Intratracheal Atomization in the Treatment of Infectious Diseases of the Respiratory System
Preliminary Report
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The treatment of infectious diseases of the respiratory tract with aerosols has become quite popular during the last few years, due in particular to the use of antibiotics. At present, nebulizers are used for this procedure in which the thick particles are condensed in the apparatus allowing only the outflow of very fine and small particles, less than two micra in diameter.

The common sprayers cause an outflow of droplets much thicker and we have demonstrated in our works on Mucosography of the Respiratory System (Radiology, July 1942) that these droplets reach by gravity and pulmonary aspiration the terminal bronchi and the pulmonary alveoli.

Harold A. Abramson of the Staff of the Commanding General Technical Division, Chemical Warfare Service, in his work on Aerosol Therapy of the Lung and Bronchi with Special reference to Penicillin and Hydrogen Peroxide (New England Medical Center, VIII, 1946), recommends the use of our technique of atomization in the general treatment of the diseases of the respiratory system where great amounts of liquids should be used.

We began our studies in the Department of Tuberculosis of the Faculty of Medicine of the University of Havana (Instituto de Vías Respiratorias, Servicio del Profesor Doctor A. Antonetti). We selected a group of patients who presented different pulmonary suppurations such as bronchiectasis, abscess of the lungs, gangrene of the lungs, etc. The first part of our investigation was directed to prove under what conditions could this method be applied. The anesthesia to be used was considered, the volume and concentration of the solution used, and its tolerance by the bronchial tract.

Tests were performed with penicillin, streptomycin, hydrogen peroxide and sulfa drugs. Finally we decided to use penicillin in the first series of applications, bearing in mind its antibiotic action and its known tolerance.

Direct examination was made of the patients sputum from the
bacteriological point of view. Cultures were carried out routinely in all the cases. Several determinations in series were performed to demonstrate the levels or concentrations of the antibiotics in the blood. Other determinations were made for the purpose of studying the conditions of absorption, retention or elimination of antibiotics in the sputum. Comparative studies with other methods of therapy by inhalation were made.

Technique

The technique of intratracheal atomization is not a difficult one. We take a long sprayer that gives a very fine atomization, the end may be placed easily in the larynx, behind the epiglottis (Fig. 1) or in the trachea under the vocal cords. The apparatus we designed is very satisfactory and we are pleased with the results obtained.

We start our procedure by anesthetizing the pharynx, larynx and the trachea by spraying a solution of ½ per cent pantocaine. During the atomization of the pantocaine we have the patient lean towards the side we are going to treat and we have him inhale strongly in order to anesthetize the trachea and the bron-
chial tract on that side. After waiting a few minutes so that the anesthesia is well established, we place our sprayer in the trachea and then commence to spray with the solution we have adopted for this technique. Before the sprayer is placed in the trachea, its container is connected to a rubber tube with an air compressor allowing a pressure of six or seven pounds. The patient must be seated in a straight position with the head straight up and the body completely bent towards the side we are going to treat, and bent to the front or to the back according to the pulmonary segment which is the object of the treatment. Right after the atomization the patient is placed in a special position corresponding to the pulmonary segments where the lesion is located and must remain in this position as long as possible trying not to cough. Trendelemburg’s position should be always used for the upper lobe. The quantity of the spray solution varies according to the kind of diseases and the substance used, 20 cc. of an aqueous solution may be sprayed in one or two minutes.

**Laboratory Investigations:**

For the exact bacteriological control of the sputum we have used 5 per cent blood-agar as culture medium. The determination of the antibiotic action was done following the technique of the Oxford investigators: in Petri dishes with solid agar medium, we add staphyloococcus aureus (strains received from Washington) culture diluted to 1/10. After keeping it 24 hours in refrigerator, it is placed on the surface of the agar. The rings are filled with the blood, sputum or other secretions to be tested for antibiotic properties. The Petri dishes are refrigerated for 24 hours, after this period of time all the liquid in the inside of the rings has disappeared by diffusion through the agar. We observed circular zones of inhibition of the culture in the dish where no bacteria develops. With a millimeter crystal ruler we determine the diameter of the zone of inhibition. This diameter demonstrates the extent of antibiotic action. In our studies a zone of 24 millimeters of inhibition corresponds to 100 units of antibiotic in each 100 cc. of material examined.

All pertinent studies, starting with those of Fleming, express the antibiotic action in units per cubic centimeter. We present our graphs in units per each 100 cc., as all humoral indexes are expressed and in this way the antibiotic action is expressed in whole numbers which are easier to handle than the decimal figures of the older method. Accordingly, all our graphs are made on millimeter paper, each millimeter equals one unit of antibiotic action per 100 cc. of the material tested (blood, sputum, etc.).
Clinical Considerations:

The cases selected were patients who formerly had received oral medication or antibiotics administered parenterally. During the trial of this method, intratracheal crystalline penicillin was used exclusively. No other antibiotic medication was employed at any other time.

