed by shaking the syringe. After dispersion in the solvent, the granules were injected into the tube. The syringe containing the mixture was always shaken during the administration to prevent granules adhering to the syringe wall. In addition, we maintained a constant injection flow rate to limit tube obstruction. The granules were then recovered in a beaker placed under the end of the tube.

### 2.3. Analysis of samples

The granules collected were analysed to determine whether PPI was lost during transit through the tube. Granules were counted and the active ingredient was assayed. In addition, the granules were examined and measured under a microscope to evaluate their dimensional homogeneity.