EFFECTS OF VENTILATORY CONDITIONS ON DEPOSITION OF NaF IN ISOLATED RABBIT LUNGS

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SUMMARY: The effects of tidal volume and respiratory frequency on the deposition of NaF aerosol particles were studied using lungs isolated from 20 rabbits. Total lung deposition decreased with increases in tidal volume and respiratory flow rate and was in the range of 20-80% when the reciprocal of the respiratory flow rate was 0.05-0.5 sec/ml. Deposition of aerosol particles in various lung lobes had a 1:1 ratio with respect to the weight of each lobe. The deposition was especially high on the right middle lobe and markedly decreased with increases in respiratory flow rate.

KEY WORDS: Lung deposition; NaF aerosol particle; Ventilatory conditions

Introduction

The toxicity of fluoride in the air of certain factories has been a health concern partly because it can cause systematic injury by absorption following inhalation. Whereas the absorption rate of fluoride through the respiratory tract has been studied for gaseous HF (1), information is unavailable concerning the particulate form of this pollutant.

Using rabbits and NaF aerosol, in previous inhalation experiments we estimated, from urinary fluoride excretion, the NaF absorption rate from the respiratory tract (2). Since, in the discussion of particle inhalation, not only its absorption, but also its deposition is of concern, the mechanism by which the particles are deposited becomes important. It is known that particle size affects the total and regional deposition of particles in the respiratory tract (3). Since the influence of tidal volume (TV) and respiratory frequency (f) on the deposition of particles has not been studied extensively, the present study was initiated to clarify this aspect by using generated NaF aerosol and lungs isolated from rabbits.

Material and Methods

Twenty rabbits were used in this study (average body weight 2.75 ± 0.30 g). The weight of the lungs ranged from 7.2 to 12.3 (average 9.9 ± 1.4g).

The apparatus, depicted in Figures 1-a and 1-b, consisted of a NaF aerosol generator, inhalation chamber and artificial thorax. The mist, formed from 0.3 M NaF solution by means of an ultrasonic nebulizer, was

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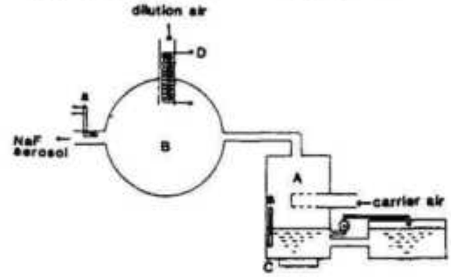
blown to the mixing chamber by the carrier air, where it was mixed with dilution air heated to 140°C with a mixing ratio of 1.24 (Figure 1a). This process produced dry solid NaF aerosol particles. The NaF aerosol concentration inhaled was maintained at approximately 10 mgF/m^3 and averaged 0.3 µm in particle diameter. The concentrations of the aerosol were monitored by a calibrated didital counter (SHIBATA KAGAKU: Type P-5). These levels were kept within 5% coefficient of variation.

The inhalation chamber was made of acrylics with a capacity of 10 liters (Fig. 1b). A constant amount of NaF aerosol, ca. 6.0 l/min was passed into the chamber with laminar flow. The chamber was maintained at 28° C with a humidity of 40%.

Figure 1-a

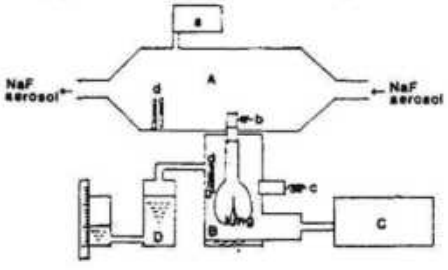
NaF Aerosol Generating System



A: NaF mist generating chamber; B: mixing chamber; C: ultrasonic nebulizer; D: heater; a: thermometer

Figure 1-b

NaF Aerosol Inhalation System



A: inhalation chamber; B: artificial thorax; C: numerical-controlled oscilator; D: pressure adjustor; a: particle counter; b: flow transducer; c: pressure transducer; d: hygrothermometer

The artificial thorax was connected with a numerical-controlled oscillator. Made of acrylics with a capacity of 1.5 liters, it was used to hold the lungs. A brass duct was placed in the trachea of the isolated lungs as a tracheal adaptor and was attached to the center of the top of the artificial thorax. The lower part of the artificial thorax was filled with water up to about 2 cm deep. The humidity of the artificial thorax was maintained at approximately 100% and a temperature of 30° C. Lung ventilation was carried out by numerical-controlled oscillator (4). TV was measured by a flow transducer (Shibata Kagaku: Type ISA-8) at the entrance of a tracheal adaptor.

Following the inhalation study, the lungs were divided according to individual lobes and the fluoride deposition determined in each of them. Each of the lobes was weighed and homogenized with distilled water. The extract was centrifuged at 1000 xg for 15 min. To the resulting supernatant was added an equal amount of TISAB, and the fluoride content was determined with an ion selective electrode (Orion Research: Model 96-09). The lung fluoride deposition was calculated by dividing the fluoride content in the lung by the amount of fluoride inhaled. Inhaled fluoride was computed by multiplying the fluoride concentration in the inhalation chamber by the f, TV and inhalation time.

