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Study of Acid Neutralizing Capacity of Various Antacid Formulations

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ABSTRACT

Background: Antacids are the substances most commonly used by the patients to obtain fast symptomatic relief from dyspepsia. They are the week base which neutralize the gastric acid and raise the pH of the gastric contents. The potency of the antacids depends upon their acid neutralizing capacity (ANC). The antacid neutralizing capacity varies from one another depending upon their formulations.

Materials and methods: The present study was undertaken to study the acid neutralizing capacity of commonly available antacids formulations using titration and pH meter method. Six liquid formulations and six solid tablet formulations were studied for their acid neutralizing capacity

Results: The acid neutralizing capacity among the liquid formulations was highest for Dioval 26.28±0.05 by pH meter method and 26.17±0.18 by titration method. Among solid antacid formulations ANC was highest with Riflux forte being 25.77±0.06 by pH meter method and 25.73±0.17 by titration method. Both the formulations had higher magnesium hydroxide concentration when compared to other antacids.

Conclusion: The acid neutralizing capacity was highest with the antacids containing magnesium hydroxide. For acute fast symptomatic relief from dyspepsia antacids containing higher concentration of magnesium hydroxide would be helpful.

Key-words: Antacids, Acid neutralizing capacity, pH meter, Titration, Magnesium Hydroxide

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Introduction:

Antacids are used for the symptomatic relief of dyspepsia which may be due to functional or associated with identifiable pathology such as esophageal reflux , peptic ulceration or gastritis.[1]Antacids are the weak bases which on ingestion lower the acidity of the gastric contents. The symptomatic relief of pain produced is mainly by reducing the acidity and partly by consequent relief of the muscle spasm. Reduction in the acidity also inhibits the activity of pepsin . Antacids also increases the tone of the lower esophageal sphincter and hence reduces the reflux of the acid and gastric contents into the esophagus.[2]

The hydroxide is the most common base, trisilicate, carbonate and bicarbonate are also used. The therapeutic efficacy and the adverse effects depend upon the metallic ion with which the base is combined. The common metallic ions combined with the base are aluminium, magnesium or sodium .[3]The antacids can be classified as systemic antacids and non systemic antacids .Systemic antacid is the one that undergoes complete systemic absorption following oral ingestion, like sodium bicarbonate .The non systemic antacids are the one that does not undergo systemic absorption following the oral ingestion. The most commonly used non systemic antacids are aluminium hydroxide, aluminium phosphate, magnesium trisilicate, magnesium hydroxide, magnesium carbonate and calcium carbonate.[4]

The systemic antacid most commonly used is sodium bicarbonate. It is white in colour, water soluble and completely absorbable antacid. It reacts with the gastric acid to form sodium chloride, water and carbon dioxide. It is an effective and rapidly acting antacid. The carbon dioxide liberated during the process of acid neutralization often gives a sense of relief from the abdominal discomfort. The adverse effect of sodium bicarbonate being it's systemic absorption producing the alkalosis. The sodium chloride formed may result in the retention of fluid and the carbon di oxide liberated may cause the feeling of nausea, belching, flatulence, fullness and rupture of the prior formed peptic ulcer.[5]

Among the non systemic antacids aluminium hydroxide reacts with the gastric acid to form aluminum chloride. The advantages of aluminium hydroxide are that it has astringent and demulcent property by which it forms a protective coating over the ulcer crater. It may also absorb toxins, bacteria and gases. Constipation being it's major adverse effect. The other adverse effects are prevention of the absorption of the phosphate from the intestine causing osteomalacia , in patients with high chronic renal failure high aluminium concentration attained in the serum may rarely cause encephalopathy and the deposition of aluminium in the bones may cause osteodystrophy.[6]

The another most commonly used non systemic antacid is Magnesium hydroxide. It is available as milk of magnesia containing 7 to 8.5% of the magnesium hydroxide. It is more palatable than the other preparation of the magnesium. The major adverse effect of the magnesium hydroxide is the diarrhea.[7]Clacium carbonate occurring as a white powder with chalky taste is also used as non systemic antacid. It reacts with the gastric acid to form the calcium chloride. The major side effect of the calcium carbonate is that it increases the gastrin and basal gastric acid secretion level above the basal level.[8] There occurs no systemic absorption of the bases among non systemic antacids, because the salt formed with combination of the gastric acid combines with the bicarbonate in the intestine to form the original base which will be excreted in the feces.[9]

