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EXPERT OPINION

Drug administration via enteral tubing: an unresolved but increasing challenge

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The number of patients with serious impairments of the swallowing function will continue to increase in the coming decades. Problems related to enteral feeding and drug administration to patients with swallowing issues is a growing concern of physicians, compounding pharmacists and nurses. The lack of information on the impact of compounding by mixing with liquid or food and/or administering through enteral or intestinal feeding tubes on the drug product safety and efficacy is problematic. In addition, there is a lack of appropriate alternative dosage forms of drugs for these routes of administration. As patients with swallowing issues represent a significant and growing patient population that is vulnerable and in need of effective drug therapy, the issue needs urgent attention by all stakeholders involved in healthcare provision. Incremental improvements at the different stages in the process, from product development to the patients' well-being are required to assure safe and effective drug therapy to an important patient population.

Keywords: drug administration, drug modification, drug safety, enteral feeding, swallowing issues

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1. Introduction

Medical and pharmaceutical sciences have made tremendous progress since the early 1960s to combat acute and chronic diseases. The results of this work are very convincing. Since 1970, life expectancy is growing on average by 3 – 4 years every decade [1]. In high-income countries like Germany, for example, this means that the average male life expectancy rose from 67.4 years in 1960 to 78.3 years in 2010, and 72.3 to 83.0 years for females in the same period. Along with this increase in life expectancy, and with the baby boomer generation starting to pass the age of 65 years, the number of older people in the society is increasing. More importantly, the number of people who reach ≥ 90 years is increasing. Age-related diseases such as cancer, cardiovascular diseases, Alzheimer's disease and dementia are expected to increase substantially within the next decades. These diseases are accompanied by age-related functional impairment like the loss in sensory functions and a potential progressing loss in the ability to swallow.

It is estimated that 15 – 40% of people ≥ 60 years currently suffer from dysphagia with substantial implications for the health and quality of life [2]. Dysphagia can be caused by the aging process [2] or as comorbidity in diseases impacting the swallowing process, such as stroke, Alzheimer's disease, Parkinson's disease, dementia, head and neck injuries or neoplastic diseases of the oropharyngeal system [3]. Dysphagia can also be induced by certain medications either through oropharyngeal or oesophageal lesions or through central nervous or neuromuscular adverse drug reactions [4]. Patients with dysphagia are highly likely to develop pneumonia which is a major cause of mortality [5]. They are highly susceptible to dehydration and malnutrition that are involved in several health complications (e.g., falls, delirium, confusion) and the

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development of frailty [6]. Affected patients, however, are very vulnerable and specifically in need of care and effective drug therapy [7]. Several studies have shown that patients with dysphagia, presbyphagia as well as age-related swallowing issues have problems swallowing oral drug products. Hence, combining nutritional intake support and oral drug administration to such patients is logical, as the principles of the problems are the same and could be solved simultaneously.

As a result, modification of oral drug products by tablet crushing or capsule opening and mixing in food or in beverages has become a frequently applied practice in nursing homes to administer medicines to the patients. This happens long before decisions are made that the swallowing issues are severe enough to require the application of enteral or percutaneous feeding tubes to the patients for nutritional and drug administration reasons [8]. The problems associated with this practice are similar and have the same magnitude of safety concerns.

Modifying drug products and dosage forms in a compounding pharmacy has to be done based on the available information about the specific product. The impact of product alterations and intended administration on product stability, compatibility, pharmacokinetics, tolerability and efficacy must be taken into account. However, the available information in product labels often only includes the warning 'do not crush the tablet' without any further details that would allow a good judgement on the risk–benefit. The number of clinical studies published in the scientific literature on the impact of dosage form modification of a specific product and mixing with liquids or food is fairly low. The few clinical studies performed on crushing tablets and suspending in water or mixing with food have shown that such modification can affect safety and efficacy [9,10]. Other studies show that bioavailability remains within the bioequivalence range defined by the regulatory authorities [11].

Looking at this scientific literature it becomes evident that the issues of administering drug therapy to patients with swallowing issues is mainly dealt with by physicians, compounding pharmacists and nurses [12]. Efforts to create awareness of the problem, developing interdisciplinary best practice guidelines and investing in professional training could improve the practice. However, the issue remains critical due to the non-availability of alternative formulations of drug products or missing guidance on drug product modification and administration with food or through enteral tubes.

2. Expert opinion

Patient populations are changing and our options for drug and therapeutic interventions are constantly growing. With the increasing awareness and focus of the regulatory authorities on the efficacy and effectiveness gap [13], the paradigm is shifting from the treatment of a disease to the treatment of a patient with individual characteristics and needs. With increasing life expectancy we will not only see more people who are 65 years and older, but we will also see many more old patients who will present with multi-morbidity and disabilities [14]. Safe and effective swallowing is an important ability for nutritional intake as well as for oral medication administration. Age and age-related disease conditions have a serious impact on swallowing, and the prevalence of swallowing disabilities will further increase. Higher prevalence of patients presenting with malignant swallowing patterns is inevitable in clinical and care practice.

Compounding pharmacists, nurses and physicians recognise the lack of product information and guidance on possible compounding, mixing with food or enteral nutrition and administration through feeding tubes. They also see the lack of appropriate alternative dosage forms. In their efforts to provide best healthcare to the patients with what is available from the pharmaceutical industry, pharmacists have to rely on their broad pharmaceutical science knowledge when making decisions but often have to work outside the legal framework. Discontinuing or changing the drug therapy to another therapeutic drug that is available in a suitable dosage form or which can be safely converted into a form to be mixed with food or administered through feeding tubes should be considered carefully and used only as the last option. Consequently, prescribing physicians, compounding pharmacists and administering nurses will increasingly face the dilemma between their legal obligation to provide best drug therapy to patients and modifying these drug products outside the label claims to enable administration to patients who are unable to swallow.

The provision of drug therapy to patients is a multidisciplinary process which basically starts with the early development of a pharmaceutical product. Quality by design requires that the product is designed to meet the clinical and non-clinical needs of the targeted patients. As old and very old patients are becoming the predominant user group especially for drugs against age-related diseases, the pharmaceutical industry must address these issues in the developmental stages. A variety of pharmaceutical drug delivery technologies exist that provide the flexibility to swallow a dosage form as a whole or to transform the dosage form easily into small distinct particles that can be added to food or administered through enteral feeding tubes safely. For example, small multi-particulates also referred to 'sprinkle formulations' filled in capsules that can easily be opened have been marketed successfully for Parkinson's disease medications. Therefore, it will be critical to involve the medical device industry, pharmaceutical industry, scientists involved in drug product development and regulatory sciences into the necessary multidisciplinary discussion groups. These groups need to build consensus on the various aspects of drug administration and improvements in enteral nutrition required to help patients with swallowing issues.

Declaration of interest

The author has no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

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