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Impact of Vocal Fold Dehydration on Vocal Function and Its Treatment

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Summary: The change of vocal function after vocal fold dehydration due to dryness was discussed along with the treatment effect of different atomizing agents. Forty-eight staffs from The Central Hospital of Wuhan were recruited. All volunteers breathed dry air for vocal fold dehydration. After dry air inhalation, the subjects were randomly divided into four groups, with 12 cases each. Three groups were treatment groups, receiving 0.9% normal saline (IS), 5% hypertonic saline (HS) and double-distilled water (SW) atomizing inhalation therapy, respectively, and the last group was the control group without treatment. Voice data were collected for all subjects before and immediately after dry air inhalation using the Multi-Dimensional Voice Program (MDVP) system. Atomizing inhalation therapy was given 10 min after dry air inhalation, and voice data were collected using MDVP system at the following time points after atomizing inhalation treatment: 5 min, 20 min, 35 min, 50 min, 65 min, 80 min, 95 min, 110 min. In the control group, voice data were collected at the same time points and compared with those of treatment groups. The vocal function parameters collected before and after dry air inhalation as well as after treatment were subjected to test using SPSS 16.0 software. In the four groups, jitter (fundamental frequency perturbation), shimmer (amplitude perturbation), and amplitude perturbation quotient (APQ) were significantly increased after dry air inhalation ($P<0.05$). In IS, HS and SW groups, after atomizing inhalation treatment, there was an obvious reduction in jitter, shimmer and APQ, showing significant differences as compared with those after dry air inhalation ($P<0.05$). Moreover, these parameters were significantly lower than those in the control group ($P<0.05$). The jitter, shimmer and APQ in the IS group were significantly lower than those in the HS and SW groups ($P<0.05$). We are led to a conclusion: Vocal fold dehydration induced by dryness can reduce the stability of voice; such decreased voice stability can be improved by atomizing inhalation therapy; without proper treatment, voice stability caused by vocal fold dehydration cannot heal spontaneously; of three atomizing agents namely, IS, HS and SW, IS had the best treatment effect for decreased voice stability caused by vocal fold dehydration.
Key words: dryness; vocal fold dehydration; vocal function; Multi-Dimensional Voice Program; atomizing inhalation

Our preliminary research[1] indicated that voice stability is impaired by vocal fold dehydration due to dryness. Atomizing inhalation can effectively reduce the short-term adverse impact on the vocal fold. However, no method has been established for treating vocal fold dehydration caused by long-term dryness[2]. In the present study, 48 volunteers were recruited to receive dryness intervention. Then these volunteers were randomly divided into 4 groups, among which 3 groups were treated by 3 different atomizing agents, and the other was control group. Voice indicators were detected by Multi-Dimensional Voice Program (MDVP) at different time points, so as to discuss the functional changes of voice before and after dryness and with or without atomizing inhalation therapy.

1 MATERIALS AND METHODS

1.1 Subjects

A total of 48 staffs from The Central Hospital of Wuhan, including 24 males and 24 females, were recruited. These volunteers were aged 28–33 years old, with an average of 30±0.6 years old. All subjects were physically healthy, without a history of voice disorders and respiratory tract diseases or smoking/

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drinking history. No pathological changes of vocal fold were found by fibrolaryngoscopy before test. All subjects had no history of upper respiratory infection within 2 months before the test and no intake of diuretics, dehydrants, antihistamines or contraceptive pills. Participant identification and recruitment methods, as well as all procedures related to the present investigation, were approved by The Central Hospital of Wuhan Institutional Review Board.

1.2 Methods

1.2.1 Data Randomized double-blind trial was adopted. Both subjects and testers were blinded to the objectives of the study. Dry air inhalation and treatment intervention were administered for all subjects, and acoustic detection was performed by the same physician at the same time point using the same MDVP system. The 48 subjects were randomly divided into 4 groups. Three groups were treated with three different atomizing agents, respectively, and the other group was the control group receiving no treatment. The three atomizing agents were prepared by the same person. The subjects and testers were blinded to the composition of the atomizing agents.