Alginic acid may be combined with the antacid to encourage the adherence of the antacid to the mucosa and it also acts like a protective to the gastric mucosa. Simethicone or dimethicone are included in the antacid as an foaming agent to reduce flatulence by lowering the surface tension and allowing the small bubbles of froth to coalesce into large bubbles that can be more easily be passed up from the stomach or down from the colon.[10]

The potency of the different antacids depends upon the acid neutralizing capacity of the individual antacid. Acid neutralizing capacity of an antacid is defined as the number of mEq of 1N HCl that are brought to the pH of 3.5 in 15 minutes by a unit dose of the antacid preparation.[11]

At presently in the market there are many antacid preparations available in different formulations. Hence the present study was conducted to identify the antacid neutralizing capacity of various different formulations.

Materials and Methods:

The antacid neutralizing capacity of six liquid and six solid antacid formulations were estimated using the titration method and pH meter method.

Each of tablet containing various ingredients was weighed and then triturated in mortar and pestle to make a fine powder .The powder was transferred to a beaker and 70ml of distill water was added and made to suspension by a magnetic stirrer.
The liquid antacid bottles were shaken well for one minute and 5ml of the preparation were poured into a 250ml of glass beaker.70ml of distill water was added to the antacid formulation in the beaker and mixed well with a magnetic stirrer for 1 minute

Titration method: 30 ml of 1N HCl was pipetted into the prepared drug solution with continuous stirring. The above preparation was stirred continuously for about 15 minutes .2-3 drops of methyl orange indicator was added to the preparation and the excess HCl was titrated with 0.5N Sodium hydroxide. At the end point the test solution changes from red to yellow.

pH meter method: 30 ml of 1N HCl was added to the 70ml of the antacid suspension with constant stirring. The stirring was continued for about 15mins.The excess of the HCl was titrated with 0.5N sodium hydroxide to attain a stable pH of 3.5
Both the above procedures were repeated for six times for each sample of drug and average was taken.

Calculations:
The number of milli equivalents (mEq) of acid consumed was calculated and the results were expressed in terms of mEq of acid consumed per gram of substance tested.

Each ml of 1N HCl consumed is equal to 1mEq of acid consumed.
mEq of acid consumed=$(V_{HCl} * N_{HCl}) - (V_{NaOH} * N_{NaOH})$
where

V_{HCl} =Volume of HCl used in ml
N_{HCl} =Normality of HCl
V_{NaOH} =Volume of NaOH used in ml
N_{NaOH} =Normality of NaOH

Table:1 List Of liquid Antacids Formulations And Their Composition Used

Sl/No	Brand name	$Al(OH)_3$mg	$Mg(OH)_2$mg	Others
1	Digene	830	185	Simethicone
2	Mucaine	291	98	Oxethazine
3	Diovol	300	250	Dimethicone,
4	Visco	125	250	Simethicone, Sodium alginate
5	Acinil O	157	125	Simethicone, Oxethazine
6	Pepticaine	250	250	Dimethicone, Sodium alginate

Table 2: List of Tablet antacids and their composition

Sl/No	Brand name	$Al(OH)_3$	$Mg(OH)_2$	Others
1	Riflux forte	300	150	Alginic acid, NaHCO3
2	Digene	300	25	Simethicone, Mg Al Silicate
3	Gelusil	250	300	Dimethicone, Mg Al Silicate
4	Diovol	240	100	Dimethicone,MgCO3
5	Ulgel	200	200	Simethicone
6	Alcid	300	25	Simethicone, Mg Al Silicate

Results: Liquid formulations

Table 3 : Digene Gel

Sample	pH	ANC pH Meter (mEq/5ml)	ANC Titration (mEq/5ml)
1	2.62	21.00	20.75
2	2.59	20.90	20.85
3	2.63	21.05	20.85
4	2.60	20.85	20.70
5	2.61	20.90	20.80
6	2.63	21.05	20.80

Mean ±SD ANC pH meter=20.96±0.09;ANC Titration=20.79±0.06

Table 4: Mucaine gel

Sample	pH	ANC pH Meter (mEq/5ml)	ANC Titration (mEq/5ml)
1	2.54	21.25	21.10
2	2.53	21.20	21.10
3	2.54	21.20	21.20
4	2.52	21.10	21.40
5	2.54	21.30	21.05
6	2.54	21.25	21.25

Mean ±SD ANC pH meter=21.22±0.07;ANC Titration=21.18±0.13

Table 5 : Diovol

Sample	pH	ANC pH Meter (mEq/5ml)	ANC Titration (mEq/5ml)
1	2.71	26.25	26.05
2	2.70	26.20	26.05
3	2.75	26.35	26.45
4	2.72	26.25	26.35
5	2.70	26.30	26.05
6	2.71	26.30	26.05

