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The Neutralizing Ability and Sodium Contents of Antacids

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Abstract: Antacids are commonly used in self-medication for gastritis and duodenal ulcer treatments. Sodium levels present in antacids, an important factor in patients with hypertension or heart diseases, are not specified in leaflets. Neutralizing abilities of commercial products are not indicated either, which is fundamental for an adequate dosage. The aim of this work is to determine the aeutralizing ability (n.a) and the amount of sodium contained in a series of antacids, in their various pharmaceutical forms, available in the Argentinean market. Adequate dosage standards are indicated and a revision of leaflets is carried out. Neutralizing ability was determined by means of an acid-base volumetric technique, whereas sodium levels were determined by Atomic Absorption Spectrometry. N.a values between 12.82 and 24.83 meq per minimum dose were obtained. These values are within the range defined by the FDA (Food and Drug Administration) for a product to be admitted as "antacid". As regards the sodium contents found in the samples studied, values ranging from 0.1 to 11.0 mg of Na per minimum dose were obtained depending on the product brand name. According to the results, in only one case the sodium level obtained was outside the limits established. It is advisable to specify both n.a values and the sodium level in leaflets to avoid irrational use of this type of medication.

Key words: Antacids, sodium contents, neutralizing ability

INTRODUCTION

Dyspepsia, in its various forms, has accompanied mankind since the arrival of bad quality cooking, food abuse and anxiety. Considerable effort has been devoted to mitigate gastric pain and peptic ulcer. Proton inhibitors like cimetidina and ranitidine are usually used in treating duodenal ulcer. However, antacids are commonly employed in self-medication as an alternative therapy[1].

Antacids aim at neutralizing HC1 secreted by gastric wall cells. The ability to neutralize acid is defined as the HC1 1N quantity expressed in miliequivalents (meq), which can get 3.5 pH in 15 min[2]. Antacids taken regularly differ in their composition and ability to neutralize acid. Aluminum and magnesium hydroxides are the main compounds frecuently used in antacids.

Sodium bicarbonate and calcium carbonate as well as other carbonates, silicates and phosphates are also employed. Antacids react by neutralizing HC1 to form chlorates, water and carbon dioxide. Most of the antacid products available in the market are usually presented together with two or more substances with an antacid activity, apart from ant-flatulent substances, such as simeticone and analgesic ones such as acetylsalicylic acid[3].

However, when selecting among several antacid products, it must not be assumed that products with higher neutralizing ability (n.a) are better, since other factors should be taken into account. For example, sodium content for high blood pressure patients, calcium content in patients with lithiasis and magnesium content that may produce colitis in chronic patients and thus they are not recommended in long-term treatments of chronic gastritis[4,5].

In spite of the fact that antacids are broadly promoted in the pharmaceutical market and that a great number of specialties are available, there is little information as regards some of its properties such as its neutralizing ability (n.a) and its sodium content[6]. It is important to carry out an investigation on such properties to have an adequate dosage mainly in certain pathologies such as high blood pressure, renal insufficiency or heart congestive insufficiency.

Patients with heart diseases or on low sodium diets must know about the sodium content of the products and

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choose the most convenient one for them. Those products containing sodium can produce hipercalcaemia in the central nervous system, renal lithasis and a decrease in the renal function.

It is not possible to have a rational dosage of antacids without the information of the properties mentioned above since there are not suiTable criteria to carry them out in clinical situations as the ones cited before. Generally accepted guidelines from information provided by Argentinean laboratories cannot be considered correct taking into account the diversity that exists as regards neutralizing ability and sodium content in other countries. This problem is even more serious if we consider that antacids belong to the group of medications people usually take without professional supervision.

The aim of this study is to obtain n.a values and sodium content in various pharmaceutical forms in Argentina in order to revise information from leaflets, have a correct dosage and check if any medication is outside the F.D.A standards[7].

MATERIALS AND METHODS

Neutralizing ability: F.D.A test[3] was the method used to determine neutralizing ability. Similar results to the ones of Fordtran [8] were obtained by this test, being F.D.A test faster and cheaper.

Determination was carried out on commercial samples on tablets and suspensions. The minimum dose was used in both, 5 mL for suspensions and the weight corresponding to one Tablet for Tablets.

Sample preparation

Tablets: 20 tablets of each sample were weighed on an analytical scale fixing each tablet average weight. They were crushed in a mortar and an equal amount to the fixed average weight was weighed and transfer to a 250 mL esrlenmeyer flask. 40 mL of bidistilled water was added and the sample was shaken in a magnetic shaker at about 300 rpm during one minute.

Suspensions: 5 mL suspension, previously shaken, was taken with a 5 mL volumetric pipette and transferred to a 250 mL erlenmeyer flask adding 40 mL of bidistilled water. It was shaken in the same way as in the previous case.

