USE OF LIQUID PHARMACEUTICAL FORMS AND CORRECT HANDLING OF SOLID FORMS IN THE DYSPHAGIC PATIENT

ABSTRACT

Introduction: The presence of dysphagia is a rather common event, both physiologically in elderly people and the presence of neurological, maxillofacial, or upper digestive pathologies. Many drugs are routinely taken in solid form for the convenience of use, however, in such patients, it becomes difficult to swallow tablets or capsules and it is important to both have liquid alternatives and possibly handle the solid forms correctly. In this article, we want to describe the correct handling of solid pharmaceutical forms or the transition to liquid ones where present
methodology: the article was written by integrating one's knowledge of pharmacology and pharmaceutical techniques with printed material and online articles extracted from databases such as google scholar and PubMed.
discussion and Conclusions: The liquid forms, where they exist, are important in the management of drug therapy in the dysphagia patient. In the absence of therapeutic alternatives or liquid forms of the same principle, the solid forms can be manipulated within certain limits, paying attention to the interactions with nutritional mixtures and other drugs and above all not obstructing the probe and not compromising the kinetic and dynamic characteristics of the active ingredient.

key words: *dysphagia, pharmaceutical forms, drug handling, clinical galenic*

INTRODUCTION

Dysphagia is a very common symptom, especially in the elderly and in patients with neurological problems, and is defined as difficulty in the formation and transit of the food bolus in the upper digestive tracts. It is so common in the elderly that it is often framed as a true geriatric syndrome. [1]The distinction between oropharyngeal and esophageal refers to the main lesion site; Oropharyngeal dysphagia is the difficulty in getting material from the oropharynx to the esophagus, caused by a functional abnormality upstream of the esophagus. Patients complain of difficulty initiating swallowing, nasal regurgitation, and tracheal aspiration followed by a cough. Generally, it's the most frequent, with a prevalence in the general population of about 16% but increases with age up to 30% in the elderly up to 40-60% in the institutionalized[2]. In particular, oropharyngeal dysphagia affects up to 80% of patients with neurodegenerative diseases and stroke outcomes. It represents the cause of mortality and morbidity due to ab ingests phenomena and the risk of malnutrition and dehydration. The swallowing system includes the pharynx, the upper esophageal sphincter (cricopharyngeal), the body of the esophagus, and the lower esophageal sphincter. The upper third of the esophagus and the structures proximal to it are made up of striated muscle; the distal esophagus and the lower esophageal sphincter are made up of smooth muscle. These components work as an integrated system that carries the material from the mouth to the stomach and prevents its reflux into the esophagus. Physical obstruction or disorders that interfere with motor function (esophageal motility disorders) can affect the system[3]. The presence of dysphagia is also a factor that complicates adherence to drug therapies: because most of the drugs used in chronic therapies are given by mouth, dysphagia implies difficulty in adherence and possible complications related not only to ab ingests phenomena but also to the underdose caused by the failure to take the prescribed doses and to the difficulty of the patient and the caregiver in long-term management[4]. These patients are often placed in enteral feeding using probes (PEG or nasogastric probes) and this further complicates the administration of oral drugs. Handling the oral solid

pharmaceutical form of drugs is a widely used practice frequently by health professionals, patients, and family members, and caregivers to encourage adherence to oral therapy in patients with swallowing difficulties[5]. The handling requires that the drug is pulverized, mixed with water, or included in fruit puree and subsequently administered to the patient. In this article we want to describe the correct methods of managing these therapies can be, paying particular attention to the administration of solid pharmaceutical forms after their handling and what is the role of liquid formulations in their replacement[6].

METHODOLOGY

The article was written by integrating the authors' individual knowledge of pharmacology and pharmaceutical technique (in addition to their practical experience) with a book of pharmaceutical techniques and printed material and online articles extracted from databases such as google scholar and PubMed. The articles used were selected by selecting those relating only to the biopharmaceutical aspects of the formulations and the relative manipulations of pharmaceutical forms for oral use.

