THERAPEUTIC ASPECTS OF ASPIRATION PNEUMONITIS IN EXPERIMENTAL ANIMALS

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THE aspiration of vomitus into the lungs has always been recognized as a dangerous complication of general anesthesia. Many authors have discussed the predisposing causes of vomiting during anesthesia, and have rightly emphasized its prevention.[1-8] However, there has been little study of the treatment of pneumonitis which constitutes the greatest hazard of aspiration of vomitus. Since this complication continues to occur, better knowledge of its treatment would be useful.

Fortunately the etiology of aspiration pneumonitis has been carefully investigated. Mendelsohn, in 1946, published the results of an extensive study of etiology of the lesions produced by inhalation of liquid vomitus.[9] He concluded that hydrochloric acid, rather than gastric enzymes or bile, caused the lesions. Teabeaut, in 1952, confirmed Mendelson's findings, and also demonstrated that in order to produce pneumonitis, the aspirated liquid must have a *p*H of less than 2.5.[10] Teabeaut also found that semisolid gastric contents composed of partially digested meat or vegetables produced pneumonitis regardless of its *p*H.

By utilizing the findings of Mendelson and Teabeaut it is possible to produce the lesions of aspiration pneumonitis in experimental animals. The present study was undertaken to test the effects of several local and systemic forms of treatment on the acid lesions. The local treatment consisted of instillations of alkaline and neutral solutions into the lungs in the hope of so diluting or neutralizing hydrochloric acid that the lesions would be altered. The systemic effects of antibiotics and hydrocortisone on acid lesions in the lung were also studied.

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METHODS

While rabbits, ranging in weight from 1.95 to 4.40 kg., were anesthetized with ether and were intubated. A light plane of anesthesia was maintained in order that breathing and the cough reflex would be present, as in the induction phase of anesthesia. Following intubation, hydrochloric acid solution, 4 cc./kg. of body weight, was instilled into the trachea. The *p*H of the solutions used ranged from 1.50 to 1.82. The animals were turned from side to side during the injection in order to insure dispersion of the acid solution into both lungs. Since the animals were breathing, extensive distribution of the solutions was usually obtained. All animals were sacrificed 48 hours following the instillation of the acid solution. Gross and microscopic examinations of the lungs were performed.

Group A (Controls). Hydrochoric acid solution, *p*H 1.60 to 1.82 4 cc./kg., was instilled into the lungs of eight animals which received no further treatment. These animals were used to assess the type and extent of the lesions produced. Six animals received no hydrochloric acid, but were used to test the effects of several treatment solutions on the lungs. Solutions of sodium bicarbonate 3.75 and 1.87 per cent, molar lactate 0.1*N*, calcium gluconate 5 per cent, and sodium hydroxide 0.1*N* were instilled into the lungs in volumes of 4 cc./kg. and the effects of these chemicals was assessed.

Group B. Nineteen animals had acid solutions instilled into the lungs in the manner explained above. Two minutes following the injection of the acid solution, treatment solutions were injected into the lungs. The volumes and concentrations of these solutions are given in detail in table 1. The animals were sacrificed and examined 48 hours following the experiments.

