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Clinical and *in vitro* evaluation of membrane humidifier that does not require addition of water

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It is well known that conventional bubbling humidifiers are capable of producing micro-aerosols contaminated with bacteria. We developed a unique humidifier, named a membrane humidifier, that does not require an external water supply. This new system obtains moisture from room air. We investigated the clinical and *in vitro* evaluation of the membrane humidifier.

Ten patients with chronic pulmonary disease participated in the study. We evaluated the partial pressure of oxygen in arterial blood (PaO_2) of 10 patients who used the new device. We conducted an *in vitro* study to determine whether the device could prevent the bacterial contamination of humidified-oxygen. We passed compressed air contaminated with *Pseudomonas aeruginosa* outside the hollow fibres of the membrane humidifier, and the humidified-oxygen passed inside the hollow fibres was sampled into nutrient broth periodically for 10 days. We also compared the relative humidity of oxygen humidified by a membrane humidifier with that of oxygen humidified by a bubbling humidifier.

There was no significant difference between measured PaO_2 while breathing oxygen humidified using a membrane humidifier and that while breathing oxygen humidified using a bubbling humidifier. Cultures of the humidified-oxygen passed through the hollow fibres were negative for bacteria. The membrane humidifier could produce good humidification.

The new device appeared to prevent bacterial contamination, and may help to reduce the risk of infection in patients at hospital and home.

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Introduction

Dry gas is conventionally humidified for clinical use by a standard bubble water humidifier (1–3). Its disadvantages include difficulty in cleaning the water reservoir and in changing the water. Furthermore, the water reservoir can become contaminated with such hydrophilic species as *Pseudomonas* and *Legionella* (4–6). Such humidifiers have been found to produce micro-aerosols that spread bacterial infection (7). Multiple use of a bubble water humidifier in the hospital can spread pathogens between patients (4,7,8). To reduce the risk of infection, the water reservoir must be cleaned periodically and the water must be changed frequently. We have developed a new humidifier, named a membrane humidifier, whose function does not require the addition of external water for humidification. This new compact device cannot only be used in the hospital, but can also be incorporated in a home oxygen concentrator (9,10). The membrane's surface consists of a dense polymer layer that is free of pinholes. If this new device can prevent bacterial contamination, it will be able to reduce the risk of respiratory infection in both hospital and home. This preliminary study evaluated the membrane humidifier to determine whether bacterial contamination could be prevented. We also evaluated the clinical utility of this new device in a small number of patients.

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Methods

PATIENTS

Ten Japanese patients (five men and five women, mean age; 66·6 years) participated in the study after giving their informed consent. They were all hospitalized for the treatment of chronic pulmonary disease with chronic respiratory failure, and were receiving oxygen therapy. Diagnoses were emphysema (three patients), sequelae of tuberculosis (three patients), diffuse panbronchiolitis (two patients), idiopathic interstitial pneumonia (one patient), and interstitial pneumonia with collagen disease (one patient). The clinical condition of each patient was stable. Local Ethical Committees approved the protocol for this study.

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STRUCTURE AND FUNCTION OF MEMBRANE HUMIDIFIER

The new membrane humidifier is composed of a steel cylinder (length: 210 mm, diameter: 45 mm) containing several hundred hollow fibres made by polyimide resin. The different permeation rate of gases is used to separate water molecules from air. Water vapor can permeate a polyimide membrane of a hollow fibre (UBE membrane, UBE Industries, Ltd., Tokyo, Japan) hundreds of times more readily than either nitrogen or oxygen. The polyimide membrane's surface consists of a dense polymer layer that is free of pinholes. Its pore size is less than 10^{-3} μm (11,12). Compressed air is passed outside the hollow fibres. The compressor can vary the air pressure in the membrane humidifier. As the room air is passed under high pressure through the space around the hollow fibres (outside passage), the water molecules in the air permeate the membrane of the hollow fibres. Dry oxygen from the hospital's oxygen supply is passed through the hollow fibres (inside passage) within the membrane humidifier, and is humidified with water vapour (Fig. 1). This device is compact and can be placed everywhere. A unit of hollow fibres is highly durable. The polyimide membrane of a hollow fibre can be sterilized by alcohol or disinfecting gases. This new system obtains moisture from room air, and the mechanism is original.