Mean ±SD ANC pH meter=26.28±0.05;ANC Titration=26.17±0.18

Table 6: Visco

Sample	pH	ANC pH Meter (mEq/5ml)	ANC Titration (mEq/5ml)
1	2.43	21.40	21.25
2	2.42	21.30	21.20
3	2.40	21.50	21.05
4	2.43	21.40	21.25
5	2.44	21.35	21.20
6	2.42	21.40	21.20

Mean ±SD ANC pH meter=21.39±0.07;ANC Titration=21.19±0.07

Table 7 : Acinil O

Sample	pH	ANC pH Meter (mEq/5ml)	ANC Titration (mEq/5ml)
1	2.45	25.60	25.45
2	2.46	25.50	25.55
3	2.45	25.65	25.40
4	2.45	25.55	25.40
5	2.46	25.50	25.60
6	2.45	25.60	25.50

Mean ±SD ANC pH meter=25.57±0.06;ANC Titration=25.48±0.08

Table 8: Pepticaine

Sample	pH	ANC pH Meter (mEq/5ml)	ANC Titration (mEq/5ml)
1	2.40	25.25	25.50
2	2.42	25.25	24.95
3	2.44	25.35	25.10
4	2.46	25.40	25.05
5	2.50	25.30	24.95
6	2.44	25.50	24.90

Mean ±SD ANC pH meter=25.34±0.10; ANC Titration=24.99±0.07

Tablet formulations:

Table 9: Riflux forte

Sample	pH	ANC pH Meter (mEq/5ml)	ANC Titration (mEq/5ml)
1	2.63	25.70	25.55
2	2.62	25.75	25.70
3	2.60	25.80	25.85
4	2.61	25.70	26.65
5	2.62	25.85	26.00
6	2.61	25.80	25.60

Mean ±SD ANC pH meter=25.77±0.06; ANC Titration=25.73±0.17

Table 10: Digene

Sample	pH	ANC pH Meter (mEq/5ml)	ANC Titration (mEq/5ml)
1	2.45	23.15	23.05
2	2.43	23.10	23.05
3	2.44	23.20	23.65
4	2.45	23.25	23.00
5	2.42	23.20	23.05
6	2.44	23.25	23.45

Mean ±SD ANC pH meter=23.19±0.06;ANC Titration=23.21±0.27

Table 11 : Gelusil

Sample	pH	ANC pH Meter (mEq/5ml)	ANC Titration (mEq/5ml)
1	2.26	12.00	11.75
2	2.30	12.30	11.70
3	2.28	12.15	11.80
4	2.29	11.95	11.85
5	2.31	12.10	11.65
6	2.28	12.30	11.70

Mean ±SD ANC pH meter=12.13±0.15;ANC Titration=11.74±0.07

Table 12 : Diovol

Sample	pH	ANC pH Meter (mEq/5ml)	ANC Titration (mEq/5ml)
1	2.45	15.85	15.75
2	2.47	15.90	15.65
3	2.47	15.60	15.55
4	2.46	15.85	15.80
5	2.45	15.75	15.70
6	2.47	15.75	15.55

Mean ±SD ANC pH meter=15.78±0.11;ANC Titration=15.67±0.10

Table 13 : Ulgel

Sample	pH	ANC pH Meter (mEq/5ml)	ANC Titration (mEq/5ml)
1	2.57	24.00	23.75
2	2.56	23.90	23.90
3	2.58	23.83	23.85
4	2.55	24.10	24.00
5	2.56	24.00	23.90
6	2.57	23.95	24.05

Mean ±SD ANC pH meter=23.96±0.09; ANC Titration=23.91±0.11

Table 14: Alcid

Sample	pH	ANC pH Meter (mEq/5ml)	ANC Titration (mEq/5ml)
1	2.39	23.10	23.00
2	2.38	23.20	22.95
3	2.40	23.25	23.45
4	2.37	23.25	22.90
5	2.39	23.15	23.05
6	2.40	23.25	23.55

Mean ±SD ANC pH meter=23.20±0.06; ANC Titration=23.15±0.28

Table 15: pH meter and titration Acid neutralizing capacity of liquid formulations