TABLE 1

RESULTS OF EXPERIMENTALLY PRODUCED LESIONS OF ASPIRATION PNEUMONITIS IN RABBITS

Animals	Agents	Amount	Concentration	Results
Group A				
5	HCl	4 cc./kg.	*p*H 1.82	Lesions involve 50 to 90 per cent of lungs.
3	HCl	4 cc./kg.	*p*H 1.60	Very extensive lung damage, approaching 100% in all animals.
1	$NaHCO_3$	4 cc./kg.	3.75%	Little gross evidence of lung damage. Some mononuclear
1	$NaHCO_3$	4 cc./kg.	1.87%	infiltration.
2	Molar Lactate	5 cc./kg.	0.1*N*	Small lesion in one lobe, peribronchial infiltration.
1	Ca Gluconate	4 cc./kg.	5%	Mild inflammatory reaction.
1	NaOH	4 cc./kg.	0.1*N*	Extensive inflammatory and hemorrhagic lesions.
Group B				
3	HCl Normal Saline	4 cc./kg. 3 cc./kg.	*p*H 1.82 0.85%	Very extensive lung damage, consisting of necrotizing lesions.
1	HCl $NaHCO_3$	4 cc./kg. 1.36 cc./kg.	*p*H 1.6 7.5%	Animal died within 1 hour, extensive necrotizing lesions.
1	HCl $NaHCO_3$	4 cc./kg. 2 cc./kg.	*p*H 1.6 1.87%	Very extensive hemorrhage and consolidation.
8	HCl $NaHCO_3$	4 cc./kg. 2 cc. each lung	*p*H 1.8 7.5%	One animal had extensive bilateral lesions. Other animals had severe damage in one lung, and small lesions in the contralateral lung.
1	HCl NaOH	4 cc./kg. 3 cc./kg.	*p*H 1.6 0.5*N*	Lungs almost completely consolidated. Died in forty-five minutes.
2	HCl NaOH	4 cc./kg. 3 cc./kg.	*p*H 1.6 0.1*N*	Lungs almost completely consolidated and hemorrhagic.
1	HCl Molar Lactate	4 cc./kg. 3 cc./kg.	*p*H 1.6 0.1*N*	Very extensive consolidation and hemorrhage. Animal died within 36 hours.
1	HCl Ca Gluconate	4 cc./kg. 3 cc./kg.	*p*H 1.5 5%	Animal died within 36 hours. Massive necrotizing lesions.
1	HCl Ca Gluconate	4 cc./kg. 3 cc./kg.	*p*H 1.5 2.5%	Animal died within 36 hours. Massive necrotizing lesions.
Group C				
6	HCl Penicillin Streptomycin	4 cc./kg. 100,000 units 0.25 Gm.	*p*H 1.75 q. 6 hours q. 6 hours	Extensive lung damage in four animals. Less widespread, but significantly large lesions in two animals.
Group D				
1	HCl Hydrocortisone	4 cc./kg. 25 mg.	*p*H 1.75 q. 6 hours	Lesions well circumscribed and much less extensive than in control animals.
3	HCl Hydrocortisone	4 cc./kg. 50 mg.	*p*H 1.78 q. 6 hours	Major portions of all lungs well aerated.
Group E				
4	HCl Hydrocortisone Penicillin Streptomycin	4 cc./kg. 50 mg. 100,000 units 0.25 Gm.	*p*H 1.7 q. 6 hours q. 6 hours q. 6 hours	No large lesions. Lungs well aerated. Lesions present well circumbscribed.

Group C. Six animals had acid solutions instilled into the lungs and then received intramuscular injections of streptomycin 0.25 Gm. and penicillin 100,000 units every six hours until they were sacrificed after 48 hours.

Group D. Four animals had acid solution instilled into the lungs and then received intramuscular injections of hydrocortisone every six hours until they were sacrificed 48 hours later. One animal received doses of 25 mg. and three animals received doses of 50 mg. of hydrocortisone.

Group E. Four animals had acid solution instilled into the lungs and then received intramuscular injections of hydrocortisone 50 mg., streptomycin 0.25 gm. and penicillin 100,000 units every six hours until sacrificed 48 hours later.

RESULTS

The results of the various experiments are summarized in table 1. The typical lesions of aspiration pneumonitis were consistently produced in the control animals, and in almost

all of these animals the damage was extensive. The treatment solutions, normal saline, sodium bicarbonate, tenth molar lactate, and calcium gluconate produced either no damage or slight damage to the lungs of the animals. One-tenth normal sodium hydroxide solution, however, was found to be as harmful to the lungs as hydrochloric acid.

The instillation of small amounts of sodium bicarbonate solution into the lungs did not consistently prevent extensive damage. In the majority of these animals lesions were much more extensive in one lung than in the contralateral lung. This could be interpreted as being due to experimental error. Perhaps, the hydrochloric acid failure to disperse well through the slightly damaged lungs, or the sodium bicarbonate solution failed to enter the badly damaged lungs. In view of the fact that some of the animals used in the experiment had extensive bilateral damage, the possibility of neutralizing hydrochloric acid by this method seems to be unlikely.

The instillation of large volumes of solutions of normal saline, sodium bicarbonate, sodium hydroxide, tenth molar lactate, and calcium gluconate aggravated the effects of hydrochloric acid rather than preventing them. It would appear that a large volume of fluid introduced into the tracheo-bronchial tree served only to push the hydrochloric acid already present into the alveoli. Mixing of diluent or neutralizing solutions with the acid is probably impossible because of the tiny interfaces existing between solutions in the bronchioles. The rapidity with which hydrochloric acid produces its damage to the alveoli is probably also a factor.