1.2.2 Relative Air Humidity of Laboratory For each test, Multifunction HTC-8 Digital Hygrometer (Zhengzhou Boyang Instrument Co., Ltd., China) was used to measure the relative humidity of the laboratory. The means and the standard deviations (SD) were calculated and one-way analysis of variance (ANOVA) was employed for statistical analysis. Results showed that relative humidity (RH)=67% (SD=±5.6%). Thus there was no statistical difference in RH of laboratory for each test (F=0.365, P>0.05).

1.2.3 Dry Air Inhalation A nose clip was used for all subjects to prevent the humidification of air in nasal cavity. The subjects wore masks to inhale dry air (RH<3%, 78% nitrogen, 21% oxygen, CO_2 content <350 ppm) for 15 min at a flow rate of 8 L/min.

1.2.4 Atomizing Inhalation Therapy Ultrasonic atomizing inhalation therapy for 10 min was given following dry air inhalation in the treatment groups using ultrasonic atomizer 402AI (Jiangsu Yuyue Medical Equipment & Supply Co., Ltd., China). Three different solutions were used as atomizing agent (20 mL).

1.2.5 Composition of Atomizing Agents in Each Treatment Group The group treated with 0.9% normal saline as atomizing agent was denoted as IS group. The group treated with 5% hypertonic saline served as HS group. The group treated with double-distilled water was denoted as SW group, and the control group denoted as C group.

1.3 Method and Time Points for the Measurement of Voice Indicators

The subjects took the most comfortable position. The microphone was placed at a distance of 10 cm from the lip. The subjects were told to utter /i/ sound 3 times, and the voice was sampled at the frequency of 44.1 kHz. The voice samples in 3 utterances were stored and input into the computer using Computerized Speech Lab (CSL) Model 4150 system (Kay Elemetrics Corporation, USA). MDVP software in CSL system was used for spectral analysis of the voices in light of three voice stability indicators, which were jitter, shimmer and amplitude perturbation quotient (APQ)[3]. Before dry air inhalation, all subjects were tested for voice stability using MDVP system. The measured data were considered as baseline. MDVP system was used to detect voice stability indicators immediately after dry air inhalation. Detections were also performed at 5 min, 20 min, 35 min, 50 min, 65 min, 80 min, 95 min and 110 min after atomizing inhalation therapy, respectively. Voice stability indicators were detected using MDVP system at the same time points for the C group, and comparison was made with the treatment groups. The voice stability indicators after dry air inhalation and atomizing inhalation therapy were compared with the baseline data for each group. The variation rates compared with the baseline were calculated, and the fitting curves were plotted[4].

1.4 Statistical Analysis

Statistical analysis was performed using SPSS 16.0 software. P<0.05 was considered statistically significant, and P<0.01 was considered highly statistically significant.

2 RESULTS

2.1 Variations of Jitter before and after Dry Air Inhalation and before and after Treatment for Each Group

After dry air inhalation for all subjects, jitter was increased significantly compared with that before dry air inhalation (P<0.01). In IS group, jitter began to decrease at 5 min after atomizing inhalation therapy, and the difference was of statistical significance at 20 min (F=12.19, P<0.05). HS group showed an obvious decline of jitter 80 min after atomizing inhalation therapy, and the difference was statistically significant (F=0.87, P<0.05). At 5 min after atomizing inhalation therapy, SW group showed a significant decline of jitter (F=2.415, P<0.05). The differences between the treatment groups and the C group are shown in table 1. The variation rates of jitter before and after dry air inhalation and before and after treatment in each group are shown in fig. 1.

