Comparative Gastroscopic Study of Choline Salicylate and Aspirin

S. C. Danao

B. M. Schuman

Follow this and additional works at: https://scholarlycommons.henryford.com/hfhmedjournal

Part of the Life Sciences Commons, Medical Specialties Commons, and the Public Health Commons

Recommended Citation

Available at: https://scholarlycommons.henryford.com/hfhmedjournal/vol20/iss1/5

This Article is brought to you for free and open access by Henry Ford Health System Scholarly Commons. It has been accepted for inclusion in Henry Ford Hospital Medical Journal by an authorized editor of Henry Ford Health System Scholarly Commons.
Comparative Gastroscopic Study of Choline Salicylate and Aspirin
A Preliminary Report

S. C. Danao, M.D.* and B. M. Schuman, M.D.*

Choline salicylate is the anhydrous choline salt of salicylic acid. It possesses the therapeutic effects of aspirin. Clinical trials suggest that it is less irritating to the gastric mucosa. A double-blind gastroscopic study of the acute effects on the gastric mucosa of choline salicylate, aspirin and matching placebo was carried out. Using the fiberoptic gastroscope, the stomach was examined and photographed before, and ten minutes after, the patient had swallowed the tablets. Results were evaluated on the basis of combined endoscopic and photographic observations. This study suggests that choline salicylate in its tablet form causes less gastric mucosal injury than aspirin. This may be due to its extreme solubility, to a relatively higher pH in solution, and to the absence of the acetyl radical in its molecular structure. Gastroscopic evaluation of acute local reaction of the mucosa to drugs is better accomplished by the combined use of endoscopic and photographic observations and by the inclusion of a placebo in the study protocol. Presence of peptic ulcer or other mucosal abnormality does not necessarily increase the susceptibility of the gastric mucosa to aspirin or choline salicylate injury.

Since 1899 when pharmacologic data about acetyl salicylic acid was first presented by Dreser, aspirin has been a mainstay in the physician’s therapeutic armamentarium. It soon became evident, however, that aspirin is capable of causing gastrointestinal bleeding. Attempts to overcome this undesirable side effect led to the appearance of various preparations including buffered, enteric-coated, and more soluble forms of aspirin.

In 1959, a new derivative of aspirin, choline salicylate, was synthesized and characterized. This is the anhydrous choline salt of salicylic acid, with a molecular weight of 241, of which 57% is due to its salicylate content. It is the most water-soluble of all salicylates and because of its hygroscopic property, it was initially available only in the liquid form (Arthropan®). Recently, however, a stable tablet preparation has been manufactured (MYBA®). A 10% solution of choline salicylate gives a pH of 6.5. Pharmacologic studies showed that choline salicylate is non-toxic, that it is absorbed about five times more rapidly than aspirin, that it maintains its plasma level as long
Danao and Schuman

as aspirin does but that peak plasma level is attained 12 times faster than aspirin (7.8). Clinical trials showed that choline salicylate possesses analgesic, anti-inflammatory and antipyretic properties equal to, if not better than, aspirin.\(^7\)–\(^10\) These studies also revealed that gastrointestinal side effects such as pyrosis, epigastric distress, and nausea are less commonly encountered in choline salicylate compared with aspirin. Pierson and his associates, using Cr\(^{51}\) tagged red blood cells, measured the fecal blood loss after administration of aspirin, calcium aspirin complex, Bufferin®, enteric-coated aspirin and choline salicylate. Of these preparations, only choline salicylate did not result in gastrointestinal blood loss.\(^11\)

Gastroscopic observation of gastric mucosal reaction to aspirin has been done many times\(^12\)–\(^17\) and found to be a valuable method for evaluating gastric mucosal injury. Our purpose was to make a double-blind comparative gastroscopic study of aspirin and the tablet preparation of choline salicylate known as MYBA\(^\text{®}\), with a matching placebo. To our knowledge no similar study has been done with choline salicylate in any form.

Materials and Methods

Forty-two patients from both the inpatient service and outpatient clinic were included in the study. There were 18 female and 24 male patients with ages ranging from 32 to 76. Seventeen patients had proven or suspected gastric ulcers; four patients had proven or suspected duodenal ulcers; six patients had complaints attributed to functional gastrointestinal disturbances; two patients had gastric cancer; six patients had unexplained upper gastrointestinal bleeding; three patients had gastritis; four patients had respectively dumping syndrome, antral polyp, functional vomiting and postgastrectomy state. Eighteen of the 42 patients received aspirin, 16 received choline salicylate and 8 received placebo.

