Alcohol Vapor by Inhalation in the Treatment of Acute Pulmonary Edema

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Accepted therapy of pulmonary edema is contraindicated in shock, central nervous system lesions, or pregnancy. Diagnosis of the underlying disease is not always immediately possible. Alcohol inhalation, previously tested in animals, changes surface tension of the foam and has beneficial effects. Clinical experience has revealed prompt relief in over one-half of the acute cases, definite improvement in another 29 per cent. Some cases with subacute edema also exhibited decreased foaming. The absence of contraindications and the possibility of using the method in conjunction with other procedures are favorable elements of alcohol therapy by inhalation.

Notwithstanding conventional therapy, mortality associated with acute pulmonary edema remains high. The need for other generally applicable methods of treatment is evident. In evaluating such new procedures, the following factors should be considered:

(a) Possibility of Shock. Several types of acute pulmonary edema occur in conditions where there is impending shock, whether cardiogenic (myocardial infarct, extreme bradycardia of A-V block) or peripheral (trauma, burns, certain cases of brain lesions). Among the accepted therapeutic procedures are the use of morphine, phenobarbital and other barbiturates, chloral hydrate, spinal anesthesia, venesection, mercurial diuretics, and positive pressure respiration. One of the main effects of these procedures is to decrease venous return which may be followed by irreversible shock.

(b) Central Nervous System Lesion. Other types of acute pulmonary edema are associated with injury to or lesions of the central nervous system (cerebral hemorrhage, thrombosis, or embolism; subarachnoid hemorrhage; poliomyelitis; tetanus; skull fracture). Anesthetics and sedatives are generally contraindicated because they may cause respiratory paralysis or shock.

(c) Pregnancy. Acute pulmonary edema may complicate pregnancy or labor. Large doses of morphine and mercurials might be detrimental to the fetus.

For these reasons, one of us studied a new approach based on the use of antifoaming agents by inhalation and demonstrated its favorable action in experimental pulmonary edema. The present study reports the first results of similar treatment in man.

Part I. Methods of Clinical Administration and Determination of Tolerance of Alcohol by Inhalation

Before attempting to administer alcohol by inhalation to patients with acute pulmonary edema, it was necessary to determine the best method for use in man and to establish the toleration of this procedure by normal subjects and cardiac patients.

Procedure

Six normal subjects, two postoperative patients, and two cardiac patients were selected for this preliminary study. Blood tests for alcohol content in the blood serum before and after 30 minutes of alcohol inhalation were done in two normal subjects. Blood pressure and pulse rate were determined in all subjects before starting the inhalation and every five minutes throughout the experiment. Reaction to stimuli was observed, and subjects were asked to state their subjective sensations at five minute intervals.

Method 1. Use was made of the standard equipment for gas anesthesia. The method of rebreathing with carbon dioxide absorption was used in order

*Titration was made by using the potassium dichromate method according to Harger.
to increase the alcohol concentration of the vapor. A wick-type vaporizer was filled with 95 per cent alcohol. Pure oxygen was administered first by bag and mask; then an increasing amount of alcohol vapor was given until the maximum capacity of the vaporizer was reached. The subjects inhaled the full concentration for about 30 minutes. The alcohol concentration thus reached was never found difficult to breath. It provoked coughing in only one person; one normal subject started to laugh. In all subjects it produced mild euphoria and slight drowsiness.

In the normal subjects, only insignificant changes in blood pressure and pulse rate were observed. In one, marked sinus arrhythmia was noted after five minutes, but subsided later. Serum concentration of alcohol was found to be less than 10 mg. per 100 cc. after 30 minutes.* The two cardiac patients, a 67 year old man with coronary heart disease and heart failure, and a 62 year old woman with hypertensive heart disease and heart failure, had been previously digitalized. Their tolerance of alcohol inhalation was good. The blood pressure rose from 160/85 to 180/95 in one case, and persisted unchanged in the other. Their pulse rates did not change. Both stated that they were feeling “better” after the inhalation.

