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Particle deposition efficiency of therapeutic aerosols in the human maxillary sinus

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SUMMARY

The deposition efficiency of therapeutic aerosol particles in the human maxillary sinus is evaluated both in the human body and in a model cast of the upper airway. In the experiments, three sample materials, such as mono-dispersed polystyrene latex particles, aqueous glucose solution and pure water, in the range of particle diameter of from 0.5 to 15.8 μm, are employed in the model cast. The radioactive labelled aerosol particle is also used in the human body. From the results of the experiment, it is confirmed that even though the maxillary sinus is a closed hollow organ, aerosol flow is able to be induced only when the pressure gradient is applied between the nasal cavity and the maxillary sinus. In this case, the particle deposition is explained in relationship to the inertia impaction of the aerosol particles on the inside wall of the maxillary sinus. The total deposition efficiencies and the deposited particle sizes in the sinus area for both experiments, with the model and in the human body, are almost the same at 3%, and 3–10 μm in diameter, respectively. A physical model for this particle deposition suggests that these experimental values change not only with the size distributions of therapeutic particles and the pressure gradient, but also with the diameter of the sinus ostium. Moreover, since the therapeutic particle might not enter the maxillary sinus when the diameter of the sinus ostium canal is less than 1 mm, some pretreatment to open the sinus ostium canal would be necessary before applying such aerosol therapy in practice.

INTRODUCTION

The deposition of aerosol particles, especially in the human nasal cavity and maxillary sinus, is important for the assessment of health hazards from environmental exposure, respiratory diseases and the delivery of various therapeutic aerosols as a prime port of entry into respiratory tract regions.

Many previous studies have been carried out on the nasal and throat penetrations of particulates in the human upper airway under various conditions (Findeisen, 1933; ICRP Task Group, 1966; Christoforidis et al., 1971). However, the deposition pattern of particles into the human maxillary sinus has not been investigated sufficiently. This is because the maxillary sinus is a closed hollow organ, and it was thought that aerosol particles might not be able to enter the maxillary sinus. Several quantitative works observed the fact that a small amount of aerosol particles deposit in the human maxillary sinus for the following sample materials; penicillin (Hyo, 1951), methylene blue (Ladouce, 1951), ^{32}P (Drabe et al., 1952), and ^{99m}Tc (Tsukiyama, 1975). However, the mechanism of particle deposition has not been discussed in relationship to physical conditions, such as particle sizes, applied pressure, and so on.

In this paper, the mechanism of this particle deposition is considered theoretically. Particle deposition is mainly induced by aerosol flow into the maxillary sinus. This, in principle, takes place under a certain optimum physical condition, and at that time the therapeutic particles including in the aerosol flow deposit on the inside wall of the maxillary sinus. Aerosol flow into the maxillary sinus is recognized by applying the instantaneous pressure gradient between the nasal cavity and maxillary sinus. This should be explained as a function of the pressure gradient and the geometrical size of the sinus ostium. Moreover, the relationship between the particle size and the deposition efficiency is considered in relationship to the unsteady state of aerosol flow into the human maxillary sinus.

PHYSICAL MODEL FOR PARTICLE DEPOSITION

Unsteady state equation of aerosol flow

In order to determine the flow pattern into the maxillary sinus, a well-known equation for the unsteady state flow was employed. It is as follows:

$$P(\mathrm{t}) = L_{\mathrm{l}} \frac{\mathrm{dq(t)}}{\mathrm{dt}} + R_{\mathrm{l}}\, \mathrm{q(t)} \qquad [1]$$

where, $P(\mathrm{t})$ is pressure variation over time, and $\mathrm{q(t)}$ is the flow rate. The first term on the right hand side of this equation is related to the inertia force of the fluid, and the second one is expressed as a parameter of resistance to the fluid flow. Although the geometrical shapes of these areas are very complicate, the most dominating part for response of the fluid is in the sinus ostium. In such a case, the fluid inertance, L_{l}, and the resistance, R_{l}, are expressed as following equations:

$$L_{\mathrm{l}} = \frac{16}{3\pi} \cdot \frac{\varrho \mathrm{l}}{\mathrm{d}^2} \qquad R_{\mathrm{l}} = \frac{128}{\pi} \cdot \frac{\nu \mathrm{l}}{\mathrm{d}^4} \qquad [2]$$

where, ϱ is the density of the fluid, ν is the viscosity of the fluid, and l and d are length and diameter of the sinus ostium canal, respectively. Here, the pressure response in the maxillary sinus, $P(t)$, is experimentally obtained with the following equation:

$$P(t) = P_0\,(1 - \exp(-t/\tau)) \qquad [3]$$

where, P_0 is the applied pressure difference between the nasal cavity and the maxillary sinus, and τ is the relaxation time of the pressure response.

Applying the Laplace transmission method to Eq. [1], solutions for the flow rate, q(t), and the total amount of fluid flow, Q_t, were obtained with the next equations:

$$q(t) = \frac{P_0\,\tau}{\tau R_1 - L_1}\,(\exp(-t/\tau) - \exp(-R_1 t/L_1)) \qquad [4]$$

$$Q_t = \int_0^{\infty} q(t)\,dt = P_0\tau/R_1 \qquad [5]$$

As shown in Figure 1, these equations suggest that the aerosol flow into the maxillary sinus occurs only when the pressure gradient is applied between the nasal cavity and the maxillary sinus, even though the maxillary sinus is a closed hollow organ. Furthermore, the total amount of fluid flow is obviously determined by three parameters, the applied pressure difference, the diameter of the sinus ostium canal, and the relaxation time of the pressure response. Here, the constant value of this relaxation time is experimentally obtained, as shown in Table 1, corresponding to this diameter.

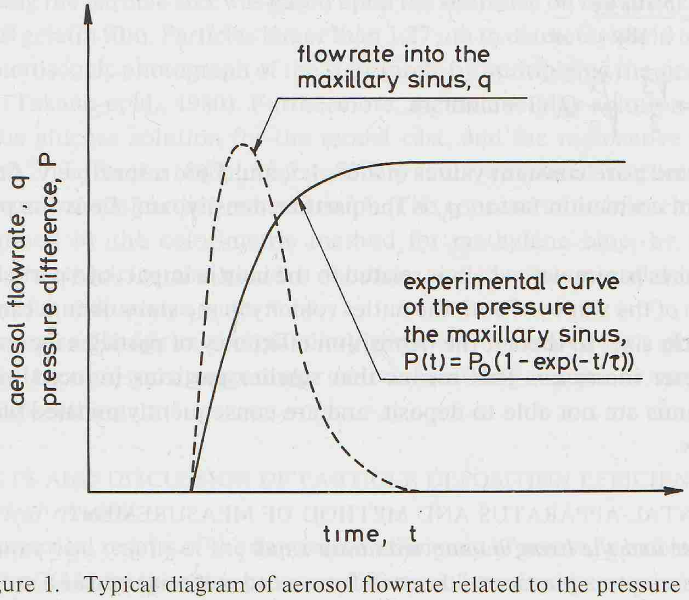


Figure 1. Typical diagram of aerosol flowrate related to the pressure variation.

Table 1. Several factors of relaxation time for negative pressure in the nasal cavity.

diameter of sinus ostium (mm)	relaxation time (ms)	pressure gradient (cm H_2O/ms)
5	0.20	68.3
3	0.33	25.0
1	0.67	16.5

The deposition efficiency of aerosol particles

The deposition of aerosol particles larger than 1 μm in diameter is mainly caused by the inertial impact of aerosol particles on the inside wall of the human airway. In this case, the deposition efficiency for each part of the respiratory tract could be expressed as a function of the Stokes number for a given flow geometry. The human upper airway consists of the nasal cavity, the sinus ostium, the sinuses, and the throat.