MEASUREMENT

We studied patients from winter to spring. Spirograms (Chestac 55V, Chest IM, Tokyo, Japan) were obtained for each patient prior to the study. The partial pressure of oxygen in arterial blood (PaO_2) was measured in the supine position after the patient had breathed each of the followings for 2 h: (a) room air; (b) oxygen via a nasal cannula that was humidified with a membrane humidifier; (c) oxygen via a nasal cannula that was humidified with a conventional bubble water humidifier (Koike Medical Co., Tokyo, Japan). The oxygen from the hospital's supply had an oxygen concentration of nearly 100%. The flow rate through the nasal cannula was 1 l min^{-1} in each patient.

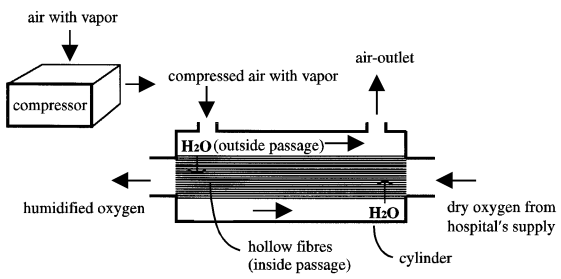

FIG. 1. Structure and function of new membrane humidifier. Compressed air with water vapor is passed through outer passage. Water vapor only permeate the hollow fibres. Dry oxygen from hospital's supply is passed inside hollow fibres, and is humidified with water vapor.

The concentrations of humidified-oxygen were measured directly with an oximeter (LC750, Toray Co., Tokyo, Japan) while using with the membrane humidifier or the conventional bubble water humidifier after the PaO_2 had been measured in each patient. We also determined the relative humidity of room air, that of dry oxygen from the hospital's oxygen supply and that of oxygen humidified by a membrane humidifier or a bubble water humidifier. The relative humidity of the dry oxygen delivered from the hospital's oxygen supply and that of the humidified-oxygen from the two different humidifiers were measured with a digital hygrometer (TRH-CA, Shin-ei Co., Tokyo, Japan) after the gases had flowed into a partially opened container (500 ml) for 30 min. The pressure of the compressed air in the membrane humidifier was either 98 kPa (1 kg f cm^{-2}) or 196 kPa (2 kg f cm^{-2}). The temperatures in the laboratory room were maintained at 20–22°C during the study. During every session, the change of temperature in the laboratory room was maintained within 1°C.

In an *in vitro* study, we evaluated whether the membrane humidifier could prevent bacterial contamination. The outside passage of the hollow fibres in that device was contaminated with 3 ml of fluid containing *Pseudomonas aeruginosa* (10^8 ml^{-1}). On the first day, the contaminated air from the air-outlet of the outside passage was passed directly for 2 h into 100 ml of nutrient broth (LB Broth, Life Technologies, Inc., ML, USA) as a control, and the humidified-oxygen (1 l min^{-1}) that had been passed inside the hollow fibres was sampled into another nutrient broth for 2 h. We also passed the compressed air contaminated with 3-ml of fluid containing 10^8 ml^{-1} *Pseudomonas aeruginosa* outside the hollow fibres of the membrane humidifier on the second, third, fourth and tenth days of 10 consecutive days, and the humidified-oxygen from the hollow fibres was sampled into the nutrient broth for 2 h. During the 10 days, we did not disinfect the membrane humidifier. Following culture, bacterial identification was performed in the hospital laboratory using quantitative cultures. A sample was taken from 100 ml of the nutrient broth into which either the contaminated compressed air from the outside passage (control) or the humidified-oxygen from the inside passage had been passed. Each sample was diluted with sterile broth to make a 10-fold dilution. We repeated the procedure and made a series of dilution from 10-fold to 10^8-fold. Each diluted sample was inoculated into a plate of trypto-soy agar (Pearlcore, Eiken Chemical Co., Ltd., Tokyo, Japan) containing 7% rabbit blood and incubated in 5% carbon dioxide and air at 37°C for 24 h. Bacterial growth was identified by genus and species.