Method 2. In order to devise a simpler and safe standard technic for routine use, another method was employed in other experiments. The device consisted of an oxygen tank, a two-stage adjustable pressure regulator, a Bourdon-type flowmeter, a positive pressure mask, and a special type of vaporizer. The vaporizer used (Model 15, Ohio Heidbrink Humidifier) utilizes the principle of jet atomization to make a gas into a fog which is further bubbled through several inches of fluid (in this case, alcohol) for increased saturation. In the course of our experiments, it soon became evident that 30 per cent alcohol in the vaporizer should be used with the meter mask. In order to achieve about 100 per cent oxygen concentration, a flow of oxygen of 10 to 12 liters per minute is necessary for the average person. Collapse of the collecting bag at the end of inspiration indicates need of higher oxygen flow. The flow of oxygen through the alcohol should be started slowly (about 3 liters per minute) in order to obtain a slight local anesthesia before higher concentrations can be tolerated. By slowly increasing the rate, a 10 liter flow was well tolerated at the end of about five minutes. It should be kept in mind that the amount of alcohol vaporized increases with the flow of oxygen.

In healthy adults studied with method 2, essentially the same results were observed as in the previous series, namely, slight euphoria and slight changes of pulse and blood pressure: slight increase of blood pressure (10 to 20 mm. systolic) during the inhalation, slight decrease after removal of the mask.

Method 3. Some patients with pulmonary edema do not tolerate a mask for any length of time because of cough and expectoration, or a smothering feeling. For these patients, an alternate method was devised during the course of the therapeutic experiment. The pressure gage, flowmeter and vaporizer all the same as described in method 2. The vaporizer is filled to the appropriate level with 95 per cent alcohol; a nasal catheter is placed into the nasopharynx and is then connected to the vaporizer. The flow is started at a rate of 2 to 3 liters per minute and then gradually increased to 7 or 8 liters per minute within three to five minutes, as tolerated by the patient. The patient should be instructed to avoid oral respiration.

Method 4. A technic of diffusing alcohol vapor into an open tent was discarded early in the therapeutic experiment because of discomfort to the patient.

Discussion

These four methods were studied in order to apply alcohol vapor inhalation to clinical cases of acute pulmonary edema. The desired effect is based on the antifoaming action of alcohol exerted locally in the air passages and not on any systemic effect. For this reason, finding that after 30 minutes of inhalation only an extremely small concentration of alcohol was present in the blood was accepted as favorable. Of the various methods, method 2 (mask) combines the effects of pressure breathing with those of alcohol therapy. On the other hand, method 3 (nasal catheter) permits the patient to expectorate; it fails to induce a feeling of suffocation; and has been found easier to use. Method 3 was used in most of the patients studied in part II of this report.

Conclusions of Part I

Alcohol vapor by inhalation is well tolerated by normal subjects and cardiac patients. Four methods have been studied. The two most practical are:

(a) One employing a nasal catheter.
(b) One making use of a positive pressure mask.

The concentration of alcohol detected in the blood was small; its general effects were negligible.

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* According to Goodman and Gilman,12 a blood concentration of alcohol of 100 mg. per 100 cc. is associated with intoxication in only about one fourth of the subjects.
PART II. Administration of Alcohol Vapor by Inhalation to Clinical Cases

Results

The results of our study are summarized in tables 1 and 2.* A total of 14 patients received alcohol treatment for 17 acute attacks of paroxysmal pulmonary edema. In addition, seven other patients with pulmonary edema of longer duration and not necessarily paroxysmal in nature also received treatment.

Classified according to primary etiologic condition, the diagnoses in the acute cases were as follows:

Hypertensive heart disease.................. 10
also coronary heart disease............. 3
also pregnancy at term...................... 1
also chronic glomerulonephritis and uremia... 1
also excoriation of the aorta........... 1
others........................................ 4
Coronary heart disease (7 weeks after a myocardial infarct)......................... 1
Rheumatic valvular disease................... 1
Various........................................ 2
Total........................................... 14

Seven of these attacks were very severe, while all others were severe. In three attacks (nos. 1, 8 and 13), the attending physicians declared that they "had never observed a more severe attack." Alcohol inhalation by nasal catheter was well tolerated by all patients, while inhalation by mask was refused by one.

