AEROSOL INSULIN INHALATION ENQUIRY

By

A. R. GOVINDA RAO

Professor of Pharmacology, Madras Medical College, Madras.

(*Received on November 15, 1958.*)

INTRODUCTION

The use of aerosol therapy in medicine is not new. The fumes of incense to drive away evil spirits, the burning of sulphur candles to disinfect the air, the spraying of operating rooms with germicidal materials have all had evolutionary significance in our thinking. Steam inhalations and the inhalations of the smoke of asthma powder are early and useful examples of aerosol therapy of the lungs.

The simplest definition of an aerosol is the suspension of particles in a gas. Usually the particles are liquid, hence the term aero, meaning air or gas, plus sol, meaning solution or moisture.

An "Atomizer" is a device which reduces a liquid to smaller particles so as to produce a spray. Air is forced into a reservoir containing air and liquid with pressure on a rubber bulb. This forces the fluid out of the reservoir through a tube, the diameter of which determines the size of the droplets in the spray. The spray is coarse or fine depending on the size of these suspended droplets. When an exceedingly fine spray is desired either a baffle is introduced to the airblowing mechanism or the outflow tube is bent to a ninety degree angle. This will reject the larger droplets and return them to the solution, at the same time, it will allow the very finely suspended droplets to emerge. This apparatus is called a "Nebuliser" which indicates the fine moist or cloud (nebula) which results.

Nebulization. It has been determined that particles of thirty microns and larger will not pass beyond the trachea when introduced into the bronchial tract. Those of ten to thirty microns will reach the terminal bronchioles; sizes of three to ten microns will reach the alveolar sacs. The choice of the nebulizer or the choice of the particle size depends on the purpose of the procedure.

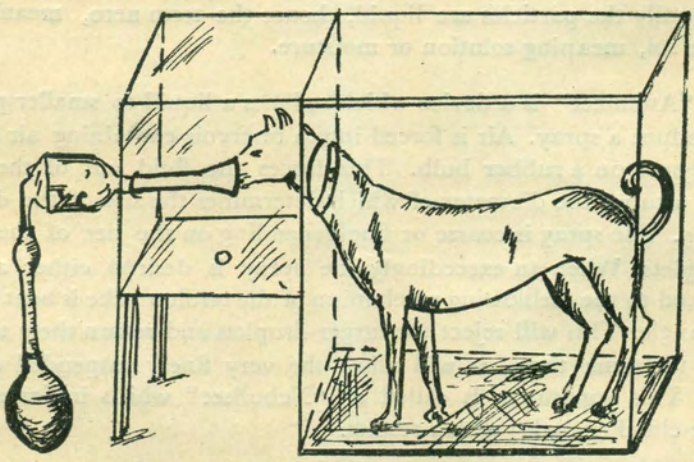
Nebulizers may be used with a hand rubber bulb to force air into the reservoir or the device may be attached to a compressed oxygen tank or air compressor. For short intermittent nebulization particularly of sympathomimetic amines and solutions of Insulin hand nebulization is adequate.

A reference to previous literature on this subject shows, that inhalation of nebulized solution of insulin could be used as a therapeutic measure in diabetic individuals; Gujral et al.(1955) have experimentally produced hypoglycaemia in rabbits by administering aerosol insulin in a chamber. Similar work was undetraken in this department using dogs as experimental animals.

METHODS AND MATERIAL

The work was carried out mostly on normal dogs except on one dog which was made hyperglycaemic by repeated intravenous administration of hypertionic glucose over a period of 4 weeks.

Dogs were obtained from Corporation lethal chamber and maintained on a nutritious diet to improve the general standard of health. Antibiotic therapy was given to such of those animals suffering from infectious skin conditions. Animals weighing between 12 and 13 Kilos were selected for the experimental work.



A special box was designed to enclose the dog excluding the head and neck which projected into a light transparent plastic mask as shown in the diagram. A special nozzle was also attached to the head of the dog to cover the mouth and the nostrils through which a fine spray of the aerosol solution was introduced. The dogs were trained to remain quiet in the box with the

masks on during the period of experiment. This training usually took a period of six to eight weeks. Animals deprived of food for fourteen hours were used for experiments. The fasting blood sugar level was taken and blood sugar estimation was done by FOLIN and WU method using Klett's Summerson colorimeter. The fall of blood sugar produced by subcutaneous method was determined by collecting samples of blood at one hour intervals and the average percentage of fall of blood sugar estimated. A similar estimation was done for insulin administered by aerosol method. In order to avoid error of undue sensitivity among the animals, the same animals were used for both subcutaneous and aerosol technique, after sufficient intervals in between the experiments. Controls were tested using isotonic saline as a spray and for injection.