DATA ANALYSIS

Data are reported as mean $\pm$SD. Evaluation of the significance of the difference between two groups utilized the Student's *t*-test. The significance of the results of multiple comparisons was calculated by two-way analysis of variance (ANOVA) using Scheffe's test. Correlation between the relative humidity of room air and that of the

oxygen flow humidified by the membrane humidifier was calculated using single linear regression and Pearson's coefficient (StatFlex, ViewFlex, Tokyo, Japan). A level of $P<0{\cdot}05$ was considered statistically significant.

Results

The mean percent predicted value of the forced expiratory volume in 1 sec (FEV1) in the 10 patients was $41{\cdot}2\pm15{\cdot}7\%$. The mean PaO_2 while the patients breathed room air was $7{\cdot}91\pm1{\cdot}31$ kPa ($59{\cdot}3\pm9{\cdot}8$ mmHg). No significant difference was observed between the PaO_2 measured while the patients breathed oxygen that was humidified with the membrane humidifier ($11{\cdot}1\pm1{\cdot}76$ kPa; $83{\cdot}1\pm13{\cdot}2$ mmHg) and with the conventional bubble water humidifier ($11{\cdot}2\pm1{\cdot}87$ kPa; $83{\cdot}9\pm14{\cdot}0$ mmHg). The mean oxygen concentration humidified with the membrane humidifier was $97{\cdot}6\pm1{\cdot}1\%$, and that humidified with the conventional humidifier was $97{\cdot}8\pm1{\cdot}2\%$ when the oxygen from hospital's supply of 100% concentration was passed into the humidifiers. There was no significant difference between them.

The relative humidity of the air in the laboratory room was $37{\cdot}3\pm13{\cdot}9\%$. The relative humidity of the dry oxygen flow delivered by the hospital's oxygen supply was $7{\cdot}1\pm1{\cdot}1\%$ after it had flowed into a partially opened 500 ml container for 30 min. A significant difference was observed between the relative humidity of the oxygen from the membrane humidifier ($82{\cdot}2\pm10{\cdot}7\%$) and that from the conventional bubbling humidifier ($89{\cdot}9\pm2{\cdot}6\%$) ($P<0{\cdot}05$) (Fig. 2). However, when the relative humidity of room air was more than 30% ($n=7$), there was no significant difference between the relative humidity of the oxygen delivered by the membrane device ($88{\cdot}6\pm3{\cdot}8\%$) and that delivered by the conventional bubbling humidifier ($90{\cdot}8\pm2{\cdot}0\%$). A significant linear relationship was observed between the relative humidity of room air and that of the oxygen humidified by the membrane device when the pressure of the compressed air was either 98 kPa (1 kg f cm^{-2}) or 196 kPa (2 kg f cm^{-2}) (Fig. 3).

The control bacterial cultures showed the presence of $3\times10^5\,ml^{-1}$ *Pseudomonas aeruginosa*, when the compressed air was contaminated by 3-ml fluid containing $10^8\,ml^{-1}$ *Pseudomonas aeruginosa*. However, when the contaminated compressed air was also passed outside the hollow fibres, the cultures of the humidified-oxygen, which had been passed inside the hollow fibres, were negative for bacteria (Table 1).