A cylindrical tubing model was applied for the sinus ostium canal (Hyo et al., 1983). It was then numerically found that the deposition efficiency in this tubing became negligibly small in comparison with other deposition factors. In the maxillary sinus, the most effective force for inducing particle deposition is inertia impact for the large sized particles. Therefore, the deposition efficiency, η, could be assumed by using the equation of impact separation on the wall of the maxillary sinus as follows (Ranz and Wong, 1952; Mercer and Stafford, 1969):

$$\eta = 3.8\sqrt{\psi} - 0.594 \qquad [6]$$

$$\psi = \frac{C_c \varrho_p D_p^2}{18\nu} \cdot \frac{\nabla}{d} \qquad [7]$$

$$\nabla = \frac{\sqrt{3}}{2} \cdot \sqrt{\frac{x}{z}\, Q_t \,(1-\tanh^2 y)} \qquad [8]$$

where, x, y and z are constant values of 7.67, 1.5, and 3.63, respectively. Cc is the Cunningham correction factor, ϱ_p is the particle density, and Dp is the particle diameter.

Ψ is the Stokes parameter, which is related to the inertia impact of a particle, and is a function of the values of both the outlet velocity in the sinus ostium canal and of the particle size. In theory, the deposition efficiency of particles increases as this parameter increases. This means that smaller particles induced into the maxillary sinus are not able to deposit, and are consequently exhaled with the aerosol flow.

EXPERIMENTAL APPARATUS AND METHOD OF MEASUREMENT

A model cast and the living human maxillary sinus

In the experiments, a plastic mold casted from a cadaver was used as a model for the nasal cavity. This model cast was connected to an especially designed hollow ball, which has almost the same volume as the human maxillary sinus and was the same size as the sinus ostium. The volume and the size were about 30 cm^3, 10 mm in length, and from 1 mm to 5 mm in diameter. Moreover, this cast was extremely convenient not only to observe the deposition at the inside of each part of the upper airway, but also to measure the size and concentration of particles, and the pressure difference over time in the maxillary sinus.

However, the real organ of this maxillary sinus is slightly changed with age, sex and the history of disease. The volume of the maxillary sinus and the diameter of the sinus ostium in normal adults are almost 30 cm^3 and 3–5 mm, respectively. Even if a small amount of the pressure gradient is instantaneously applied, these values do not seem to change considerably in practice because this organ is supported by the bone wall of the nose.

Sample materials and measuring method

Three kinds of sample aerosols, monodispersed polystyrene latex particles, aqueous glucose, and pure water in the size range from 0.5 to 15.8 μm in diameter were produced by using an ultrasonic aerosol generator (UDV generator, Carl Hyer Co.), or by a jet nebulizer.

Two devices were provided for particle size measurement in water mist. One of them was an on-lined He-Ne laser beam light-scattering particle counter which was used to simultaneously measure both particle diameters up to 2.7 μm and concentrations of aerosol particles (Takano et al., 1980). The other method for analyzing the particle size was based upon the stain size on the surface of naphtol green *B* gelatin film. Particles larger than 1.27 μm in diameter could be measured by a microscopic photograph of the stain circle by multiplying the size correction factor (Takano et al., 1980). Furthermore, methylene blue solution and 20 wt% aqueous glucose solution for the model cast, and the radioactive water mist, labelled ^{99m}Tc for the real human maxillary sinus, were used in order to quantitatively confirm the particle concentration. The concentration of each aerosol was determined by the colorimetric method for methylene blue, by the glucose oxidase method for the glucose solution, and by the scintillation counting method for radioactive water mist.

The pressure change in the maxillary sinus was measured by a diffusion-type piezo balance pressure gauge under various breathing conditions, such as deep or natural breathing.

RESULTS AND DISCUSSION OF PARTICLE DEPOSITION EFFICIENCY

Numerical results

The numerical results of the deposition efficiency of aerosol particles are shown in Figure 2. Under the same pressure difference between the nasal cavity and the