Sl/No	Brand	ANC pH Meter (mEq/5ml)	ANC Titration (mEq/5ml)
1	Digene	20.96±0.09	20.79±0.06
2	Mucaine	21.22±0.07	21.18±0.13
3	Diovol	26.28±0.05	26.17±0.18
4	Visco	21.39±0.07	21.19±0.07
5	Acinil O	25.57±0.06	25.48±0.08
6	Pepticaine	25.34±0.10	24.99±0.07

Table 16: pH meter and Titration ANC of the solid tablet formulations

Sl/No	Brand	ANC pH meter mEq/gm	ANC Titration mEq/gm
1	Riflux forte	25.77±0.06	25.73±0.17
2	Digene	23.19±0.06	23.21±0.27
3	Gelusil	12.13±0.15	11.74±0.07
4	Diovol	15.78±0.11	15.67±0.10
5	Ulgel	23.96±0.09	23.91±0.11
6	Alcid	23.20±0.06	23.15±0.28

Discussion:

Antacids are the weak bases used to obtain fast symptomatic relief from dyspepsia. The potency of the antacids purely depends upon the acid neutralizing capacity of the individual. In the above study the acid neutralizing capacity of six liquid and six solid antacids formulations were estimated using titration method and pH meter method. The liquid antacids used were the Digene, Mucaine, Divol, Visco, Acinil O and Peticaine. The solid antacids used were Riflux forte , Digene, Gelusil, Diovol, Ulgel and Alcid tablets.

The liquid formulation Digene had ANC by pH meter 20.96±0.09 and titration 20.79±0.06, which had composition of 830mg of aluminium hydroxide and 185mg of magnesium hydroxide. Similarly mucaine gel had ANC 21.22±0.07 and 21.18±0.13 by pH meter method and titration method respectively .The composition of mucaine gel was 291mg of aluminium hydroxide and 98mg of magnesium hydroxide. The Diovol liquid formulation with composition of aluminium hydroxide 300mg and magnesium hydroxide 250mg had the ANC pH meter method of 26.28±0.05 and titration method 26.17±0.18.The ANC of the liquid formulation Visco by pH meter was 21.39±0.07 and by titration method was 21.19±0.07. 125mg of aluminium hydroxide and 250mg of magnesium hydroxide was its composition. The other two liquid formulations acinil O and pepticaine had composition of aluminium hydroxide 157mg and 250 mg and magnesium hydroxide 125mg and 250mg .Their ANC by pH meter method was 25.57±0.06 and 25.34±0.10 respectively. Similarly ANC by titration method was 25.48±0.08 and 24.99±0.07 respectively. From the above results the Diovol had the highest ANC by both pH meter method and titration method. It might be due to highest composition of the magnesium hydroxide which provides the fast acid neutralization when compared to aluminium hydroxide. The order of acid neutralizing capacity of the liquid formulations were Diovol, Acinil O, pepticaine, visco, mucaine and digene.

The solid tablet formulation Riflux forte had ANC 25.77±0.06 by pH meter method and 25.73±0.17 by titration method. The Riflux forte had the combination of 300mg of aluminium hydroxide and 150mg of magnesium hydroxide. Similarly digene tablet having aluminium hydroxide 300mg and magnesium hydroxide 25mg had the ANC 23.19±0.06 by pH meter method and 23.21±0.27 by titration method. Similarly the ANC of the gelusil tablet by pH meter method was 12.13±0.15 and by titration method was 11.74±0.07.It had a combination of aluminium hydroxide and magnesium hydroxide 250 mg and 300mg respectively. The ANC of 15.78±0.11 by pH meter method and 15.67±0.10 by titration method was obtained by the solid formulation diovol tablets having combination of aluminium hydroxide and magnesium hydroxide 240mg and 100mg respectively .The ANC of the

other two Ulgel and Alcid tablets by pH meter method was 23.96±0.09 and 23.20±0.06 respectively and ANC by titration method was 23.91±0.11 and 23.15±0.28 respectively. They had aluminium hydroxide 200mg and 300mg and 200mg and 25mg of magnesium hydroxide. Among the solid antacids ANC was found highest in riflux forte which had highest magnesium and aluminium concentration. The order of ANC of solid formulations are riflux forte, ulgel, alicid, digene, diviol and gelusil respectively.

Conclusion:

Acid neutralizing capacity is the most important factor in determining the potency of the antacid in providing the symptomatic relief. Acid neutralizing capacity varies among different antacid and their formulations. It was observed that the formulation with increased magnesium hydroxide had higher acid neutralizing capacity .The treating physician can use the antacids with higher neutralizing capacity to obtain faster symptomatic relief from dyspepsia .

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