The patients were prepared for the examination by intramuscular injection of 50 mg of meperidine hydrochloride and 0.4 mg of atropine sulfate given 30 to 45 minutes before the procedure. The fiberoptic gastroscope (Olympus Model GTF-A) was used to survey the stomach, with 12 to 15 pictures taken of the antrum, body of the stomach and the fundus at the area of the mucosal pool. Endoscopic observations were made and recorded by at least two endoscopists. After the instrument was removed, the patient swallowed three tablets with water ad lib. All tablets were identical in appearance and the constituents unknown to the endoscopist. The pharyngeal mucosa was swabbed with 5% hexylcaine. Ten minutes after the tablets were swallowed, the fiberoptic gastroscope was re-introduced. The stomach was surveyed and pertinent areas rephotographed. Pictures were taken of the disintegrated tablets at various areas of the stomach. Endoscopic observations were recorded. The gastroscope films were read independently by the two endoscopists two to three days later. The degree of severity of mucosal reaction was graded according to the following scale: 1 point for erythema; 2 points for hemorrhage; 2 points for petechiae and 2 points for erosion. This rating scale was used for both the endoscopic and photographic observations. After completing the tabulation of the results for each of the 30 patients, the code was broken to match the patient treatment groups.
was broken and the tablets given each patient identified.

Results

Of the 42 examinations, 22 showed no gastroscopic evidence of gastric mucosal injury. Of these 22 negative cases, 4 occurred in the placebo group, 9 in the aspirin group, and 9 in the MYBA group. The other 20 showed varying degrees of mucosal injury. Of these 20 positive cases, 9 occurred in the aspirin group, 7 in the MYBA group, and 4 in the placebo group. Therefore, 50% of the aspirin cases were positive, 50% of the placebo cases were positive, and 43.8% of the MYBA cases were positive. Using our rating scale, the nine positive aspirin cases had 23 points, the seven positive MYBA cases had 16 points, and the four positive placebo cases had 18 points. These points represent the total of both endoscopic and photographic observations for each individual case.

Particles of the tablets in varying degrees of disintegration were consistently demonstrated in the antrum, body, or the mucus pool of the fundus. The most common reaction was erythema localized around the tablet particles, noted in 15 patients. Diffuse erythema was seen in only one case. A hemorrhagic reaction was noted in eight patients, with free blood in the gastric lumen seen in three cases. Two patients exhibited petechiae and one showed erosions at the vicinity of the dissolved tablets.

Of the 20 positive cases, 8 patients showed mucosal reaction in both gastroscopic and photographic observations. Six patients did not show mucosal reaction during gastroscopy, but review of the photographs revealed evidence of mucosal injury. The remaining six patients showed mucosal reaction during gastroscopy but photographic evidence was normal.

Eighteen patients received aspirin. Nine showed a positive reaction. Of these nine who reacted, six had normal gastric mucosa, one had a gastric ulcer, one had an antral polyp and one had antral gastritis. Of the nine patients who did not react to aspirin, two had duodenal ulcer, four had gastric ulcer, one had gastritis, and two had normal mucosa.

Sixteen patients received choline salicylate. Seven showed a positive reaction. Of these seven, one had gastric carcinoma, two had gastric ulcer, one had gastritis while the other three showed normal mucosa. Of the nine patients who did not react to choline salicylate, two had duodenal ulcer, three had gastric ulcer, one had gastric carcinoma, one had mucosal telangiectasia and two had normal mucosa.

Six patients in the study had upper gastrointestinal bleeding of undetermined etiology. One had a positive reaction with the placebo. Three patients received aspirin with one showing a positive reaction. The other two patients received choline salicylate with one showing a positive mucosal reaction.

Fifteen patients of the entire group were past users of aspirin. Eight patients were using aspirin regularly, taking several tablets almost daily while seven patients used it occasionally. Among the eight regular users, three received aspirin with one showing positive reaction, two received choline salicylate to which one showed a reaction, and the other three received placebo tablets with no reaction.
Of the nine patients who showed reaction to aspirin, four gave a history of aspirin intake. Among the nine patients who did not show reaction to aspirin, only two had used aspirin previously. Of the seven patients who showed reaction to choline salicylate, two had a history of aspirin intake. Among the nine patients who did not react to choline salicylate, two had a history of aspirin intake.

Comment

Analysis of the raw data suggests that choline salicylate causes less mucosal injury than aspirin. Because analysis of the present study does not yield statistically significant differences between the experimental groups, further studies are in order. We believe these additional studies are likely to sharpen the differences already observed in the experimental groups.

This study suggests that choline salicylate in its tablet form causes less gastric mucosal injury than aspirin. Previous studies comparing these two forms of salicylates agree. Clinical trials using the liquid form of choline salicylate have shown that it is better tolerated and causes less gastrointestinal side effects than aspirin. This was especially true when larger doses of salicylates were administered. It was also noted that most patients who developed epigastric distress with aspirin tolerated comparable doses of choline salicylate very well. Measurements of fecal blood loss, using Cr-labeled red blood cells, revealed that of six salicylate preparations used, only choline salicylate did not result in gastrointestinal blood loss.