RESULT AND DISCUSSION

Today the preferred mode of administering drugs is the oral one. Solid oral pharmaceutical forms (SODFs) include tablets, capsules, and granules. The advantages of these forms of administration are the simplicity in the methods of preparation and packaging, product stability, ease of administration and dosing accuracy, and greater microbiological stability[7]. One of the factors that influence the functionality of the drug is the choice of excipients, according to which SODFs is classified as conventional and modified release. In the first case, the dissolution of the drug depends on its intrinsic properties of solubility. In the second case, on the other hand, the type of formulation modulates the release of the active ingredient and therefore the relative trend of the blood levels. SODFs must be swallowed intact, because only through the correct intake can they meet disintegration, dissolution, and release of the contents into the lumen gastrointestinal[8]. Despite the administration of these pharmaceutical forms being advantageous because it is simple and non-invasive, it starts from the assumption that swallowing is a stable function time. Inappropriate handling of the drug is a common practice to remedy the problem both in general populations and in health care settings. Manipulations consist of splitting or crushing the tablets and opening out the capsules to mix them with food or dissolve them in water[9]. These practices lead to the loss of efficacy of the drug because they modify its absorption, stability, and effect. They also increase the likelihood of administering an incorrect or insufficient dosage and, in the case of dragees or film-coated forms, the result can be an unpleasant tasting preparation. It should also be noted that for drugs with a low therapeutic index (for example antiepileptics, digoxin, anticoagulants, antibiotics, etc.) there may be the risk of exposure of the operator to toxic doses of the substance and also of iatrogenic damage from overexposure of the patient to toxic quantities of the substance[10]. An initial assessment should be made if alternative pharmaceutical forms of the same drug exist on the market, now available for most of the more commonly used products. The distinction between:

- LAF (long-acting formulations), such as example transdermal patches, subcutaneous implants, depot preparations, or pharmaceutical forms with modified release, gastroprotective or delayed-release, which release the active ingredient very slowly into the circulation, reaching lower maximum doses and in a long time but kept longer[11]
- SAF (short-acting formulations), all those with an immediate release such as sublingual, buccal, effervescent tablets, liquid formulations (oral drops), transmucosal, etc ... which give rapid absorption peaks and in higher concentrations[12].

When a drug should be administered orally to a patient with difficulty swallowing, in the phase of prescription, it must be previously assessed whether it is possible to avoid manipulation and therefore if there is an alternative route of administration of the drug (e.g. transdermal, injection) which, at the same of clinical indications and efficacy, does not require manipulations or if there is

an alternative oral pharmaceutical form of the drug that requires less handling (oral drops, syrup, effervescent tablet, gold-dispersible tablet, granules for oral suspension, etc.) or if there is another drug in therapeutic equivalence that does not require manipulation[13]. If the patient is being treated with a prolonged-release formulation, for example, tablets, switching to a transdermal patch or liquid formulation (for example syrup) of an equivalent compound with a long half-life may be valid alternatives, as well as switching from a solid to a liquid formulation both with the rapid release. [14]The liquid formulations have interesting advantages, first of all, the possibility of being administered using a probe in general after dilution with saline without obstructing the probe or adhering excessively to its walls causing underdosing. On the other hand, the direct manipulation of solid formulations in the absence of therapeutic alternatives is more complex. this provides for crushing and pulverizing tablets or granules and opening of the hard capsules with the withdrawal of the solid content, both followed by liquid dilution of the obtained compounds and subsequent administration. [15]Atenction must always be paid to the package leaflet (product characteristics) as it is always reported, among the methods of administration, the possible possibility of dividing/crushing tablets or opening the capsules. It should also be noted that different pharmaceutical forms of the same drug may have different indications; for example, trazodone exists in both scored and extended-release, non-divisible tablets. [16]To avoid errors in administration, always read the single package leaflet first. In summary, the manipulation of tablets (trituration) and capsules (opening) can only be carried out when it is guaranteed that:

• the patient is given the full dose of medication prescribed (there should be no loss of drug during handling)
• the manipulated drug maintains its stability until it is taken
• the manipulated drug is absorbed in the desired rate, to ensure the therapeutic effect
• there is no toxicity caused by the manipulation either for the patient or for the healthcare worker
• there is no interaction with food and drink so that both the drug and the nutrient come absorbed effectively and the site of administration is still the site of absorption of the drug
• the manipulated drug does not obstruct the gastrointestinal probe and/or does not cause gastrointestinal symptoms resulting from incorrect administration in the probe[17,18,19].

They must not be manipulated in soft capsules (there is no accurate and complete withdrawal of the dose), coated tablets (they do not maintain stability due to exposure to air, humidity, light or become irritating to the mucous membranes or take on unpleasant organoleptic characteristics), tablets/capsules and micro granules with a gastro-resistant coating (acid-labile drugs are exposed to gastric acidity and are inactivated by it, consequently losing their effectiveness) and modified-release forms (the drug is not released gradually to maintain a constant plasma concentration and evoke a maintained therapeutic effect over time, but everything is released immediately, with an initial risk of overexposure and toxicity, followed by under-exposure and lack of efficacy)[20]. Moreover, in case you decide to carry out the manipulation, specific tools such as pill cutters or pill crushers must be used, available in pharmacies at low prices and which allow greater accuracy in the procedure.

SPECIFIC INDICATIONS FOR SOME PHARMACEUTICAL FORMS

For oral administration, if the drug can be manipulated:
• crush the tablet, dissolve in a little water or mix in apple puree and administer immediately
• open the capsule, dissolve in a little water or mix in apple puree and administer immediately

In case of administration by the gastrointestinal probe (SNG, PEG), If the drug can be manipulated:
• do not use syringes with a volume of fewer than 20 ml (to avoid excessive pressure exerted on the probe)[21]
• stop feeding and wash the probe with 30 ml of water

• do not mix the drug in the nutritional product: the drug potentially interacts with the nourishing and alters the chemical-physical characteristics of the nutritional product
• prepare the drug immediately before administration
• prepare and administer one drug at a time
• wash the probe with 30 ml of water between one drug and another and at the end of the administration of the medications, before eventually resuming nutrition
• respect the time of administration of the nutrient concerning the drug.
For drugs that must be taken on an empty stomach, suspend the nutritional product one hour before and resume it 1-2 hours later; for drugs that must be taken on a full stomach: administer the nutritional product in time near the drug. Do not administer SNG / PEG drugs in sublingual tablets (not adequate absorption of the drug and not immediate effect of the drug).

Finally, in the case of patients with prevalent dysphagia for liquids, it is possible to use aqueous preparations with the addition of thickeners or directly gelled water as a vehicle to allow oral intake, paying attention to the fact that the rheological modification of the liquid can, in any case, modify the properties of the release of the active ingredient, especially for gastric emptying and possible disintegration or dissolution from the gel mesh and passage into solution in intestinal fluids[22].

CONCLUSIONS

The liquid forms, where they exist, are very important in the management of drug therapy in the dysphagia patient[23]. In the absence of therapeutic alternatives or liquid forms of the same active ingredients, the solid forms can be manipulated within some limits, with big attention to the interactions with nutritional mixtures and other drugs and above all not to obstruct the probe and not to compromise the kinetic and dynamic characteristics of the active ingredient[24]. Clinical galenic allows for obtaining customized forms of solutions, suspensions, emulsions, or syrups and also mixing some active ingredients in gelled water or by formulating solutions and then using thickeners for patients with dysphagia for liquids[25]. However, it must be said that these procedures must be performed only if you are sure of the stability of the active principle in the various excipients/vehicles and paying attention to interactions with other drugs or nutritional mixtures and not to compromise the kinetic and dynamic properties of the drugs[26].

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