Experimental Intrabronchial Administration of Neomycin in Man and Animals

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Ten years ago, Waksman and Lechevalier demonstrated the important antibiotic action of neomycin against the Koch bacillus. The effect of neomycin is even greater than that of streptomycin.

Rake, Hobby and Donovick have also demonstrated the antibiotic effect of neomycin in experimental tuberculosis.

Because of its toxicity, Grumbach and Rist considered that parenteral neomycin injection was dangerous. However, Dumon and Courtreux have shown that the blood concentration is minimal (injection of 0.33 gm. gives a maximum blood level of 1.6 microgram/ml.) after intrabronchial administration. These workers describe good clinical results with toxic side effects following intrabronchial application.

Previous investigations have shown that when streptomycin and oxytetracycline are administered intrabronchially, their pulmonary concentration is much higher for much longer periods than the level obtained after parenteral administration with the same dose.

Therapeutic concentrations of chlorotetracycline, tetracycline, and penicillin are maintained for only five to six hours after administration. The pulmonary tissue concentration of erythromycin, and hydrazide (INH), as well as sulfathiazole, immediately after intrabronchial, is similar to the low content found after parenteral or oral application. This is indicative of a higher diffusion rate from the point of application.

In order to study this application method, for neomycin, we administered it both intrabronchially and parenterally in patients, and intratracheally in guinea pigs and rabbits. Intrabronchial administration was effected by means of catgut tubes, since aerosols gave less satisfactory results. The pulmonary tissue concentration of all the subjects was determined after various time intervals.

Materials and Methods

A series of 18 patients was given intramuscular injections of neomycin (250 mg. per 60 kg. body weight). Another group of patients was given the same neomycin dosage intrabronchially by means of Metras catgut tubes. After neomycin administration, the entire group of 36 patients underwent pulmonary resection after varying time intervals.

Neomycin was administered to 110 guinea pigs and 14 rabbits intramuscularly or by intrapulmonary (tracheal) route. Animals from each group were sacrificed and their lungs examined at various time intervals after application.

The concentration of Neomycin in the pulmonary tissue has been determined by the method described in 1959.*

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The results of the observations on 36 patients, 220 guinea pigs and 28 rabbits have been arranged in the following tables.

Results

The table based upon results in patients demonstrates that pulmonary neomycin concentration is greater after intrabronchial administration than after parenteral administration. Neomycin pulmonary concentration three hours after intrabronchial application was 1300 microgram/ml, which is 700 times greater than the pulmonary concentration three hours after parenteral injection. An effective antibiotic concentration of 30 to 40 microgram/ml was still present 24 hours after intrabronchial application. The animal experiments completely confirm the results obtained with humans.

Since neomycin is relatively toxic when administered parenterally, it has been discarded in ordinary practice in spite of the fact that it is a powerful antituberculosis antibiotic with a wide spectrum. Blood levels of neomycin after intrabronchial administration are very low (Table 1), explaining the high tolerance of it even during prolonged treatment (daily, for over four months).

SUMMARY

Neomycin was administered to 36 patients, 220 guinea pigs and 28 rabbits either intrabronchially or parenterally and the pulmonary neomycin concentration was determined bacteriologically. Those who received the intrabronchial administration showed a pulmonary neomycin concentration after three hours 700 times higher than those which received parenteral injection. Concentration of 1360 mcg./ml in the pulmonary tissue were found four hours after intrabronchial application. After 24 hours, the level was 40 mcg./ml. Therefore, intrabronchial administration of neomycin is advisable in neomycin-sensitive pulmonary infections.

RESUMEN

Se administró neomicina a 36 enfermos, a 220 cuyes y a 28 conejos, ya sea intrabronquial o parenteralmente y se determinaron las concentraciones de la neomicina bacteriológicamente. Los que recibieron la droga intrabronquial, mostraron concentraciones de neomicina pulmonar después de 3 horas, 700 veces mayor que los que la
recibieron parenteralmente. La concentración de 1360 microgramos/ml en el tejido pulmonar se encontraron cuatro horas después de la aplicación intrabronquial. Después de 24 horas, el nivel fue de 40 micro gr./ml. Por tanto, la administración intrabronquial de neomicina es aconsejable en las infecciones pulmonares que sean sensibles a esa droga.

RESUMÉ

La neomycine fut administrée chez malades, 220 cobayes et 28 lapins soit par voie intrabronchique, soit par voie parentérale, et la concentration pulmonaire de néomycine fut déterminée bactériologiquement. Ceux qui reçurent une administration intrabronchique montrèrent une concentration pulmonaire en néomycine après trois heures 700 fois plus élevée que ceux qui reçurent une injection parentérale. Des concentrations de 1360 mcg. par ml. de tissu pulmonaire furent trouvées quatre heures après application intrabronchique. Après 24 heures le taux fut de 40 mcg. par ml. Donc l'administration intrabronchique de néomycine est souhaitable dans les infections pulmonaires sensibles à ce produit.

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REFERENCES


RESPIRATORY DISTRESS IN THE NEWBORN

Eighty-five newborn and 36 adult rats subjected to laboratory procedures designed to stimulate adverse perinatal influences showed difficulties and developed pulmonary lesions similar to those seen in infants of respiratory distress. The miliary atelectasis seen in the experimental animals may be the result of an interplay of complex mechanical, neural and most important of all, obstructive influences. The miliary atelectasis may be associated with a reversion to the fetal circulatory pattern which, with other factors, result in flooding of the pulmonary capillary bed. Increased pulmonary blood volume and capillary pressure are reflected in engorgement of the pulmonary venules and capillaries found in the lungs of all newborns dying of respiratory distress. As a result of uncompensated increased capillary hydrostatic pressure and increased capillary permeability, formed or nonformed elements to the blood may pass into the air spaces leading to pulmonary lesions of hemorrhage, hyaline-like membranes or edema. Hyaline-like membranes, although contributing to hypventilation, are merely a pathologic result in the same category as pulmonary lesions of hemorrhage.