The pathogenesis of the aspirin-induced injury in the gastric mucosa has been reviewed recently. While the exact mechanism has not been elaborated, several factors have been incriminated.

Davenport felt that the absorption of aspirin causes damage to the gastric mucosal barrier allowing back diffusion of hydrogen ions which induces bleeding. At pH 2.5, aspirin exists in the un-ionized, lipid-soluble form which is more rapidly absorbed through the lipoprotein membrane of the gastric mucosal cells. At pH 6.5, aspirin becomes poorly absorbed by the gastric mucosa. The importance of intragastric pH in the production of bleeding by aspirin has been well documented in both animal experiments and in experiments with volunteers. Choline salicylate in solution has a pH of about 6.5.

Another important factor is the dissolution rate of the salicylate preparation. There appears to be an inverse correlation between solubility and amount of blood loss as measured in the feces. Calcium-aspirin complex, which is more soluble than aspirin, caused a smaller amount of blood loss compared to aspirin. In this respect, choline salicylate is the most soluble of all salicylate preparations.

Another interesting observation is the absence of gastrointestinal bleeding when enteric-coated sodium salicylate was given. This is probably unrelated to the coating of the tablet since both uncoated and enteric-coated aspirin produced significant bleeding. On the other hand, sodium salicylate and choline salicylate have one common characteristic in their chemical structure which is not found in aspirin: the absence of the acetyl radical.
possibility is raised therefore that the presence of the acetyl radical in the molecule of aspirin may be a factor in causing gastric mucosal injury. This study utilizes both endoscopic and photographic observations in evaluating gastric mucosal injury. Similar studies with aspirin had employed either purely gastroscopic observation or blind intragastric photography. Our findings show that mucosal reaction varying from erythema to hemorrhagic changes can be missed if only one procedure is used. Vigorous peristalsis and the effect of antral spasm and retained secretions occasionally may afford only fleeting views of some areas of the stomach, thus hampering mucosal evaluation by even the experienced endoscopist. This disadvantage is obviated by a detailed leisurely review of photographs taken during the endoscopy. On the other hand, blind intragastric photography cannot always be a substitute for gastroscopy. This has been pointed out by Schindler and Nelson. It is our impression that gastroscopy and gastrophography complement each other and that the optimum result is obtained when both procedures are used.

An unexpected finding is the positive reaction of four patients who received placebo tablets. All four showed mucosal hemorrhagic changes. The placebo tablets (composed of Lactose) contain no constituent known to cause gastric mucosal injury. It is possible that a pre-existing gastric lesion may result in an altered mucosal reactivity so that even inert substances may provoke mucosal change. Three patients had no demonstrable gastric pathology while the fourth had a gastric ulcer which was completely healed at the time of the study. Another important consideration is the emotional state of the patient during the time of examination. It has been demonstrated that mucosal changes varying from erythema to hemorrhage can be provoked by emotional upset. These four patients, however, did not show any unusual reaction to the examinations we performed. While we have no definite explanation for these placebo reactors, our findings emphasize the importance of including a placebo in the protocol of any similar study.

Weiss' gastroscopic study of aspirin and gastric bleeding led him to conclude that persons with peptic ulcer and abnormal mucosa are more susceptible to mucosal injury by aspirin. Our data suggests that susceptibility of the gastric mucosa to injury by aspirin and choline salicylate is not necessarily increased by the presence of pre-existing peptic ulcer or other mucosal abnormality.

REFERENCES

Danao and Schuman


6. Broh-Kahn R. H.: Pharmacologic and clinical studies with choline salicylate, abstracted in 

7. Broh-Kahn R. H.: Choline salicylates: A new, effective and well-tolerated analgesic, anti-
   inflammatory, and anti-pyretic agent. 

   salicylate therapy. 

9. Scully F. J.: Choline salicylate: An effective, well-tolerated drug for treatment of rheu-
   matic diseases. 


    aspirin and certain other substances on the stomach. 

    action. 

    *Gastroenterology* 44:419-23, April 1963.

    gastroscopic study. 

    of the effect of pH. 

    observations, with review of literature. 


    in the rat. 

22. Davison, C., Hertig D. H., and DeVine, R.: Gastric hemorrhage induced by nonnarcotic 
    analgesic agents in dogs. 

23. Levy G.: Comparison of dissolution and absorption rates of different commercial aspirin 
    tablets. 


25. Matsumato K. K. Grossman M. J., Quantitative measurement of gastrointestinal blood 
    loss during ingestion of aspirin. 