The validity of the method for determination of fluoride in lung tissues was established by a study on recovery of fluoride from spiked samples. For this purpose, 12 lung tissues, each weighing about 1 g, were used. A 2 ml solution, containing 0.5, 1, and 2 ppm F, respectively, was added to the tissue sample; the mixture was homogenized, and the homogenate, centrifuged. The fluoride content of the supernatant was determined by the method described previously. The percentage recovery from these experiments ranged from 92.0 to 106.0%, with an overall average of 98.3±4.2%.

Results

Several mechanical factors, for each of the rabbits used in this work, were studied. The total lung capacity (TLC), static lung compliance (Cst), and pulmonary resistance (Rp) were determined. Average values, for the 20 rabbits, follow: TLC, 95.4 16.5 ml; Cst, 13.0 3.5 ml/cm H_2O; Rp, 0.019 ± 0.007 cm H_2O/ml/sec.

The TLC and Cst were measured from the volume-pressure curve, and the Rc was obtained by the oscillation method. When TLC was 95.4±16.5 ml and the Cst 13.0±3.5 ml/cm H_2O, the Rp was 0.019±0.007 cm H_2O/ml/sec. Little variation was observed in these values which confirms earlier reports concerning mechanical factors of pulmonary ventilation (5).

The TV, f, V, reciprocal of respiratory flow rate (1/V), ventilation time (T), fluoride concentration in the air (Fair), amounts of fluoride inhaled (Finh), amounts of fluoride deposited in the lungs (Fdep), and total lung deposition (D) are shown in Table 1).

Table 1

Ventilatory Conditions and Amounts of Fluoride in Inhalation

No.	f (Hz)	TV (ml)	$\dot{V}$ (ml/sec)	1/$\dot{V}$ (sec/ml)	T (min)	Fair (mg/m^3)	Finh (µg)	Fdep (µg)	D (%)
1	0.25	4.3	2.4	0.42	20	10.1	13.0	10.2	78.5
2	0.25	6.7	3.9	0.26	30	11.1	33.5	17.8	53.1
3	0.25	3.3	2.0	0.50	20	10.8	10.7	8.1	75.7
4	0.25	9.9	5.1	0.20	30	11.3	50.3	11.3	22.5
5	0.25	8.7	5.8	0.17	30	9.9	38.8	15.2	39.2
6	0.5	8.0	9.3	0.11	30	12.8	92.2	24.6	26.7
7	0.5	5.2	6.1	0.16	30	15.6	73.0	30.7	42.1
8	0.5	7.0	8.2	0.12	30	12.0	75.6	27.2	36.0
9	0.5	4.5	5.3	0.19	10	12.2	16.5	7.9	47.9
10	0.5	7.9	9.3	0.11	20	11.8	55.9	19.8	35.4
11	0.5	2.7	3.1	0.32	20	11.4	18.5	8.9	48.1
12	1.0	6.5	15.1	0.066	20	9.7	75.7	17.3	23.0
13	1.0	5.1	11.9	0.084	20	10.9	66.7	12.8	19.2
14	1.0	8.5	19.8	0.051	15	8.2	62.7	13.6	21.7
15	1.0	7.8	18.5	0.054	15	9.5	66.7	11.6	17.4
16	1.0	5.3	12.2	0.082	15	11.9	56.3	11.0	19.5
17	2.0	6.4	30.2	0.33	6.5	10.7	53.4	7.5	14.0
18	2.0	2.1	9.7	0.10	12	12.0	36.3	7.1	19.6
19	2.0	4.7	22.2	0.045	15	10.6	89.7	14.0	15.6
20	2.0	7.6	34.2	0.029	15	11.3	154.6	13.7	8.9

f = respiratory frequency; TV = tidal volume; $\dot{V}$ = respiratory flow rate; 1/$\dot{V}$ = reciprocal of respiratory flow rate; T = ventilation time; Fair = fluoride in air; Finh = fluoride inhaled; Fdep = fluoride deposited in lung; D = total lung deposition

The relationship between total lung deposition (D) and TV to f frequency is shown in Figure 2. D tended to increase with decreases in TV and f. The V is the product of f and TV in sinusoidal ventilation. To examine the relationship between V, and D, I/V and D were used to plot Figure 3. A linear relationship existed between the two variables (r= 0.803 and n=20) and was significant at the 99% level. D was in the range of 20-80% when I/V was 0.05-0.5 sec/ml (Figure 3).