The result of alcohol inhalation in the acute and severe attacks was as follows:

(a) The beneficial result was prompt and marked in 10 attacks (nos. 1, 2, 3, 4, 7, 8, 10, 11, 14, 17) or 58 per cent.
(b) There was definite improvement in five attacks (nos. 9, 12, 13, 15, 16) or 29 per cent.
(c) No improvement was noted in two attacks (nos. 5, 6) or 13 per cent, but in one of them the patient did not tolerate alcohol and in the other the patient objected to it at first and possibly received an inadequate dose.

(d) There was only one fatality (case 5). This patient died four hours after treatment was discontinued.

The seven cases of pulmonay edema of long duration were classified according to the following primary diagnoses:

- Coronary occlusion.......................... 2
- Heart failure (with coronary heart disease in one)................................. 2
- Postoperative complications................. 2
- Pneumonia and anemia........................ 1

Three of the attacks were severe, the other four of medium severity. Marked improvement was observed in one patient (case 4); moderate to slight improvement in two (cases 3 and 6); and doubtful result or no improvement in the other four. When improvement was noted, the sputum lost its foamy quality, becoming more liquid and more easily expelled. The general condition of all patients in this group was very poor to terminal when therapy was instituted.

Case Reports

The following clinical case reports have been selected as illustrative of the dramatic improvement which followed administration of alcohol vapor by inhalation.

Case 1. A woman of 72 years was suffering from hypertensive heart disease with cardiac enlargement and repeated episodes of paroxysmal nocturnal dyspnea. Her blood pressure varied between 150/80 and 180/110, with occasional further increases to 230/130; the latter usually followed by paroxysms of dyspnea or pulmonary edema. Several electrocardiograms, recorded during two years prior to admission, showed evidence of coronary insufficiency.

On Feb. 15, 1951, at 4:45 a.m., the patient experienced a severe choking sensation and started gasping for breath. Soon afterward, yellow-tinged foam poured repeatedly from the nostrils and mouth. The pulmonar squad, immediately called, started oxygen administration at once. An internist, who had been treating the patient, reached the patient’s home at 5:30 and later described the attack as "the most severe observed in his life.” Foam kept pouring from the nostrils and from the patient’s mouth. The pulse was 120; the blood pressure, 170/100. Both lung fields presented diffuse and numerous rales of various caliber up to the gurgling of foam in the trachea. The patient was only partly conscious.
Within a few minutes after the physician arrived, the following medication was given: (a) Pantopon, 1 cc., subcutaneously; (b) aminophyllin, 0.25 Gm., intravenously; (c) Demerol, 100 mg., intravenously. Some degree of general sedation ensued, but the foamy expectoration continued unabated. The nose and pharynx of the patient were cleaned through suction, again without improvement.

At 7 a.m. (more than one hour after the last medication), a large gauze pad, soaked with 40 per cent alcohol was applied over the mouth and nose of the patient and covered with the oxygen mask so that the oxygen flow reached the respiratory passages after becoming surcharged with alcohol vapor. Within 10 minutes, foaming decreased and tracheal gurgle disappeared. At 7:15 a.m. the patient was comfortable and conscious; the number of rales over the lung fields had decreased remarkably. The oxygen mask was removed and the patient was sent to the hospital by ambulance. Upon arrival, only minimal traces of pulmonary edema were found, so that no further medication was considered necessary. The patient was sent home three days later.

The patient died six weeks later following thrombosis of the abdominal aorta and unsuccessful surgical intervention. An electrocardiogram, recorded a few hours before death, revealed a supraventricular tachycardia. No autopsy was obtained.

The impression of the internist concerning the effectiveness of alcohol treatment was so definite that he insisted in reporting the case, in spite of the unusual way by which alcohol had been administered as an emergency procedure. It is noteworthy that all drugs administered should have passed their peak of action long before administration of alcohol vapor.

**Case 8.** A 43 year old Negro woman was admitted to the hospital on Jan. 9, 1951, because of hypertension complicating pregnancy. A para XII, gravida XV, she offered no complaints. Hypertension had been noted during two earlier pregnancies; however, no interim examinations had been performed. Physical examination revealed an obese woman with blood pressure 230/140, pulse 84, temperature 98.6° F., and respirations 20. The size of the uterus was consistent with a nine month pregnancy. Fetal heart tones were heard at a rate of 152 per minute.