Reagents and apparatus:

- 0.9944 N HC1 solution (standardized with 0.1000 N $Na_2 CO_3$ standard solution in presence of methyl red indicator).
- 0.4852N NaOH solution (standardized by means of HCl with methyl red).
- Water: deionised, distilled, 18 MΩ.cm, obtained from a NANO pure (Barnstedt, Iowa, USA).
- Titrimetry equipment: burette, erlenmeyer flask and glass accessories.
- Analytic Scale Mettler-Toledo AG 245.
- Magnetic shaker
- pHmeter Mettler Delta 320

Neutralizing ability test: Once the samples were prepared, the titration technique was equally applied to all the pharmacological forms. 30 mL of 0.9944 N HCl was added to each sample while shaking during fifteen minutes. HC1 excess was titrated with a 0.4852 N NaOH solution until a sTable 3.5 pH was obtained during 10-15 s.

The number of miliequivalents (meq) of acid neutralized by the sample was calculated as follows:

Total meq $= V_1 \times N_1 - V_2 \times N_2$ where:

V_1 = 30 mL of HCl

N_1 = normalityof Hcl = 0.9944 N

V_2 = mL de NaOH wasted

N_2 = normality of NaOH = 0.4852 N

Determination was duplicated for each sample taking the averages of both as the representative datum of the neutralizing ability.

Sodium contents

Sample preparation: For determination by Atomic Absorption Spectrometry (AAS), samples in both pharmaceutical forms had to be digested.

Suspensions: The following procedure was duplicated:

a) A burnt and empty crucible was weighed on the scale.
b) 5 mL (minimum dose) of the sample was added and it was weighed again.
c) It was heated slowly on a hot plate until it dried.
d) It was burnt at 900° C in muffle furnace during two hours.
e) It was left to cool in a desiccator.
f) The crucible with the burnt sample was weighed and the ash weight was obtained.
g) The ash was transferred into a beaker adding 50 mL of 2 N HNO_3.
h) It was heated slowly to allow dissolution; the remainder was filtered to be thrown away and then the sample dissolved was put into the 100 mL volumetric flask with deionized water.

Tablets: 20 tablets were finely crushed in a mortar; an amount equivalent to a tablet was weighed on an analytical scale; 1 mL of 0.5% HNO_3 was added and then taken to 100 mL with deionized water in a volumetric flask.

The solutions prepared were directly nebulized in the AA equipment. At the same time a survey was carried out to find the recovery in the process of ashing and in the digestion.

Atomic Absorption Procedure: The sodium determination was realized by an Atomic Absorption Spectrometer Perkin-Elmer AAnalyst 100 (Norwalk, CT, USA), using the air-acetylene flame. Measures of sodium absorption were realized at 589.0 nm Data were obtained with a standard nebulizer and flow spoiler. The ionization should be controlled by the addition of cesium chloride 0,1%.

The quantitation by direct calibration against aquous standards was realized. The six working calibration standards, between 1 to 5 mg L^{-1}, were prepared from the sodium stock standard solution. The calibration graph was linear with a correlation coefficient of 0.9997. Sample solutions were analyzed by triplicate.

The results of sodium levels in the samples were obtained in mg Na per 1g of tablets and later the meq per minimum dose was calculated. In the case of suspensions the results were expresed in mg Na per 5 mL.

The method of standard addition was used as a validation method[9] in order to demonstrate the validity of our method. A portion of each antacid sample was spiked with an appropiate volume of sodium stock standard solution. All the samples were prepared following the procedure proposed (section 2.2.1). The average quantity of sodium found in the samples without addition was taken as the base value. The recovery obtained was 96.95%.

RESULTS AND DISCUSSION

Table 1 and 2 show the neutralizing ability values (n.a) obtained for the various antacids analyzed together with their composition, both for suspensions and tablets.

A stressed variation between n.a obtained from 12.8 meq values to 24.83 meq. per minimum dose can be appreciated. According to FDA, a product must neutralize 5 meq of acid at least and it must keep a 3.5 pH during ten minutes in an "*in vitro* test" to be called antacid. Taking this criterion into account, the values of the products evaluated are over that limit showing an adequate neutralizing ability.