Figure 2

Relationship Between Tidal Volume and Total Lung Deposition

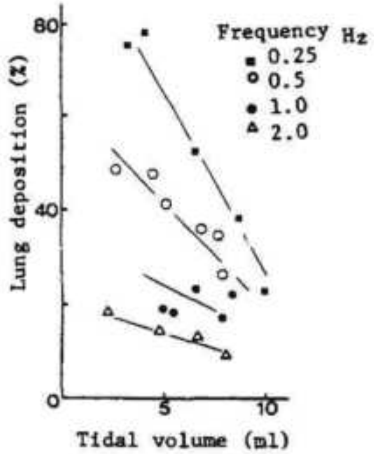
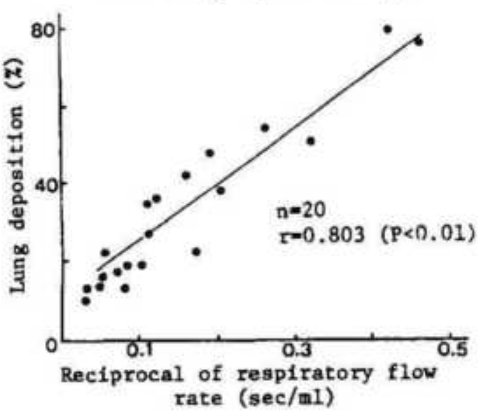


Figure 3

Relationship Between Reciprocal of Respiratory Flow Rate and Total Lung Deposition (D)



The distribution of deposited fluoride onto various lung lobes (Df) and distribution of various lung lobe weight (Dw) are shown in Table 2. Deposition of the fluoride in the lung lobes was in a 1:1 ratio with the weight of the lung lobes. However the right middle lobe received a disproportionate deposition. To examine the influence of $\dot{V}$ on the Fdep in each lobe, an adjusted distribution of fluoride deposited into various lung lobes was computed. This was done by dividing Df by Dw in each category in Table 2. The values obtained were averaged, and the results are

Table 2

Deposited Fluoride and Distribution of Lung Lobes Weight

	Distribution of Deposited Fluoride (Df)					Distribution of Lobe Weight (Dw)				
No.	R-u (%)	R-m (%)	R-l (%)	L-u (%)	L-l (%)	R-u (%)	R-m (%)	R-l (%)	L-u (%)	L-l (%)
Av.	8.9	14.5	37.2	10.5	29.4	8.5	11.4	39.9	10.2	30.0
S.D.	3.2	3.0	6.4	2.3	5.4	0.8	1.2	2.2	1.3	1.8

R-u = right upper lobe; R-m = right middle lobe; R-l = right lower lobe; L-u = left upper lobe; L-l = left lower lobe; Av. = average; S.D. = standard deviation.

shown in Table 3. The ratio for the right middle lobe tended to decrease as $\dot{V}$ increased and was more affected by $\dot{V}$ than the other lobes.

Table 3

Respiratory Flow Rate and Adjusted Distribution of Deposited Fluoride onto Various Lung Lobes

$\dot{V}$(ml/sec) lobe	-4.9 (n = 4)	5.0-9.9 (n = 8)	10.0-19.9 (n = 5)	20.0- (n = 3)
R - u	1.10	0.93	1.27	0.80
R - m	1.45	1.29	1.25	1.05
R - l	0.81	1.04	0.99	0.92
L - u	0.83	1.04	1.03	1.30
L - l	0.82	0.82	0.86	1.06

These values were obtained as the Df/Dw ratio to compensate the deposited fluoride by each lung lobe weight. Df = distribution of deposited fluoride onto various lung lobes. Dw = distribution of various lung lobes weight. $\dot{V}$ = respiratory flow rate; R-u = right upper lobe; R-m = right middle lobe; R-l = right lower lobe; L-u = left upper lobe; L-l = left lower lobe.

Discussion

The influence of f and TV on particle deposition in the respiratory tract has been investigated by several workers. Hatch and Gross (5) pointed out that increases in f would lower the respiratory tract deposition. Lippmann (6) attributed this to decreased residence time of particles with increasing f. Kimura (7) suggested that increased TV enhanced the respiratory tract deposition. Lippmann, on the other hand, claimed that when TV was increased, particles penetrated deeper in the lung, resulting in increased particle residence time.

The results obtained in our study using sinusoidal ventilation demonstraded that increases both in TV and f lowered the D. The data on TD are in contrast to the report made by Kimura (7). Presumably this is due to the different experimental conditions used in our study. The physiological ventilatory conditions used by Kimura were different in its ventilation patterns from the sinusoidal ventilation employed in our study (8), and an increase in TV does not necessarily result in lowered residence time.

Heyder et al. (9) reviewed the regional deposition of aerosol particles in the human respiratory tract and demonstrated that increase in $\dot{V}$ would lower the deposition in the respiratory tract. As seen in Figure 3, the results that D increased with increases in I/V agree with observations made by Heyder et al. (9). It is noted from these observations that the ventilatory conditions that influence deposition in the respiratory tract could be examined by using a parameter such as $\dot{V}$.

As shown previously increases in $\dot{V}$ caused a greater decrease of deposition in the right middle lobe than in other lobes, suggesting that the right middle lobe is different from other lobes in its response to changes in ventilatory pressure. This may be justified in view of the developmental and anatomical differences between the right lobe and other lobes of the lung.

It is concluded that $\dot{V}$ is an important ventilatory condition parameter which influences particle deposition in the respiratory tract.

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