Acid-neutralizing capacity and acid-neutralizing profile of various antacid formulations available in Nepal

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abstract

The relative effectiveness of treatment, acid-neutralizing capacity and acid-neutralizing profiles are inter-related. Their inter-relation is evaluated *in-vitro* by USP/BP method and encouraging results are found. Hydroxide forms of aluminium and magnesium combination are found to be more effective than the combination of aluminium hydroxide and magnesium trisilicate. Rationality of choosing solid or liquid form of antacid formulations are also discussed.

Keywords: Antacid; acid-neutralizing capacity

Introduction

Antacids are prescribed for symptomatic relief of hyperacidity associated with peptic ulcer, gastritis, gastric hyperacidity etc., which on ingestion react with HCl of gastric juice to lower the acidity of the gastric contents. Different antacid formulations are widely available in the market containing different combinations of active ingredients in varying concentrations in different brand names and varying prices.

Antacids are substances that react with acid in the stomach and ideally, raise the pH of the stomach contents to between 4-5. Ideal antacid product should be efficient, effective, safe, inexpensive and palatable.2

In terms of peptic ulcer disease, the attitude in the late 1950s and 1970s that antacids should be taken only on demand was erroneous. The most appropriate and economical antacid regimens for the treatment of duodenal ulcer disease should include tablets or liquid that have acid neutralizing capacity of 400 mmol/day, given at least an hour after meal.1

The main criterion for evaluation of the antacid activity is to find out the acid neutralizing capacity (ANC).3-5

To show the efficiency of an antacid, acid neutralizing profile (ANP) has to be evaluated.6 ANP test is based on Rosset-Rice activity test7, which provides information on both the total amount of neutralized acid and the rate of neutralization. The monitored events are the onset of action (time from when the product is first added until the pH rises to 3), maximum pH, and maintenance of pH above 3.7

The aim of this study is to evaluate both the rate and extent of acid neutralization capacity of different formulations available in the Nepalese market and to help pharmacists and practicing physicians to choose the best formulation in the least price among a very large number of formulations.

materials

All the reagents and chemicals used in the experiment were of reagent grade.

Methods

Different brands of antacid suspensions and tablets were purchased from the market. Preliminary antacid test was performed according to USP XXII.4 10 ml of 0.5N HCl was added to a fixed amount of suspension or fixed amount of powder equivalent to one tablet and stirred for 10 minutes. For antacid pH should be greater than 3.5.

Neutralization capacity was performed according to BP6 or, USP XXII.6 Fixed amount of suspension or fixed amount of powder equivalent to 1 tablet was added to 150 ml of 0.1N HCl and stirred for 1 hour at 37o centigrade. Excess acid was titrated using 0.1N NaOH up to pH 3.5 and ANC was calculated.

Tablets and suspension were also assayed for the active ingredients according

to BP.6 Neutralization profile was performed according to Rosset and Rice test.7 The methods based on the fact that an antacid tablet was added in 3 equal installments within 15 minutes time as to mimic chewability of the tablet, but the suspension was added at a time to a 125 ml of 0.1N HCl at 37o+2o centigrade. With continuous agitation more acid was added from buret continuously
at the rate of 1 ml per minute analogous
to the *in-vitro* gastric acid secretion.
pH was continuously monitored with
the electrode dipped in the antacid-acid mixture.

Result and discussion

Randomly sampled antacid tablets and suspension dosage forms were examined for preliminary antacid test according to USP XXII. All of the products were found to confirm USP antacid test. These products were tested for active constituents according to BP/USP specification and were found to comply those requirements.

Suspensions were evaluated by different physical parameters viz. pH, wt/ml etc. The pH was found to range from 7.5–9.5 for different brands. Similarly, weight per millilitre varied greatly.

Tablets were crushed into powder and sieved through 100 mesh screen and pH was noted according to BP specification. Results were in the range of 7.5–9.5.

The acid neutralizing capacity and ANP of all of the products were evaluated according to established standards. (figures 1 & 2 and Table I.