The results of a research carried out by Viñuelas *et al.*[6] about antacid products commercialized in Spain, showed that they have a great variation in their n.a as regards Argentinean antacids and in some cases they are outside FDA standards. However, low n.a products differ considerably in their composition from the ones analyzed in the present work, e.g: aluminum phosphate and magnesium trisilicate. In comparing Spanish and Argentinean products with the same label and composition, as in the case of Pepsamar tablets, it can be observed that the Spanish product contains a 10.54 value, whereas the Argentinean one has a 12.82 n.a. N.a values were in the same order in cases of antacids with a similar composition

Table 1: Neutralizing ability (n.a) and antacids composition in suspensions

Name	Composition (mg per 5mL)	n.a (meq per 5 mL)
Mylanta II	Magnesium hidroxide.....400 mg Aluminum hidroxide.....400 mg Simeticone.....40 mg	22,90
Aludrox	Aluminum hidroxide .....307 mg Magnesium hidroxide.....103 mg	16,88

Table 2: Neutralizing ability (n.a) and antacids composition in tablets

Name	Composition (mg per tabs.)	n.a (meq per tabs)
Mylanta II	Magnesium hidroxide.....400 mg Aluminum hidroxide.....400 mg Simeticone..... 40 mg	24,83
Pepsamar	Aluminum hidroxide.....233 mg	12,82
Rennie	Calcium carbonate .....680 mg Magnesium carbonate ..... 80 mg	15,84

Maalox suspension can be mentioned to make a comparison with an antacid product widely spread in the United States. It is composed of aluminum hydroxide (200 mg) and magnesium hydroxide (155 mg) per each 5 mL, similar to the Argentinean Aludrox suspension. The American product has 13 meq. n.a whereas Aludrox is about 17 meq. However, since the composition of both products is not exactly the same, there could be a slight variation in their values. These differences show possible mistakes made when product lists that come from other countries are taken as source of information.

According to what has been said, it is logical to think that antacid doses should be expressed in meq of neutralizing ability. The protocols recommended for chronic treatment of peptic ulcer are of 80 meq per day for gastric ulcer and of 160 meq per day for duodenal ulcer.

Considering the values recommended for protocols and taking into account the different pharmaceutical specialties obtained, the necessary dosage for a correct therapy was calculated, as Table 3.

Table 3 shows that doses expressed in mL or in tablet units would be excessive in some cases not only for the patient lack of cooperation in the treatment but also for its economic cost plus its adverse reactions.

According to its n.a, the calculated dosage for most of the pharmaceutical specialties analyzed, agrees with the dose suggested in leaflets by the laboratories. Information from leaflets is not accurate as regards time intervals in

Table 3: Laboratory recommended dose (*) and efficient dosage (**) calculated according to the n.a found and to the values recommended by protocols

Name	Dosage (prospectus)*	Gastric ulcer (**)	Duodenal ulcer (**)
Mylanta II, tab.	Until 9 tab./ day	3 tab. $d.^{-1}$	6 tab./d.
Rennie, tab.	3-6 tab./day	5 tab. $d.^{-1}$	10 tab./d.
Pepsamar, tab.	4-8 tab./day	6 tab. $d.^{-1}$	12 tab./d.
Aludrox, susp.	5 mL, 3 times/day	15 mL d^{-1}	30 mL/d.
Mylanta II, susp.	7,5-15 mL 2 times/d.	25 mL d^{-1}	50 mL/d.

Table 4: Sodium contents in antacid suspensions

Name	Na (mg per 5mL)	Na (meq per 5mL)
Mylanta II	4.12	0.18
Aludrox	3.52	0.15

Table 5: Sodium contents in antacid tablets

Name	Na (mg per tab.)	Na (meq per tab.)
Pepsamar	10,82	0,47
Rennie	0,1030	0,0045
Mylanta II	0,8915	0,039

which the product should be taken. They usually indicate for example "1 or 2 tablets three times a day", when in fact time interval should be from one to three hours after meals, when going to bed or when there is pain. Leaflet recommendation should not be made in general but considering the variations in n.a values to prescribe dosage.

When recommending the selection of a product, not only should the n.a be considered but also other substance contents that may affect the patient such as sodium content in a patient that takes antacids and is hyper tense. Leaflets never mention sodium contents for an adequate therapy. They should be a guide for the patient and the doctor providing accurate and complete information. According to FDA antacids and antflatulent products should not contain more than 0.2 sodium meq per minimum dose. If they contain more than 5 meq per day/dose, sodium content should be clearly specified in the leaflet.

Sodium levels obtained both for suspensions and tablets are indicated in Table 4 and 5.

According to the results observed, Pepsamar tablets should indicate sodium meq quantity in its leaflets according to FDA requirements. The rest of the samples analyzed are within the standards.

It is necessary to have precise information as regards sodium content since it is one of the factors that highly contribute in the selection of a product.

CONCLUSION

Neutralizing abilities obtained in Argentinean antacid products analyzed are within the values recommended by FDA. Sodium content over the limit established was detected in only one case among the ones studied. If such a value is obtained, it should be specified in the leaflet.

This study suggests including both, neutralizing ability and sodium levels of antacid products in leaflets. In this way, such information may be available for health professionals to be able to inform the patient correctly and select the product. Leaflets should include updated recommended guidelines for the treatment of gastric ulcer.

Prescriptive rules to control antacid use and overuse should be carried out since antacids are expended without prescription and leaflet information is not enough for medical treatments.

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