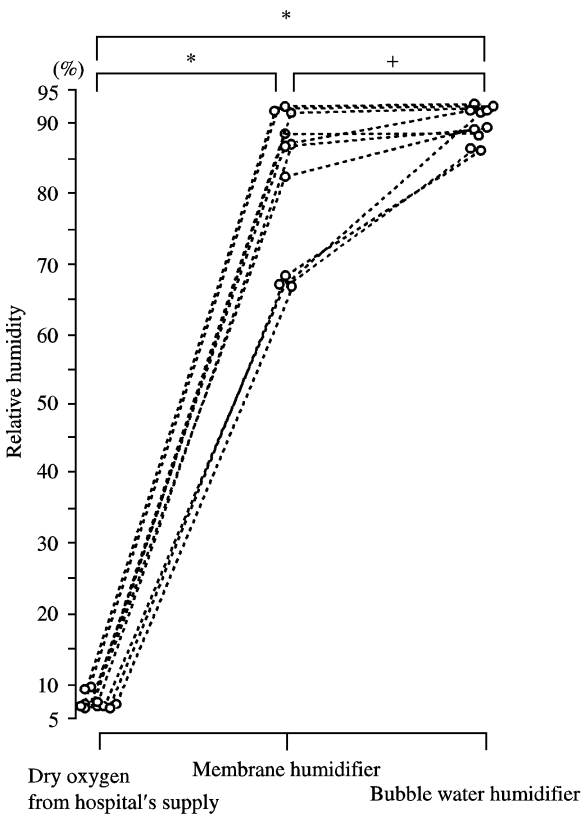

FIG. 2. Relative humidity of dry oxygen from hospital's supply, oxygen humidified by membrane humidifier, and oxygen humidified by bubble water humidifier.
$^*P<0{\cdot}0001$, $^+$: $P<0{\cdot}05$ (Scheffe's test).

Discussion

Although several reports indicate that routine humidification of oxygen for administration by nasal cannula is not necessary for low flow inhalation (13,14), a reduction in humidity could cause discomfort and adversely affect the respiratory mucosa and ciliary activity (2,3). In many countries, when supplement of dry oxygen is provided by nasal cannula, the oxygen is generally humidified by sterile distilled water using a standard bubble water humidifier. However, sterile distilled water is expensive. We developed a new humidifier, which can humidify dry oxygen without the use of water.

The present study showed that the mean PaO_2 in patients was not adversely affected by the new membrane humidifier, because no significant difference was observed between the PaO_2 measured while they breathed oxygen from the membrane humidifier or from the conventional bubble water humidifier.

A significant linear relationship was observed between the relative humidity of room air and that of the oxygen humidified by the membrane humidifier. Since this system obtains its water vapour from room air, it appears that its efficiency is diminished when the relative humidity of room air is low (9,10). In previous studies, the pressure of the compressed air in the membrane humidifier was about 98 kPa (1 kg f cm^{-2}) (9,10), but the pressure could be variable in this study. The relative humidity of oxygen humidified by the membrane humidifier was increased when the air pressure was increased (Fig. 3).

A significant difference was observed between the relative humidity of the oxygen humidified by the membrane humidifier and that humidified by the conventional

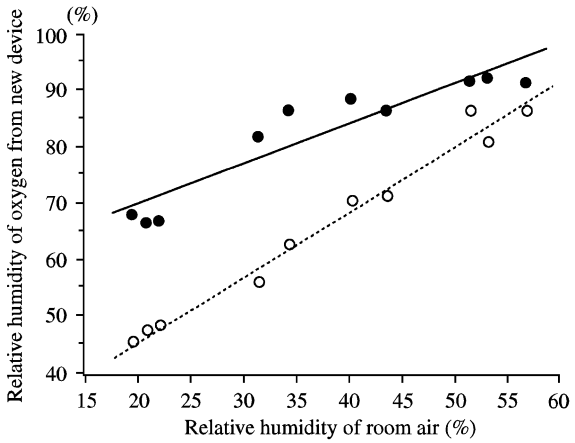

FIG. 3. Single linear regression observed between the relative humidity of room air and that of the oxygen humidified by the new membrane humidifier. ●: significant relationship between the relative humidity of room air and that of oxygen humidified by membrane humidifier when 196 kPa (2 kg f cm^{-2}) pressure was added to air ($r^2 = 0{\cdot}87$, $P < 0{\cdot}0001$); ○: significant relationship between the relative humidity of room air and that of oxygen humidified by membrane humidifier when 98 kPa (1 kg cm^{-2}) pressure was added to air ($r^2 = 0{\cdot}98$, $P < 0{\cdot}0001$).