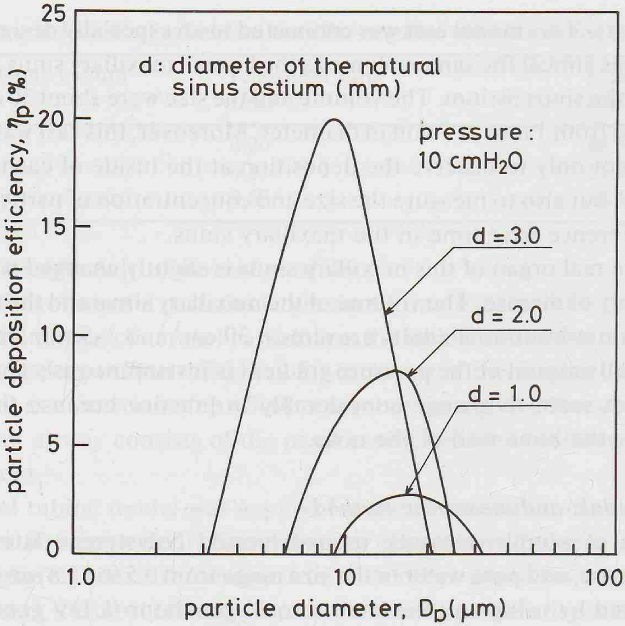


Figure 2. A calculated results of partial deposition efficiency in a human maxillary sinus.

maxillary sinus, partial deposition efficiency was increased with a larger natural sinus ostium, and the particle diameter deposited on the inside wall of the maxillary sinus was decreased.

In practice, the pressure gradient will change under various physical conditions, and also the aerosol flow rate corresponding to the total airflow into the maxillary sinus is decreased with increase in the size of the sinus ostium. Therefore, it might not be suitable to compare such deposition efficiency at the same total aerosol flow, as shown in Figure 2. This is because this flow will be changed with the relaxation time which is a function of the diameter of the sinus ostium canal. However, this figure indicates only the qualitative tendency of the partial deposition efficiencies.

Particle deposition in the model cast

Two kinds of experiments were done by using a model cast to evaluate both the overall and partial deposition efficiencies.

To measure the overall deposition efficiency, the aerosol particle was produced by the ultrasonic generator. The aerosol had a log-normal distribution, and the particle size and its geometric standard deviation were 4.0 μm and 1.4, respectively.

The particle deposition strongly depends on the following parameters: the aerosol flow rate into the maxillary sinus, the pressure difference between the nasal cavity and the maxillary sinus, the particle size distribution of aerosols, the response characteristics of the aerosol flow, and the diameter of the sinus ostium canal. Using normal medical aerosol therapy, the parameters related to the particle properties, such as size distribution, are fixed for each method of aerosol generation. However, the pressure difference is usually changeable up to 60 cm H_2O for the measurement of unpleasantness in the human body. The diameter of the sinus ostium canal was varied from 1.0 to 3.0 mm, the same as the possible degree of deformation due to disease. In this way, the experiments were performed under conditions where the diameter of the sinus ostium canal was between 1.0 and 5.0 mm, and the pressure difference was a constant 10–15 cm H_2O. If the pretreatment of the opening of the sinus ostium up to 5.0 mm is possible, this aerosol therapy would be effective in increasing the particle deposition into the maxillary sinus.

Table 2a indicates the measured values of overall particle deposition efficiency using the 20 wt% solution of aqueous glucose. The deposition efficiency was increased from 1.32 to 2.76% as the diameter of sinus ostium increased. This means that the most important factor determinating particle deposition is the size of the entrance to the sinus ostium. Thus, the value of the sinus ostium diameter is of importance in determining the deposition properties of aerosol particles.

The partial deposition efficiency was examined by using the water mist and the polystyrene latex. As shown in Table 2b for the water mist and in Table 2c for the polystyrene latex, the partial deposition efficiency also changed in accordance

Table 2. Experimental results of particle deposition efficiency.

sample aerosols	diameter of sinus ostium (mm)	deposition fraction (%)		
a) 20 wt% aqueous glucose solution (glucose oxidase method)	5	2.76		
	3	2.66		
	2	2.01		
	1	1.32		
		particle size (μm)		
		0–5	5–10	10–15
b) water mist (stain size ratio method)	3	44	51	5
	2	53	45	2
	1	87	12	1
		particle size (μm)		
		5.7	11.9	15.8
c) polystyrene latex (particle counter)	3	42	50	8
	2	56	42	2
	1	80	19	1

with the diameter of the sinus ostium. The experimental result indicated that larger sized particles passed through the sinus ostium with increase of the sinus ostium diameter. In another words, smaller sized particles could enter the maxillary sinus in the case of a smaller diameter of the sinus ostium. However, as the particle deposition is mainly caused by the force of inertia in the size range larger than 1.0 μm, much smaller sized particles could not be deposited on the surface wall of the maxillary sinus. Therefore, a certain suitable range of particle size could be assumed to exist, from 3 to 10 μm for the maxillary sinus, as mentioned before.