Laboratory findings on admission were: hemoglobin 50 per cent (7.8 Gm.); red blood cells 3,120,000, white blood cells 14,200; traces of acetone and protein in the urine; nonprotein nitrogen 19 mg. per 100 cc.; serum protein 5.7 Gm. per 100 cc. (albumin 3.1 Gm. per 100 cc., globulin 2.6 Gm. per 100 cc.); blood uric acid 6.1 mg. per 100 cc.; negative Kahn. The chest film was reported as being within normal limits. The electrocardiogram was interpreted as being within normal limits, with left axis shift.

Shortly after admission, the patient, considered to be a pre-eclamptic, was placed on a modified Stroganoff regime. This included the periodic use of morphine sulfate, magnesium sulfate, and 25 per cent dextrose in water parenterally, and ammonium chloride by mouth. By January 10, the patient's blood pressure dropped to 154/92 and the fetal heart tones could not be heard with certainty. At 1:15 p.m., spontaneous rupture of the fetal membranes was noted.

While lying supine upon a delivery table following sterile vaginal examination, the patient complained of flushing and a choking sensation. She became severely dyspneic, cyanotic, and developed acute pulmonary edema of the greatest severity. At 8:30 p.m., positive pressure oxygen by mask was instituted. Successively, morphine sulfate, 30 mg.; aminophyllin, 0.5 Gm.; atropine sulfate, 0.5 mg.; sodium amytal, 0.5 Gm.; and Digalen, 1 cat unit, were administered intravenously within 15 minutes after the onset. At 9:10 p.m. (40 minutes after these measures were completed), frothy sputum was still being emitted in copious quantity from the delirious patient's mouth.

Administration of alcohol-oxygen vapor according to method 2 was then started by mask, intermittently, under variable pressure and rate of oxygen flow. Improvement was prompt, dramatic and progressive. Within 15 minutes, the foam became more liquid in character so that more effective expectoration was possible. Within 20 minutes, the patient was no longer in severe distress. At the end of 30 minutes, the patient was able to sit up and speak clearly, although with some effort. Bubbling and crepitant pulmonary rales were markedly reduced in quantity. No further alcohol vapor was given. Approximately seven hours later, the patient spontaneously delivered a female infant who required resuscitation.

The patient was re-examined on January 15. Her blood pressure was 185/110 and the pulse, 82. The conjunctivae were pale. A grade 2 apical systolic murmur and grade 3 hypertensive retinopathy (Keith-Wagener) were present. Otherwise, the findings were noncontributory. Seven weeks post partum the patient's status was re-evaluated at the Cardiac Clinic. Although free of complaints, she was found to have a blood pressure of 230/120 and pulse of 88 in both arms; the apex was 4 cm. outside of the left midclavicular line, and a trace of pretilial edema was present. Fluoroscopy revealed left ventricular and probably also left auricular enlargement. A 12 lead electrocardiogram, including standard and unipolar extremity and chest leads, was interpreted as being abnormal and consistent with left ventricular hypertrophy and "strain." Final diagnosis was hypertensive cardiovascular disease and term pregnancy. The infant is free of illness, but somewhat retarded in growth and development.

In summary, this 43 year old woman with asymptomatic hypertensive cardiovascular disease and
term pregnancy developed acute paroxysmal pulmonary edema of the utmost severity. After an unsuccessful trial of conventional forms of medical therapy, oxygen-alcohol vapor was administered and was followed by prompt and dramatic recovery.

Case 14. A 58 year old Negro was admitted to the hospital on April 17, 1951. He was severely dyspneic and gravely ill. History, obtained from relatives and corroborated later by the patient, revealed that the patient had been engaged in his usual occupation of stoking furnaces until 3 p.m. At approximately 6:15 p.m. he experienced a choking sensation and became extremely dyspneic. A physician administered 1 mg. Adrenalin hydrochloride hypodermically, penicillin and Terramycin intramuscularly, and a 0.1 Gm. Nembutal suppository, between 7 and 7:45 a.m. All persons questioned stated that the symptoms continued to increase in severity in spite of the medication.

Past history revealed that the patient had experienced severe headaches and occasional mild dyspnea for more than a year. For six months, the patient had been under medical supervision for hypertension. During the three weeks prior to admission, he had been unable to lie flat in bed.