As shown by the variations of jitter, the jitter after treatment in all 3 treatment groups declined significantly, while that of the C group increased obviously. Among the treatment groups, jitter of the IS group declined to the minimum 35 min after atomizing

Table 1 Variations of Jitter before and after dry air inhalation and after treatment in 4 groups [Jitter (%), $\bar{x}$±s]

Groups	Before[1]	After[2]	After treatment							
			5 min	20 min	35 min	50 min	65 min	80 min	95 min	110 min
IS	0.57±0.30$^{\Delta}$	0.87±0.40$^{\Delta}$	0.48±0.11	0.43±0.08*	0.49±0.16	0.34±0.12	0.45±0.17	0.47±0.15	0.56±0.25	0.46±0.10
HS	0.46±0.19$^{\Delta}$	0.81±0.25$^{\Delta}$	0.71±0.28	0.64±0.33	0.72±0.23	0.58±0.29	0.66±0.30	0.39±0.18*	0.78±0.48	0.64±0.33
SW	0.49±0.12$^{\Delta}$	0.85±0.29$^{\Delta}$	0.50±0.14*	0.57±0.05	0.49±0.13	0.59±0.20	0.54±0.20	0.69±0.4	0.86±0.38	0.73±0.31
C	0.64±0.12$^{\Delta}$	0.90±0.34$^{\Delta}$	0.90±0.28	0.96±0.36	1.12±0.50	1.09±0.52	0.99±0.30	1.09±0.32	1.01±0.21	1.17±0.32

Before[1], before dry air inhalation; After[2], after dry air inhalation; IS, 0.9% normal saline; HS, 5% hypertonic saline; SW, double-distilled water; C, control.

The data before dry air inhalation were taken as baseline data.

$^{\Delta}$indicates significant differences before and after dry air inhalation in the four groups, P<0.05

*indicates significant difference *vs.* Jitter after dry air inhalation, P<0.05

Comparison between IS group and C group at each time point indicated F=92.539, P<0.05; comparison between HS group and C group at each time point indicated F=51.354, P<0.05; comparison between SW group and C group at each time point indicated F=66.616, P<0.05.

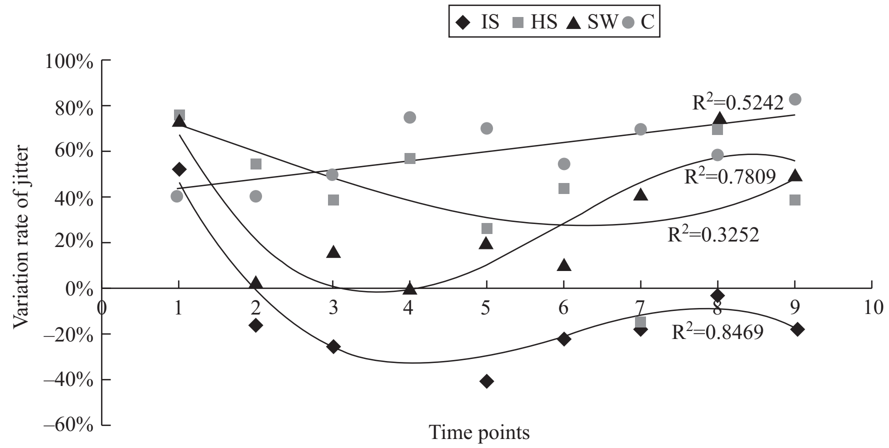

Fig. 1 Variation rates of jitter after dry air inhalation and at different time points after treatments compared with the baseline
IS: 0.9% normal saline; HS: 5% hypertonic saline; SW: double-distilled water; C: control group; 1: before dry air inhalation; 2: after dry air inhalation; 3–10: 5, 20, 35, 50, 65, 80, 95 and 110 min after treatment, respectively.

$$\text{Variation rate of Jitter}=\frac{\text{Jitter measured at different time points–Jitter measured before dry air inhalation (baseline)}}{\text{Jitter measured before dry air inhalation (baseline)}}\times 100\%$$

inhalation therapy, and the variation rate was negative. This indicated the jitter was restored to the level before dry air inhalation.

