Evaluation of Oral Dilution as a First Aid Measure in Poisoning

By METTA LOU HENDERSON, ALBERT L. PICCHIONI, and LINCOLN CHIN

Dilution with large volumes of water is a widely recommended first aid measure for the treatment of poisoning from ingested chemical agents. In view of the lack of experimental work to support its clinical application and of possible adverse effects that may attend its use, further investigation was undertaken to determine the influence of oral dilution on blood levels of sodium pentobarbital, quinine hydrochloride, and aspirin. The results indicate that oral dilution with large volumes of water increases the rate and degree of gastrointestinal absorption of pentobarbital and quinine, although it has no significant effect on the absorption of aspirin. In view of the possibility of enhanced gastrointestinal absorption of certain chemicals caused by oral dilution, it is suggested that this procedure not be employed as a first aid treatment for ingested systemic poisons.

DILUTION with large volumes of water or other fluids is a widely recommended first aid measure for the treatment of poisoning from ingested chemical agents (1–4). This procedure is based on the belief that dilution will slow absorption of a chemical from the gastrointestinal tract by increasing the amount of fluid that must be absorbed for a given amount of poison (4). However, no experimental evidence has been presented to support this view. Indeed, a study by Ferguson (5) showed that oral median lethal doses (LD_{50}s) of a number of drugs in rats vary inversely with the volume of water in which a drug is administered. In contrast to the above view, the observations of Ferguson would seem to imply that dilution of an ingested chemical may enhance rather than retard its absorption from the gastrointestinal tract.

In view of the lack of experimental work to justify the use of oral dilution in poisoning, and of the possible adverse effects that may attend its use, further investigation of this recommended procedure seems warranted.

The present investigation was designed to determine the influence of oral dilution with water on blood levels of certain chemicals, since the blood concentration of a chemical compound is related to its rate of absorption from the gastrointestinal tract. Sodium pentobarbital, quinine hydrochloride, and aspirin were selected as representative chemical compounds for this project. Barbiturates, in general, are absorbed from the stomach (6, 7) and small intestine (6–9). Quinine is predominantly absorbed from the small intestine (10, 11). Aspirin is considered to be readily absorbed from both the stomach and small intestine (7, 12, 13). The results obtained constitute the basis of this report.

EXPERIMENTAL

Female Sprague-Dawley rats weighing 170–295 Gm. were fasted for 24 hr. and divided into control and test groups of five to nine animals. They were allowed free access to water except during the last hour prior to testing. All drugs were given by oral intubation in a volume of 2 ml./Kg.; 1 min. later the control animals were administered a small volume of water (1 ml./Kg.) by gavage and the test animals were administered a large volume of water (20 ml./Kg.). At each time period after drug treatment, as indicated below, a control group and a test group of animals were anesthetized with ether and blood samples collected from the abdominal aorta for analyses. The difference in the concentrations of each drug in the blood of test and control animals at each time period was statistically compared by means of Student's t test (14).

Pentobarbital.—Control and test animals were administered sodium pentobarbital,[1] 25 mg./Kg., calculated as the base. Blood samples were collected 10, 20, 40, 80, 160, and 320 min. after drug treatment and extracted and analyzed for pentobarbital by the method of Goldbaum (15) as modified in this laboratory (16).

Quinine.—Control and test animals were administered quinine hydrochloride, 100 mg./Kg., calculated as the base. Plasma samples were collected 15, 60, and 120 min. after drug treatment and extracted and analyzed for quinine by the fluorimetric procedure described by Brodie and Udenfriend (17); measurements of fluorescence were made with an Aminco-Bowman spectrophotofluorometer.

Aspirin.—Control and test animals were administered aspirin, 200 mg./Kg., as an aqueous suspension.[2] Plasma samples were collected 5, 15, and 60 min. after drug treatment and analyzed for salicylate by the method of Trinder (19). At the 5-min. time period, the plasma samples were incubated in a water bath at 37° for 2 hr. to ensure that all of the aspirin was hydrolyzed to salicylic acid (20).[3]

RESULTS

Pentobarbital.—The results of the pentobarbital study are presented in Fig. 1. Ten minutes after the administration of pentobarbital the blood concentration of the drug in test animals was 33% higher than in control animals, but the difference is not statistically significant ($p > 0.05$). At the 20- and 40-min. time periods, the pentobarbital levels of test animals were 90 and 78% greater than those of corresponding control animals, respectively. These elevated blood levels of pentobarbital are significantly higher than the control levels ($p < 0.01$). By the 80-, 160-, and 320-min. time periods

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[1] Sodium pentobarbital was supplied through the courtesy of Abbott Laboratories, Chicago, Ill.