Among the cases selected, one patient had a neoplasm with abscess in the middle lobe of the right lung who entered the hospital for an operation. Before his admission to the hospital no diagnosis of lung tumor had been made and suspecting an abscess of the lung, high doses of penicillin were given simultaneously with sulfa drugs. There was no reduction in the amount of bronchial secretions which reached 300 cc. in 24 hours and were bloody and purulent. The patient was quite toxic, had moderate anemia with much cough, especially at night and a most aggravating dyspnea. The bronchoscoptic examination did not show tracheobronchial lesions. Five intratracheal applications were given to him by our method, one every day, using crystalline penicillin in maximal doses of 400,000 units in each application and in solutions of 15 to 20 cc. of isotonic saline. We noticed in the first application a definite pharyngeal reflex. We obviated this in the following treatments by giving previously an injection of 1.0 mg. of morphine with atropine. Following the second application, the continuous coughing of the patient was relieved, the expectoration began to diminish and at the end of the fourth application it had come down to 15 cc. in 24 hours. The patient’s general condition improved and his recovery was maintained for several weeks, when refusing surgical intervention, he left the hospital.

In bronchiectasis we have observed quick reduction of expectoration in 24 hours with a modification of the bacterial flora.

The graphic curve of concentration of antibiotic of sputum and blood simultaneously obtained in this group have been very interesting. We observed that the concentration of antibiotic in the blood was maintained during the first eight hours, fluctuating between 15 and 2 units per each 100 cc. In the sputum, in the same number of hours, the antibiotic action fluctuated between 125 and 35 units per each 100 cc. In case number 5 (Fig. 2), multiple bronchiectasis of both lung bases, using always 300,000 units of penicillin at a time, with our method a remarkable difference has been observed in the levels simultaneously obtained from sputum and blood.

In case number 2 (Fig. 3), abscess of the vertex of the lower lobe of the left lung cleared promptly under the effect of our treatment. This case, a 31 year old farmer, with a lung affection
FIGURES 2 and 3: Comparative concentration curves of the antibiotic action in sputum and blood.
of seven months' duration, was characterized by pain in the flank, high temperature, coughing, abundant purulent expectoration, with asthenia, loss of energy and anorexia. During his second month of illness sulfa drugs were given orally and penicillin parenterally, with no improvement in his condition. The physical examination showed a noticeable oral sepsis, "watch glass" nails and a condensation syndrome at the left-scapular-vertebral zone, with several subcrepitant rales. Mucopurulent sputum showed numerous pyogenic cocci. Its culture revealed the presence of staphylococcus aureus. There was slight anemia, with 15,000 leucocytes, young cells predominating. On bronchoscopic examination we found very fetid secretions originating from the left lower lobe bronchi.

In all, twenty-five intratracheal applications were made in this case, with maximum dose of 400,000 units of penicillin in a solution of 5 cc. of isotonic saline. After the fourth application we noticed that the expectoration diminished, coughing at night was less, his appetite and general condition improved. After every application the patient felt better and at the end of the first 20 applications his general condition was good. His expectoration, coughing, fever and asthenia had ceased. He had his normal weight. Nothing important was noticed in the physical examination of the chest. In the x-ray picture we only observed traces of the contrast medium used in the bronchographic examination (Fig. 4). In the final culture of the patient's sputum only catarrhalis cocci were observable (Fig. 5). Concentration of peni-

**FIGURE 4**
*Fig. 4: Pulmonary abscess of the apex of the left lower lobe.*

**FIGURE 5**
*Fig. 5: One month later: Complete resorption of the process.*
Penicillin in the blood and sputum curves during treatment was similar to those described in our former observation. This patient was kept in the hospital for several weeks after treatment, without observing any further clinical or radiographic manifestations of the infection.

SUMMARY AND CONCLUSIONS

1) We have used a technique developed by us for mucosography of the respiratory tract and applied to the treatment of suppurative diseases of the lung.

2) This preliminary report covers a group of cases treated with penicillin which we have used in different concentrations, between 100,000 and 500,000 units dissolved in isotonic saline solution. The application was made daily with progressive increase in the doses of penicillin.

3) We preferred crystalline penicillin because it is better tolerated; the volume used has been 5 cc. Larger amounts show no advantage, for it delays the method, and the patient develops pharyngeal irritation.

4) It is an easy method to use, with no risk or disturbance to the patient. The amount of anesthesia used is very small, atomization of 2 cc. of ½ per cent pantocain solution is sufficient. In some patients we have sprayed without anesthesia, and noticed good tolerance.