Physical examination revealed a semicomatose patient with blood pressure 240/140; pulse 156; respiration 60; and rectal temperature 99.2 F. Pink foam was noted at the corners of his mouth. Examination of the ocular fundi revealed mild narrowing and tortuosity of the arterioles. The neck veins were markedly distended. Cardiac dullness extended to the left anterior axillary line in the sixth intercostal space; the heart sounds could not be heard. Loud, moist, crepitant and subcrepitant rales, and rhonchi, were present over both lung fields. Expiration was prolonged. All deep reflexes were hypoactive.

Within a few minutes after arrival at the ward, alcohol-oxygen vapor was administered to the patient by nasal catheter according to method 3. After 15 minutes of therapy, the patient began to expectorate pink liquid material. At the end of 30 minutes, dyspnea had decreased remarkably and the patient was able to speak clearly. Improvement was progressive, subjectively and objectively, being marked at the end of one hour. Thirty minutes later, alcohol therapy was no longer considered necessary. Chest rales were still present but were decreased in number. Later, when the patient was resting, Mercuhydrin, 1 cc., and digitoxin, 1.2 mg. in divided doses, were given. No further digitalization was necessary.

On the following morning, the patient's blood pressure was 170/120; pulse, 102; respiration, 28; and rectal temperature, 101 F. A harsh, short, grade 3 systolic murmur over the aortic area and a loud reduplicated first heart sound at the apex were heard.

Laboratory findings were: urine, specific gravity 1.008 with 3 plus protein on admission and 1 plus protein at the time of discharge; maximum urine concentration of 1.010 and dilution of 1.008 during convalescence; nonprotein nitrogen 43; Kahn test negative. Chest films revealed cardiac enlargement and a "hypertensive contour." Circulation time (magnesium sulfate), during convalescence, was 25 seconds. Serial electrocardiograms, including standard and unipolar limb and chest leads, were recorded. The interpretation was: "abnormal tracing consistent with left ventricular hypertrophy and strain; vertical position with clockwise rotation."

On April 27, the patient was discharged free of symptoms to the Cardiac Clinic with the diagnosis of "hypertensive cardiovascular-renal disease."

In summary, this 58 year old Negro with hypertensive cardiovascular-renal disease developed acute paroxysmal pulmonary edema of the utmost severity. After approximately two and one-half to three hours of unabated progression, during which time no medication generally considered useful in this condition was given, alcohol-oxygen vapor was administered. Progressive and prompt recovery ensued.

Discussion

Selection of Cases. Evaluation of the usefulness of a new method of treatment in a paroxysmal, often fatal, syndrome is by no means easy. In order to insure the maximum objectivity of judgment, these patients have been observed by several members of the house staff in two different hospitals. In addition, most of the patients have been studied during and after the attack by one of us. The possibility of statistical comparison between two groups of patients, those tested with accepted procedures only, and those treated with these plus alcohol was considered at first; however, it did not seem practical because of the wide variety of causes, the extreme variability in the severity of the attacks, the differences in age and general health of the patients studied, and the fact that the judgment of various physicians was involved. Such variables would make the statistical validity of even a much larger group questionable. Therefore, the following plan was devised:

(a) The severity of the attacks was graded from 1 plus to 4 plus as follows: slight, 1 plus; moderate, 2 plus; severe, 3 plus; extremely severe, 4 plus. Only severe and extremely severe
cases of acute pulmonary edema (table 1*) were considered for alcohol treatment in order to exclude spontaneous recovery. In general, only the acute cases were accepted (table 1). However, early in the study, cases with a prolonged course were also accepted for treatment (table 2*) in order to evaluate the results in this type of pulmonary edema.

(b) The responsible physician was allowed to use any of the accepted procedures including drugs, venesection, oxygen, and positive pressure respiration. If, a suitable interval having elapsed, the attack continued unabated in spite of the above procedures, then alcohol inhalation was started. This plan was adopted in order to avoid the objection that life-saving procedures and drug therapy had been omitted to the possible detriment of the patients. Moreover, some patients came to the hospital after having received initial medication. On the other hand, in spite of this program, in three attacks (nos. 12, 14, 17) no other accepted treatment for acute pulmonary edema was received before or during alcohol vapor therapy since response to this method was prompt and most satisfactory.