2.2 Variations of Shimmer before and after Dry Air Inhalation and before and after Treatment for Each Group

We found through experiment that shimmer after dry air inhalation increased significantly for all subjects (P<0.01). For IS group, shimmer decreased significantly at 5 min after atomizing inhalation therapy compared with that after dry air inhalation (F=0.29, P<0.05). HS group showed an insignificant decrease of shimmer after atomizing inhalation therapy compared with that after dry air inhalation. SW group had a significant decrease of shimmer 35 min after atomizing inhalation therapy (F=1.082, P<0.05). The differences between the treatment groups and the control group are shown in table 2. The variations of shimmer before and after dry air inhalation and before and after treatment as compared with the baseline are shown in fig. 2.

As shown by the variations of shimmer, all three treatment groups had an obvious decrease of shimmer after treatment, while the control group had an increase of shimmer. Normal saline group showed an obvious decrease of shimmer 20 min after atomizing inhalation therapy. Shimmer reached the lowest at about 30 min, which was basically the level before dry air inhalation.

2.3 Variations of APQ before and after Dry Air Inhalation and before and after Treatment

We found that APQ increased obviously in all subjects after dry air inhalation (P<0.01). Furthermore, APQ decreased greatly in IS group 5 min after atomizing inhalation therapy, reaching the lowest at 30 min. However, the APQ immediately after dry air inhalation was not significantly changed. At each time point after treatment, HS group and SW group

Table 2 Variations of shimmer before and after dry air inhalation and before and after treatment in each group [Shimmer (%), $\bar{x}\pm s$]

Group	Before[1]	After[2]	After treatment							
			5 min	20 min	35 min	50 min	65 min	80 min	95 min	110 min
IS	2.66±0.36$^{\Delta}$	3.04±0.66$^{\Delta}$	1.94±0.85*	2.12±0.62	2.25±0.36	2.24±0.52	2.35±0.27	2.46±0.68	2.87±0.55	2.66±0.59
HS	2.57±0.27$^{\Delta}$	3.30±0.85$^{\Delta}$	2.95±0.55	2.91±0.54	2.88±1.06	3.27±0.98	3.19±1.66	2.81±0.57	3.10±0.56	3.03±0.85
SW	2.01±0.39$^{\Delta}$	3.16±0.84$^{\Delta}$	2.48±0.79	2.53±0.75	2.25±0.51*	2.23±0.50	2.26±0.60	2.94±1.02	2.67±0.68	2.99±0.86
C	2.15±0.56$^{\Delta}$	2.68±0.37$^{\Delta}$	3.47±0.66	3.54±1.02	3.09±1.24	3.46±0.82	3.43±0.87	3.55±0.87	3.31±0.85	3.12±1.06

Before[1]: before dry air inhalation; After[2]: after dry air inhalation; IS, 0.9% normal saline; HS, 5% hypertonic saline; SW, double-distilled water; C, control group

Data before dry air inhalation were taken as baseline data.

$^{\Delta}$indicates significant differences before and after dry air inhalation in each group, $P<0.05$

*indicates significant difference *vs.* Shimmer after dry air inhalation, $P<0.05$

Comparison between IS group and C group at each time point indicated $F=5.839$ and $P<0.05$; comparison between HS group and C group at each time point indicated $F=1.467$, $P<0.05$; comparison between SW group and C group at each time point indicated $F=0.392$, $P<0.05$