5) We perform the atomization continuously. That is, in both phases of respiration, in order that the patient may keep open the glottis to avoid coughing and pharyngeal contractions.

6) We have used the supra and infraglottic technique. We prefer the supraglottic technique because it is better tolerated.

FIGURE 6: Petri dishes showing the different intensity of the antibiotic action of sputum and blood.
7) The results obtained are definitely encouraging. We have succeeded in improving and curing suppurative lung conditions some of which were of more than six months' duration and having been previously treated without success with penicillin and sulfa drugs.

8) It is interesting to point out that the simultaneous study of sputum and blood in our patients shows high antibiotic action in the sputum and quite low antibiotic action in the blood. It is easy to see in our graphs that the antibiotic action of the sputum fluctuates between 130 units as maximum and 40 units as minimum, the antibiotic action of the blood fluctuates between 30 units as maximum and 2 units as minimum.

These facts bring forth certain questions which we shall try to explain:

(a) Does the high bacteriostatic power found in the sputum represent the whole penicillin concentration or is it related to any other antibiotic action?

(b) Does the high bacteriostatic action found correspond to accumulative or eliminative action?

(c) Do proteins of the expectoration (mucins, mucoids, etc.), have anything to do with the "delayed effect" in connection with the penicillin deposited in the bronchi?

9) The results obtained point toward the extraordinary importance of the topical action of antibiotics.

10) Finally, with this method we can direct to a certain pulmonary area the highest percentage in volume and concentration of the drug used, which, to our belief is not obtainable by any other method of inhalation used up to the present moment.

Atomizer described manufactured by the DeVilbiss Company.

**FIGURE 7:** Petri dishes showing the different intensity of the antibiotic action of sputum and blood.
RESUMEN Y CONCLUSIONES

1) Hemos empleado una técnica perfeccionada por nosotros para la mocosografía del aparato respiratorio y aplicada al tratamiento de las enfermedades supuradas del pulmón.

2) Este informe preliminar incluye un grupo de casos que hemos tratado con penicilina en concentraciones de 100,000 a 500,000 unidades disueltas en una solución isotónica de cloruro de sodio. Se aplicó el tratamiento diariamente, con aumento progresivo en la dosis de penicilina.

3) Preferimos la penicilina cristalina porque es más tolerable. Se ha usado un volumen de 5 cc. Cantidad más grandes no ofrecen ventaja, pues demoran el método y el paciente sufre de irritación faríngea.

4) Es un método fácil de usar que no tiene peligro ni causa desasosiego al paciente. Es muy pequeña la cantidad de anestésico empleada, es suficiente la pulverización de 2 cc. de una solución de pontocaina al 0.5 por ciento. Hemos rociado sin anestesia a algunos pacientes y lo han soportado bien.

5) Ejecutamos la pulverización continuamente, es decir, en las dos fases de la respiración, a fin de que el paciente mantenga la giotis abierta para evitar la tos y las contracciones faríngeas.

6) Hemos empleado la técnica supraglótica e infraglótica. Preferimos la técnica supraglótica porque es más tolerable.

7) Los resultados obtenidos son definitivamente alentadores. Hemos logrado la mejoría o la curación en estados supurados del pulmón, algunos de los cuales habían existido por más de seis meses y habían sido tratados previamente sin buen éxito con penicilina y sulfonamidas.

8) Es interesante indicar que, en nuestros pacientes, el estudio simultáneo del esputo y de la sangre demostró una acción antibiótica elevada en el esputo y una acción antibiótica bastante baja en la sangre. Se puede ver en nuestras gráficas que la acción antibiótica del esputo fluctúa entre 130 unidades como máximo y 40 unidades como mínimo, y la acción antibiótica de la sangre fluctúa entre 30 unidades como máximo y 2 unidades como mínimo.

Estos hechos sugieren ciertas preguntas que trataremos de contestar:

(a) ¿Representa el elevado poder bacteriostático del esputo la entera concentración de la penicilina, o está relacionado con alguna otra acción antibiótica?

(b) ¿Corresponde la elevada acción bacteriostática a una acción acumulativa o eliminativa?
(c) ¿Tienen algo que ver las proteínas de la expectoración (mucinas, mucoides, etc.) con el "efecto demorado" de la penicilina depositada en los bronquios?

9) Los resultados obtenidos demuestran la extraordinaria importancia de la acción tópica de los antibióticos.

10) Finalmente, con este método podemos aplicar a una zona pulmonar el porcentaje más alto, en volumen y en concentración, de la droga empleada, lo que, en nuestra opinión, no es obtenible mediante ningún otro método de inhalación usado hasta la actualidad.