Evaluation of the Results. As already stated, only severe and very severe acute attacks were treated. In most of them, accepted procedures had been proved unsuccessful or no other treatment had been given. In some of them, death was considered imminent. Survival could not be taken as the only measure of success because in several clinical conditions the attack of pulmonary edema is merely one of the aspects of the syndrome and death may take place hours or days later because of the underlying basic disease (myocardial infarct, heart failure). For this reason, great attention was paid to objective and subjective evidence of improvement. Change from unconsciousness to consciousness; from labored respiration to even and slower breathing; from inability to speak to ability to even hold one's breath; from pale, taut face to a more normal aspect; slowing of the pulse; reduction of cyanosis; and auscultatory evidence of decrease in number and extension of pulmonary rales, were accepted as evidence of improvement. In particular, evidence that the sputum decreased in quantity, and that from a foamy, bubbling, abundant material it changed to small amounts of liquid or thick expectorate was taken as indication that the surface tension of the foam had been changed and that its content of air was diminished.

On the basis of the above data, it was considered that alcohol therapy was useful in 87 per cent of the attacks and dramatically so in 58 per cent of them.

This study suggests that the new method of treatment being discussed is worthy of use in cases of acute pulmonary edema of varied etiology whether or not other drugs or devices are also used.

Alcohol inhalation should be started at the earliest possible time and continued as long as required to produce a desirable effect. It should be tried again after initial sedation in the exceptional cases of poor toleration. When only the usefulness of therapy is involved, no waiting period should be allowed, and full use should be made of the combined effect of alcohol vapor and therapy of any other kind not specifically contraindicated.

In the acute, severe type of pulmonary edema, it is frequently impossible to ascertain the specific underlying disease responsible during the critical period. For this reason, a universally applicable treatment is particularly desirable.

Conclusions of Part II

Alcohol vapor has been administered to patients with acute pulmonary edema of severe or extremely severe type after failure of conventional medication. Improvement was prompt and marked in 58 per cent, definite though less prompt in another 29 per cent. Tolerance of this therapy has been generally good. No specific contraindications to its use have been established.

Alcohol vapor was also administered to seven patients with subacute, prolonged pulmonary edema, all of whom were considered unlikely to survive. Clinical evidence of decrease of the foaming process was observed in three cases, even though the fatal course of the underlying
condition (myocardial infarct, heart failure) caused death later on. Improvement was neither as prompt nor as marked as in the previous group.

Summary

Following experimental studies, clinical therapy of acute pulmonary edema utilizing the antifoaming effect of alcohol vapor by inhalation was studied.

Preliminary studies indicated that alcohol vapor by inhalation is well tolerated by normal subjects and cardiac patients. Four methods were tried. The two most practical are (a) one employing a nasal catheter, and (b) one making use of a positive pressure mask. The amount of alcohol detected in the blood was found to be small; its general effects, negligible.

Alcohol vapor was administered to 14 patients during 17 severe or extremely severe attacks of pulmonary edema. In general, alcohol was given after failure of routine medications; however, three cases received no conventional therapy prior to alcohol inhalation. In 58 per cent of the attacks, the result was favorable and there was good evidence of prompt relief. In 29 per cent of the attacks, the improvement was definite though less dramatic, so that improvement in a total of 87 per cent was noted. The clinical records of three selected cases are reported.

Alcohol vapor was also administered to seven patients with severe and prolonged pulmonary edema with poor to terminal status. In three, evidence of decrease of the foaming process was noted even though the fatal course of the underlying disease was not modified.

This preliminary study indicates that alcohol inhalation has a favorable action in clinical pulmonary edema, particularly of the acute paroxysmal variety. The desirability of a mode of therapy free of contraindications is noted and the possibility of using alcohol vapor in conjunction with conventional therapy is stressed.

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Addendum

Since completion of this report, 14 attacks of acute pulmonary edema in 12 patients have been treated with alcohol-oxygen vapor per nasal catheter according to the method described above. Several patients received no other treatment during the attack. The results of therapy parallel very closely those included in this report.

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