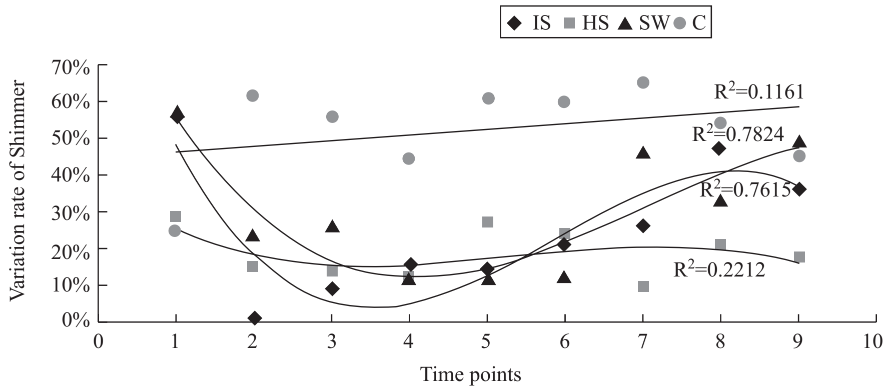

Fig. 2 Variations of shimmer after dry air inhalation and at different time points after treatment for each group compared with the baseline

IS, 0.9% normal saline; HS, 5% hypertonic saline; SW, double-distilled water; C, control group; 1: before dry air inhalation; 2: after dry air inhalation; 3–10: 5, 20, 35, 50, 65, 80, 95 and 110 min after treatment, respectively.

$$\text{Variation rate of Shimmer}=\frac{\text{Shimmer measured at different time points–Shimmer measured before dry air inhalation (baseline)}}{\text{Shimmer measured before dry air inhalation (baseline)}}\times 100\%$$

exhibited an obvious decline of APQ. But the difference was of no statistical significance compared with that immediately after dry air inhalation. The differences between the treatment groups and the control group are shown in table 3. The variation rates of APQ after dry air inhalation and after treatment compared with the baseline are shown in fig. 3.

As shown by the variations of APQ, all treatment groups showed an obvious decline of APQ after treatment, while the control group showed an obvious increase. IS group had an obvious decline of APQ at 20 min after atomizing inhalation therapy, reaching the lowest at about 65 min.

Table 3 Variations of APQ before and after dry air inhalation and after treatment using MDVP in each group [APQ (%), $\bar{x}\pm s$]

Groups	Before[1]	After[2]	After treatment							
			5 min	20 min	35 min	50 min	65 min	80 min	95 min	110 min
IS	2.01±0.33$^{\Delta}$	2.10±0.59$^{\Delta}$	1.76±0.54	1.95±0.43	1.68±0.35	1.57±0.36	1.62±0.43	2.04±0.74	1.99±0.59	1.87±0.20
HS	1.96±0.35$^{\Delta}$	2.37±0.64$^{\Delta}$	2.28±0.62	2.14±0.40	2.26±1.14	2.06±0.43	2.27±0.97	2.07±0.52	2.29±0.42	1.87±0.33
SW	1.58±0.53$^{\Delta}$	1.72±0.61$^{\Delta}$	1.67±0.68	1.56±0.51	1.78±0.47	1.73±0.54	1.65±0.23	1.71±0.53	1.99±0.45	1.83±0.46
C	2.11±0.94$^{\Delta}$	3.35±2.23$^{\Delta}$	2.88±1.34	2.73±0.91	2.19±1.10	2.41±0.57	2.57±0.94	2.58±0.77	2.78±1.29	2.63±0.86

Before[1], before dry air inhalation; After[2], after dry air inhalation; IS, 0.9% normal saline; HS, 5% hypertonic saline; SW, double-distilled water; C, control group

The data before dry air inhalation were taken as baseline.

$^{\Delta}$indicates significant difference before and after dry air inhalation in each group, $P<0.05$.