[2] The aspirin was triturated in a mortar and sifted through a 100-mesh sieve in order to provide a more uniform suspension and to reduce variability in absorption (18).

[3] Preliminary studies in this laboratory demonstrated that aspirin was completely hydrolyzed to salicylic acid in plasma collected 15 and 60 min. after drug treatment; hence, plasma was not incubated at these two time periods.

the blood pentobarbital concentrations of the test animals were similar to those of the corresponding control animals ($p > 0.05$).

Quinine.—The results of the quinine study are presented in Fig. 2. At the 15-, 60-, and 120-min. time periods the plasma concentrations of quinine in the test animals were 138, 72, and 62.5% higher than those of the corresponding control animals. These values are statistically significant ($p < 0.05$).

Aspirin.—The results of the aspirin study are presented in Fig. 3. The plasma levels of aspirin in test animals did not differ significantly from those of the corresponding control animals during the 5-, 15-, and 60-min. time periods ($p > 0.05$).

DISCUSSION

The results of the present study indicate that oral dilution with large volumes of water increases the rate and degree of gastrointestinal absorption of pentobarbital and quinine, although it has no significant effect on the absorption of aspirin.

Some factors which influence the absorption of drugs from the gastrointestinal tract include: (*a*) degree of ionization of the drug, (*b*) lipoid solubility of the nonionized form of the drug, (*c*) gastric emptying time, (*d*) concentration of the drug in the digestive system, (*e*) solubility of the drug in the digestive system, and (*f*) size of the area over which the drug is spread (6–10, 21–24). Oral dilution with a large volume of water would affect factors (*c*), (*d*), and (*f*).

Since barbiturates are absorbed from the intestine (6–9) as well as from the stomach (6, 7) by nonionized diffusion (8), gastric emptying time probably has only a slight influence on the absorption rate of pentobarbital. The large volume of water administered to the test rats would decrease the concentration of pentobarbital in the gastrointestinal tract and tend to reduce the rate of absorption. However, oral dilution causes a marked increase in surface area over which absorption may take place; this factor undoubtedly exerts a more significant effect on gastrointestinal absorption of pentobarbital than does the factor of concentration of the drug in the digestive system.

Quinine is poorly absorbed from the stomach (7, 10), but it is readily absorbed from the small intestine (10, 11). Hence, hastening the passage of the drug from the stomach into the intestine by oral dilution would tend to allow intestinal absorption to start sooner in the test animals than in the control animals. However, the higher plasma quinine levels in the test animals are most likely due to the increase in surface area for absorption in the intestine.

Aspirin is readily absorbed from the stomach and small intestine (7, 12, 13). Martin (12) states that gastrointestinal absorption is very rapid and complete. In the present study, since the plasma salicylate concentration of the test rats is no higher than that of the control rats, it could be postulated that aspirin is absorbed so rapidly and completely that oral dilution has no significant effect on gastrointestinal absorption of this drug.

Dreisbach (4), who has recommended oral dilution as a first aid treatment in poisoning, warns that the volume of fluid given should not exceed the capacity of the stomach, otherwise the noxious material may be forced into the intestine and absorption would be increased. However, due to the increased surface area for absorption in the stomach following oral dilution, absorption is likely to be enhanced even in the absence of gastric emptying.

Although the present investigation involves only three chemical agents, it appears logical to conclude that oral dilution would generally be ineffective in retarding the gastrointestinal absorption of ingested chemicals. The act of dilution with water cannot occur without a concomitant increase in volume and a consequent increase in surface area from which absorption of a chemical can take place. In view of the possibility that oral dilution may enhance gastrointestinal absorption of chemicals, it is suggested that this procedure not be employed as a first aid treatment for ingested systemic poisons.

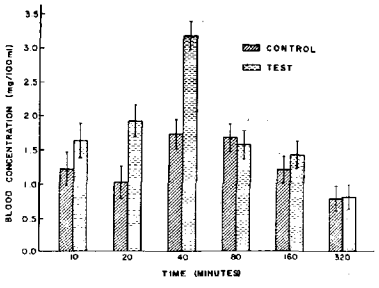

Fig. 1.—The effect of oral dilution on blood pentobarbital concentration. Bracketed lines represent 95% confidence limits. Key: control, 1 ml. water/Kg.; test, 20 ml. water/Kg.