bubble water humidifier (Fig. 2), because the mean relative humidity of the oxygen humidified by the new device was 67% when the relative humidity of room air was low (about 19–22%) (Figs. 2 and 3). However, when the relative humidity of room air was above 30%, we found no significant difference between the relative humidity of the oxygen humidified by the membrane humidifier ($88{\cdot}6 \pm 3{\cdot}8\%$) and that humidified by the conventional bubble water humidifier ($90{\cdot}8 \pm 2{\cdot}0\%$). The new membrane humidifier supplied well-moistured nasal oxygen without the need of water. This new device can be incorporated in pressure swing adsorption (PSA) type oxygen concentrator (9,10). Since it eliminates the laborious cleaning of the reservoir and changing of the water, it will be beneficial to the patients in home oxygen therapy.

TABLE 1. Bacterial culture of the air contaminated with 3 ml of fluid containing *Pseudomonas aeruginosa* (10^8 ml^{-1}) and cultures of the oxygen humidified with a membrane humidifier on the first, second, third, fourth and tenth days of 10 consecutive days

Day	1	2	3	4	10
Culture of contaminated-air as control	(+)				
Culture of humidified-oxygen	(−)	(−)	(−)	(−)	(−)

+: positive, 3×10^5 ml^{-1} *Pseudomonas aeruginosa*; −: negative, no presence of bacterial growth.

The use of prefilled disposal oxygen humidifier units can reduce the risk of contamination during handling and attachment (5,6). Even though they are sealed, the prefilled disposable oxygen humidifier bottles should be reportedly used within 30 days (6). The new membrane humidifier does not need water for humidification, and the unit of hollow fibres can be durable for about 8 y. In our study, when the compressed air contaminated with *Pseudomonas Aeruginosa* was passed outside the hollow fibres in the new device, cultures of humidified-oxygen that had been passed inside the hollow fibres were negative for bacteria on the first, second, third, fourth and tenth day of 10 consecutive days. If the humidified-oxygen is contaminated with bacteria, the results of cultures from the gas samples will show the positive bacterial growth (4,7). The polyimide membrane used for the hollow fibres in this humidifier has a dense layer of pinhole-free surface. The size of the hole on the surface is considered to be less than 10^{-3} μm (11,12). The size of bacteria is reportedly 0·2–10 μm, and fungi are generally larger (15). Water vapour that is present in the air dissolves and diffuses into the membrane wall. Since bacteria and fungi cannot permeate the membrane, this new type of membrane humidifier may be less prone to the bacterial contamination than conventional bubbling humidifiers. The new device appears to prevent bacterial contamination of the humidified-oxygen, and its use in the hospital or home setting may reduce the risk of bacterial infection. This device may be used by patients, who need the inhalation of oxygen, in a clean room which no people should enter.

The cost of a unit of the hollow fibres in the membrane humidifier is 30 000 yen. The cost of a compressor used in the membrane humidifier is 50 000 yen. On the other hand, the cost of a conventional bubble water humidifier (Koike medical, Tokyo, Japan) is 20 000 yen. The noise from the compressor is small. When the membrane humidifier is incorporated into PSA type oxygen concentrator, the compressor of the oxygen concentrator can be shared with a membrane humidifier (9), and the cost of the new device is only 30 000 yen.

This new device has many advantages. Detailed, controlled long-term studies are required to delineate further utility of the new membrane humidifier.

Acknowledgement

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