Comparison between IS group and C group indicated $F=25.942$ and $P<0.05$; comparison between HS group and C group indicated $F=13.863$ and $P<0.05$; comparison between SW group and C group indicated $F=28.177$ and $P<0.05$

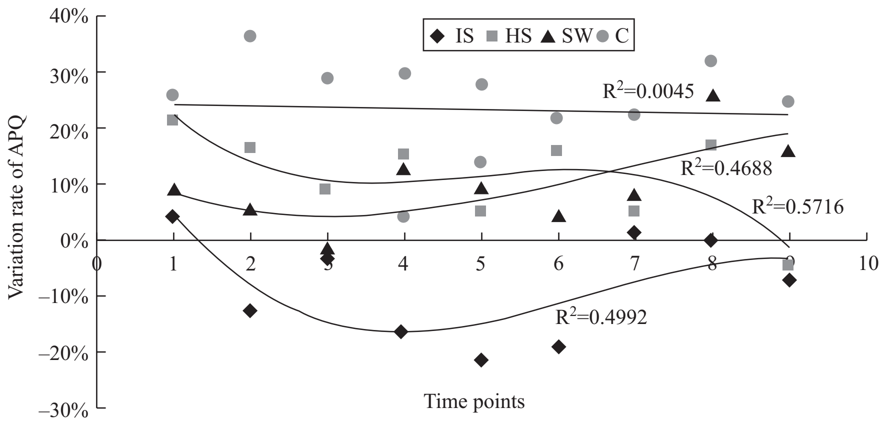

Fig. 3 Variation rates of APQ after dry air inhalation and at different time points after treatment in each group compared with the baseline

IS, 0.9% normal saline; HS, 5% hypertonic saline; SW, double-distilled water; C, control group; 1: before dry air inhalation; 2: after dry air inhalation; 3–10: 5, 20, 35, 50, 65, 80, 95 and 110 min after treatment, respectively.

$$\text{Variation rate of APQ}=\frac{\text{APQ measured at different time points–APQ measured before dry air inhalation (baseline)}}{\text{APQ measured before dry air inhalation (baseline)}}\times 100\%$$

3 DISCUSSION

3.1 Variations of Each Indicator after Dry Air Inhalation

Our experiment indicated that jitter, shimmer and APQ of the 4 groups varied greatly before and after dry air inhalation. Perturbation, including jitter and shimmer, increased considerably after dry air inhalation. Jitter is the variation rate of sound wave frequency between two adjacent cycles. It reflects the cycle-to-cycle variability of pitch and hence the irregularity of vocal fold vibration. Shimmer is the measure of cycle-to-cycle variability of amplitude and reflects the degree of hoarseness. Lieberman first proposed the concept of perturbation as a measure of cycle-to-cycle variability of voice signals in 1961[5]. Perturbation indicates the stability of vocal fold vibration, and a smaller perturbation means a lesser variability of acoustic signals during phonation. Such variability is induced by differences in vocal fold quality, tension and biomechanical properties. Theoretically, biomechanical properties of vocal fold are closely related to its thickness, elasticity and the stiffness of vocal fold surface mucus[5]. In our subject, we only changed the stickiness of vocal fold surface mucus by dry air inhalation, so we considered such change of stickiness as the reason for variations of perturbation. The hydration degree of normal vocal fold surface is regulated by the following three factors: water regulation of mucous blanket, vocal fold epithelial cells and aquaporins on vocal fold surface and laryngotracheal gland secretion. Desiccated air flow will take away most water molecules on vocal fold surface. Desiccated air flow applied for a short period of time causes a significant reduction of water molecules in mucous blanket and laryngotracheal gland secretion, leading to an increase of stickiness of vocal fold surface mucus and stiffness of vocal fold. According to the vibration-based sound production theory, an increased stiffness of vocal fold will affect voice frequency, amplitude and stability. Fisher *et al* believed that vocal fold dehydration would lead to dysphonia or even hoarseness[6]. Tao and their colleagues established the dynamic model representing the relationship between vocal fold vibration and movement of vocal fold surface mucus with the aid of computer. The model showed that phonation threshold pressure (PTP) increased gradually as the water content in vocal fold surface mucus decreased. When PTP increased to a certain value, vocal fold vibration and movement of vocal fold surface mucus would cause damage to vocal fold, or even lead to vocal fold edema and vocal nodules[7]. A large number of clinical trials indicate that vocal fold dehydration has an adverse impact on vocal fold functions. Systemic dehydration and dehydration of vocal fold surface mucus will both cause the impairment of biological features of vocal fold, thus reducing the phonation efficiency of vocal fold. Although PTP cannot directly reflect the situation of vocal fold vibration and the voice quality, it is an indicator of the phonation function of larynx[8]. An increased PTP is usually associated with dysphonia and fatigue in sound production. Fisher *et al*[6] believed that the loss of extracellular fluid can lead to dysphonia or even hoarseness in severe cases. Verdolini *et al*[9] observed through experiments that PTP increased obviously after the intake of diuretics, which was accompanied by dysphonia and hoarseness. Fisher[10] observed the same phenomenon in patients receiving dialysis. Dehydration of vocal fold surface mucus can also cause the impairment of sound production function. Solomon *et al*[11] carried out an experiment in which the subjects were required to phonate for 2 h in dry and humid environment. It was found that the subjects had more difficulties in phonation in dry environment and that PTP increased obviously in humid environment. As the air is humidified in the nasal cavity, PTP in people breathing through the mouth is obviously higher than that in those breathing through the nose under the same environment[12, 13]. Vintturi *et al*[14] proved that dry environment (humidity 25%±5%) was more likely to cause vocal fatigue than humid environment (humidity 65%±5%). Thus jitter and shimmer reflect the degree of hoarseness and vocal roughness, respectively. Hemler *et al*[15] performed an acoustic voice analysis for subjects breathing for 10 min under the humidity of 2%±4% and those breathing for the same time under 100% humidity. The results showed that jitter and shimmer of the former were obviously higher than those of the latter. Thus a dry environment was more likely to cause hoarseness and vocal roughness than a humid environment.