Fig. 1: T1, T2 and T3 = 400 mg Almunium hydroxide and 400 mg Magnesium hydroxide

T4 and T5 = 300 mg Almunium hydroxide and 150 mg Magnesium hydroxide

T6 and T7 = 250 mg Almunium hydroxide and 250 mg Magnesium Trisilicate

T = Tablet

Fig. 2: S1, S2, S3 and S4 = 500 mg Almunium hydroxide and 500 mg Magnesium hydroxide

S5 = 600 mg Almunium hydroxide and 600 mg Magnesium hydroxide

S = Suspension

Table I: In-vitro evaluation of different antacid products.

Sample No.	*ANC mEq acid/dose*	*Acid Neutralizing Profile (ANP)*			
T = Tablet *S = Suspension*		*Onset (time to reach pH 3) (Min)*	*Speed (time to reach max pH)*	*Capacity of buffering (Max, pH)*	*Duration at which pH is above 3 (Min)*
T1	25	19	24	3.71	52
T2	21.4	18	23	3.94	58
T3	20.75	16	25	3.84	51
T4	10.4	-	48	1.54	-
T5	17.2	-	50	1.69	-
T6	10.9	-	30	1.38	-
T7	11.8	-	30	1.59	-
S1	23.4	15	20	3.79	53
S2	26.2	17	22	3.87	61
S3	25.1	18	25	3.68	59
S4	22.9	19	24	3.72	53
S5	24.9	17	25	3.92	55

Key: T1, T2, T3 = 400 mg Al(OH)3 + 400 mg Mg(OH)2

T4, T5 = 300 mg Al(OH)3 + 150 mg Mg(OH)2

T6, T7 = 250 mg Al(OH)3 + 250 mg Mg-trisilicate

S1, S2, S3, S4 = 500 mg Al(OH)3 + 500 mg Mg(OH)2

S5 = 600 mg Al(OH)3 + 600 mg Mg(OH)2

In-vitro evaluation in this study shows that there is not much difference in acid neutralizing capacity of formulations containing following combinations: 400, 500 and 600 mg of both aluminum and magnesium hydroxide which complies with the previous research.9 The marketed antacid formulations are diverse in Nepal. There are two most common types: *Type I* includes the combination of hydroxides form while *Type II* includes Aluminum hydroxide and magnesium trisilicate. It appears from the observation that *Type I* has better ANC than that of *Type II.* Moreover, for *Type I*, ANP is far better than that of *Type II.* This observation was in agreement with the general concept that magnesium trisilicate is less potent antacid than magnesium hydroxide. However, there is one added advantage of using trisilicate form of magnesium that the hydrated silicon dioxide which is a by-product, is thought to have adsorbent qualities and unreacted magnesium trisilicate may coat the ulcer crater and produce some cytoprotective action.2 It has been reported that magnesium hydroxide has faster onset of action and higher antacid activity than magnesium trisilicate, aluminum hydroxide and magaldrate although acid neutralizing properties of antacids in the stomach more or less parallel those observed in-vitro. However, mucoproteins and other substances tend to slow the rate of neutralization and decrease ANC, especially of Al(OH)3.7

The rate of neutralization of gastric acid by Al(OH)3 is usually too slow relative to gastric emptying time to neutralized gastric acid when the stomach is empty. The concurrent use of Mg(OH)2 and Al(OH)3 provide both fast acting component, which can achieve neutralization within a few minutes, and a more sustained effect. Food in the stomach delays emptying and allow more time for Al(OH)3 to react.8

There is a minor variation among the same type of antacid formulations. The quality of raw materials, concentration of binder in chewing tablet, different formulation factors and pH of the preparation influence the antacid activity.

It is interesting to note that similar amount of raw materials even in a similar dosage form varies in ANC and of course ANP. Thus, formulation of an effective antacid is a great challenge for a product development pharmacist. Generally, it is thought that liquid dosage forms are more effective, but less convenient than tablets. In our observations, acid neutralization can be more effective and quickly achieved with liquid antacids. However, better tablet formulation can be accomplished. It may thus be irrevalent except in terms of cost-effectiveness to choose between liquid and tablet forms for symptomatic relief. It seems wiser to recommend antacids with high neutralizing capacity that are inexpensive.

Conclusion

In-vitro evaluation of antacid is a very simple and rapid means of selecting best formulation among host of hundreds of available formulations in the market. For better product development, antacid manufacturer should consider the test of neutralization profile while formulating tablet or suspension. Hospital pharmacist should carry out this test before selecting an ideal product for hospital use.

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