Persistent hyperglycaemia was produced in dogs as follows: Two hours after their regular normal diet the dogs were anaesthetised with 250 mg. of Pentothal sodium in 10 c. c. of normal saline given intravenously. This procedure was continued for three days and on the fourth day intravenous glucose was withheld. From the next day the cycle of operations was continued on similar lines. Water was allowed ad libidum. After about four weeks it was possible to raise the fasting blood sugar level from about 70 mg. percent to 110 to 120 mg. percent.

RESULTS

Aerosol insulin was also tried on the hyperglycaemic dog produced by the above method. (Table I – Dog No. 7).

At the end of two hours, however, the mean fall in Blood sugar level by the subcutaneous route exceeded that by the aerosol route by 4.3 mg per cent. The difference is, however, statistically insignificant as is shown in table 3.

DISCUSSION

A number of drugs like Epinephrine, Isoprenaline, Penicillin, local anaesthetics, have been successfully administered by aerosol spray.

As the treatment in diabetes is a replacement therapy with insulin throughout life, it would be of immense benefit if the hormone could be administered in the form of aerosol. Then the painful daily injections with possibility of sepsis and other concomittents could be avoided. A diabetic could carry a small plastic nebulizer in his pocket and use it for insulin at regular intervals.

CONCLUSION.

An attempt has been made to successfully administer Insulin in the form of fine spray (by aerosol method) to normal and hyperglycaemic dogs.

TABLE 1.

No. of Dog.	Weight in Kilograms	Route of Administration	Initial blood Sugar Level Mgms%	Blood sugar level after		
				One hour	Two hours	Three hours
1.	12.3	Aerosol	92	75	69	61
		Subcut	90	74	67	59
2.	13.0	Aerosol	80	69	61	58
		Subcut	82	68	50	50
3.	12.2	Aerosol	96	86	81	76
		Subcut	98	82	76	76
4.	11.8	Aerosol	82	69	61	59
		Subcut	78	65	57	55
5.	12.5	Aerosol	88	80	73	68
		Subcut	85	74	66	61
6.	13.0	Aerosol	98	75	60	48
		Subcut	96	74	63	52
7.	13.5	Aerosol	110	86	79	73

EFFECTS OF INSULIN ON BLOOD SUGAR BY AEROSOL AND SUBCUTANEOUS ROUTES.

TABLE 2

No.	Aerosol Route				Sub-cutaneous route.			
	Initial Level	Fall in Blood Sugar level			Initial Level	Fall in Blood Sugar level		
		1 hour	2 hours	3 hours		1 hour	2 hours	3 hours
1.	92	17	23	31	90	16	23	31
2.	80	11	19	22	82	14	32	32
3.	96	10	15	20	98	16	22	22
4.	82	13	21	23	78	13	21	23
5.	88	8	15	20	85	11	19	24
6.	98	23	38	50	96	22	33	44
	89.3	13.6	21.8	27.6	88.1	15.3	25	29.3
Percentage Fall of Blood Sugar.		15.2%	24.4%	30.9%		17.3%	28.3%	33.2%

TABLE 3

Fall in Blood sugar with		Difference	Deviation from mean difference y	y^2
Aerosol Insulin	Subcutaneous Insulin			
23	23	0	4.8	23.04
19	32	13	−8.2	67.24
13	22	7	−2.2	4.84
21	21	0	4.8	0.64
15	19	4	.8	
38	33	5	−0.2	

From the data gathered so far it can be concluded that the effect of aerosol Insulin administration is almost as efficient as subcutaneous injection.

Clinical studies on normal and diabetic persons are Being instituted and the effect would be reported after adequate observations.

ACKNOWLEDGEMENT

I am grateful to Madras State Research Committee for providing necessary funds for conducting this enquiry and permitting me to publish the same and to Dr. A. A. Aiyer for his kind help and guidance.

I am thankful to M/S Burroughs Welcome & Co. for their kindness in supplying me the insulin.

REFERENCES

1. Gaddum, J. H. (1948): *Pharmacology – Oxford Medical Publications.*
2. Gujral, M.L. et al. (1954): *Indian Medical Gazzette*, **89**, *141.*
3. Ayer. (1954): *The Antiseptic.*
4. Gujral, M. L. et al. (1955): *Journal of the Indian Medical Profession*, **2**, *No. 4.*