Particle deposition in the real human sinus

The deposition pattern of aerosol particles in the sinus area would essentially be the same for a living human and for the model cast, even though there are several differences between them such as, the model cast does not have adjustment functions for simultaneously controlling temperature and humidity as well as ciliary movement. Furthermore, the general value of internal pressure in the maxillary sinus is changed with the flowrate and the diameter of nasal ostium, as shown in Table 3.

In order to confirm this similar deposition pattern between them, the radioactively labelled aerosol particles were performed on an actual human sinus in the case where the pressure difference was 10 cm H_2O. The experimental results for six samples are shown in Table 4, and the deposition pattern was also indicated in Figure 3 as an example of the samples. The average value of the deposition efficiency of the aerosol particles was 3.34%, which was similar to the value of 5% corresponding to the case where the diameter of the sinus ostium is 3.0 mm, and the particle diameter is 4.0 μm in Figure 2.

Table 3. Data on the internal pressure in maxillary sinus in the case where the flowrate of aerosol is 15 lpm.

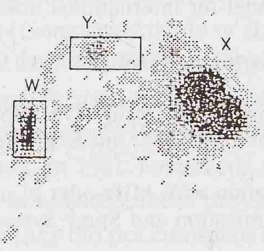
conditions	diameter of nasal ostium (mm)		
	5	3	1
breath			
inspiration	−3	−2	−1
expiration	+3	+2	+1
deep breathing	−30	−20	−12
swallow	+60	+60	+30
Politzel's method			
open epipharynx	+18	+15	+10
swallow	over +300	+300	+200

Table 4. Average value of the deposition efficiency by means of radioactive aerosol particle.

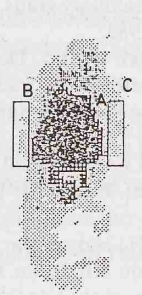
run no.	total deposition efficiency (%)
1	3.59
2	1.90
3	2.40
4	3.14
5	4.92
6	4.11
average	3.34%

Assuming that the diameter of the sinus ostium is about 3 mm in these samples, this result was similar to the experimental values using the aqueous glucose solution in the model cast, as shown in Table 2a. Furthermore, this tendency could be applied to the numerical results of the physical model. The calculated value for the diameter of the sinus ostium of 3 mm was nearly the same as an average one.
Therefore, judging from the experimental analysis using the radioactive particles, the validity of the physical model for the deposition efficiency was confirmed when using the same experimental parameters.

(a) side view



(b) front view



radioactive counting

key	total	mean	area
W	662	16.55	40
X	6892	430.75	16
Y	288	5.75	50

radioactive counting

key	total	mean	area
A	19160	638.667	30
B	311	11.519	27
C	377	13.963	27

Figure 3. Experimental results of particle deposition efficiency by using a radioactive aerosol (^{99m}Tc).

CONCLUSION

By acting on the pressure gradient between the nasal cavity and the maxillary sinus, the aerosol flow through the sinus ostium was induced even for such a closed organ, and the aerosol particles were then deposited on the surface wall of the maxillary sinus. According to the physical model, particle deposition instantaneously took place in the sinus area, and its mechanism is mainly explained as the inertia impact of aerosol particles ejected from the sinus ostium onto the inside wall of the maxillary sinus. In the experiments, it was indicated that the deposition efficiency in this sinus area was about 3% under conditions where the mean particle diameter and the pressure difference were 3–10 μm and 10–15 cm H_2O respectively.

Consequently, this aerosol therapy is applicable where the diameter of the sinus ostium canal is larger than 1 mm, which means a middle and slight degree of the disease.

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