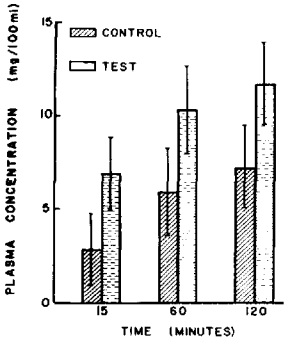

Fig. 2.—The effect of oral dilution on plasma quinine concentration. Bracketed lines represent 95% confidence limits. Key: control, 1 ml. water/Kg.; test, 20 ml. water/Kg.

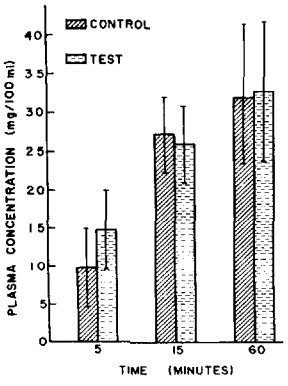

Fig. 3.—The effect of oral dilution on plasma aspirin concentration. Bracketed lines represent 95% confidence limits. Key: control, 1 ml. water/Kg.; test, 20 ml. water/Kg.

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Quantitative Determination by Thin-Layer Chromatography of Anhydrotetracyclines in Degraded Tetracycline Tablets

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A two-dimensional thin-layer chromatography (TLC) procedure on microcrystalline cellulose is presented for the quantitative determination of anhydrotetracycline and epianhydrotetracycline in degraded tetracycline tablets. Initial development is performed with 0.1 *M* EDTA–0.1 per cent ammonium chloride solution to separate the anhydrotetracyclines (R_f 0.34–0.38) from the tetracycline (R_f 0.72) and methanol-soluble excipients. Anhydrotetracycline (R_f 1.0) and epianhydrotetracycline (R_f 0.52) are then resolved by developing the chromatogram with chloroform which has been saturated with the same EDTA–ammonium chloride solution. A complete assay for these anhydro compounds can be performed in less than 2 hr.

POOR RESOLUTION and/or excessive development time has characterized previous chromatographic attempts to separate tetracycline (TC) and its major degradation products, anhydrotetracycline (ATC) and 4-epianhydrotetracycline (EATC). The latter was recently incriminated in the reversible renal dysfunction (Fanconi-type syndrome) caused by the ingestion of degraded TC products (1–7).

In a qualitative examination of TC and its anhydro derivatives by radial chromatography, using water-saturated butanol on silica gel, Rustici and Ferappi (8) obtained the following similar R_f values after 2 hr. of development: TC (0.36), ATC (0.50), and EATC (0.40). When Kelly and Buyske (9) employed paper which had been impregnated with 0.1 *M* EDTA solution and the solvent system *n*-butanol–ammonium hydroxide–water (4:1:5), they obtained the following 16 hr. R_f values: TC (0.39), ATC (0.62), and EATC (0.40). In a recent paper (10) the authors reported the quantitative analysis of ATC from TC test mixtures by TLC on microcrystalline cellulose. This method required only 20 min. development with 0.1% ammonium chloride solution to give R_f values of 0.38 and 0.72 for the ATC and TC, respectively. Subsequent experiments revealed that mixtures of EATC, ATC, and TC are partially resolved by the same chromatographic system, but overlapping of the ATC (0.38) and EATC (0.34) occurred. In order to completely resolve the two anhydro-compounds, two-dimensional chromatography was attempted. The findings of Kelly (11) that ATC and EATC can be separated by partition chromatography employing buffered 0.1 *M* EDTA solution (pH 7.8) as stationary phase and buffer saturated chloroform as moving phase, prompted the authors to utilize these findings in their search for a suitable second solvent system. By developing the chromatogram with 0.1 *M* EDTA (disodium salt)–0.1% ammonium chloride solution (pH 4.5), followed by chloroform which had been saturated with the same EDTA–ammonium chloride solution, complete resolution of the ATC (1.0) and EATC (0.52) occurred. On altering the pH of the aqueous phase between 3.5 and 8.0, R_f values for ATC (1.0) and TC (0.17) were observed to remain constant in the second development;

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