The administration of streptomycin and penicillin failed to protect the lungs from the effects of hydrochloric acid in all instances. This would only tend to confirm Teabeaut's conclusion that microorganism play no part in producing aspiration pneumonitis.

Hydrocortisone administered following the instillation of hydrochloric acid appeared to restrict the effects of the acid to much smaller areas than were found in the control animals. While typical lesions were found in some animals, the lesions involved much smaller portions of the lungs. In one animal, so treated, neither gross nor microscopic lesions were found. In animals receiving both hydrocortisone and antibiotic therapy the lesions were found to be insignificant on gross and microscopic examination.

Discussion

The results of the experiments performed in this study reveal that irrigation of the lungs with large volumes of alkaline or neutral solutions following the instillation of hydrochloric acid is dangerous. The volumes of the irrigating solutions used in these experiments were quite large, being comparable to volumes of fifty to two hundred cubic centimeters in an adult human. It is not necessary to infer from these results that irrigation of a patient's trachea with small amounts of normal saline for the purpose of loosening secretions is contraindicated. It does appear to be wise, however, to restrict the volumes of irrigating solutions to ten cubic centimeters and to aspirate it promptly. The danger of spreading the vomited material should be borne in mind when the anesthetist employs tracheal irrigation.

On the other hand, the administration of hydrocortisone to have afforded protection against extensive lung damage. (Cross examination of the lungs of animals treated with hydrocortisone revealed much smaller areas of damage than were found in the control animals. Microscopic examination showed that the histology of the lesions in the hydrocortisone treated animals was similar to that found in the controls. Hydrocortisone, thus appears to have prevented the extension of the acid lesions in all animals which received this hormone.

While the anti-inflammatory effect of the adrenocortical steroids has been studied for over ten years, the mechanism by which the steroids produced this effect has not been discovered. One theory which may explain the experimental findings of this study has been stated by Dougherty and Schneebeli as follows: "Cellular injury is not in itself an inflammatory response. It is rather a stimulus to the development of the series of events grouped inclusively under the term inflammation. For example, burned tissue is not an inflammation, but the reaction to the burned tissue is an inflammation. It is clear, then,

that adrenocortical hormones do not inhibit the production of the initiating stimulus which triggers the chain reaction of the inflammatory response. These hormones probably exert their antiphlogistic action by interrupting the chain reaction of cellular destruction triggered by the injurious stimulus. According to this point of view, inhibition of inflammation is exerted by preventing the release and enhancing the removal of substances coming from injured cells." [11]

The lethal effects of aspiration of vomitus into the lungs appear to be caused by the overwhelming inflammatory reaction to the lesions which the acid produces in the alveoli. This appeared to be true in one fatal case of aspiration pneumonitis which occurred at Hartford Hospital. The lungs of this patient were found to be almost completely consolidated by inflammation at the time of death, three days following aspiration. The conclusion seems inescapable that this patient survived the lesions produced by the aspirated vomitus, but failed to survive the overwhelming inflammatory response to the initial lesions.

Clinical evidence supports the experimental findings of this study. Marshall and Gordon reported that hydrocortisone ameliorated the effects of aspiration pneumonitis in twelve patients whom they observed.[12] Four patients with radiologic evidence of extensive pneumonitis following aspiration were treated with hydrocortisone at Hartford Hospital. All four patients had a benign course and prompt recovery. While clinical impressions must be carefully evaluated, especially when they are based upon only a few patients, they may provide some aid in judging the effectiveness of therapy. The value of hydrocortisone as an adjuvant to the treatment of aspiration pneumonitis is supported by both experimental and clinical evidence.

Summary

Etiology of aspiration pneumonitis has been reviewed.

Aspiration pneumonitis was produced experimentally by introducing hydrochloric acid solution into the lungs of rabbits.

Attempts were made to prevent pneumonitis by introducing a diluent solution (normal saline) and neutralizing solutions (sodium bicarbonate, sodium hydroxide, tenth molar sodium lactate and calcium gluconate) into the rabbit lungs, following the introduction of hydrochloric acid. No beneficial effects of this type of therapy were noted, rather the pneumonitis was worse in many cases.

Antibiotic therapy following the instillation of hydrochloric acid solution in rabbit lungs also failed to alter the severity of the pneumonitis.

Hydrocortisone administered to the animals when given alone and in combination with antibiotics strikingly alleviated the severity of pneumonitis following the instillation of hydrochloric acid in the rabbit lungs. The anti-inflammatory effects of hydrocortisone have been discussed.

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