3.2 Variations of Indicators after Treatment in Each Group

Jitter, shimmer and APQ decreased significantly after atomizing inhalation therapy in IS group, HS group and SW group compared with those immediately after dry air inhalation (P<0.05). Our previous studies also confirm this view[1]. The reduction in jitter, shimmer and APQ in IS group, HS group and SW group was statistically significant compared with the control (P<0.05). Atomizing inhalation therapy can effectively reduce the adverse impact of dry air flow on vocal fold. This can be explained by two reasons: first, the water loss in mucous blanket and laryngotracheal gland secretion is directly supplemented; secondly, the water regulation in vocal fold epithelial cells and aquaporins in vocal fold surface plays a regulatory role. Tanner *et al*[16] found that PTP increased considerably in subjects inhaling dry air (5% relative humidity) for 15 min. The subjects were randomly divided into four groups. For the 3 treatment groups, normal saline, double-distilled water and 7% hypertonic saline were given, respectively. The results showed that PTP decreased greatly in the 3 treatment groups compared with the control group, and the three treatment groups did not differ significantly in terms of long-term effect. Jiang *et al*[17] observed that when the canine larynx was immersed in saline solution *in vitro* after drying treatment, PTP declined considerably compared with that immediately after drying treatment. Yiu *et al*[18] discovered that drinking water and stopping phonating could also improve vocal fold dehydration. Thus PTP, jitter and shimmer were decreased, and vocal fatigue was alleviated. Some drugs (eg., decongestants and expectorants) can also relieve vocal fold dehydration and thus the vocal fatigue[19].

The results in figs. 1, 2 and 3 showed that the parameters of jitter, shimmer and APQ in the control group increased significantly with time after the intervention of dry air, which indicated that the vocal cord pronunciation was significantly affected and its stability decreased after drying and dehydration. With the increase of dehydration degree, the vibration amplitude of the vocal cord decreased significantly[20]. After three different atomizers (IS, HS, WS) were given, the parameters of jitter, shimmer and APQ decreased significantly with the passage of time, which indicated that the vocal cords could be partially restored early after atomization treatment. This may be due to the rapid formation of water film on the surface of vocal cords by atomization, which reduces the vibration tension of vocal cords and increases their stability. At the same time, we also observed that after aerosol treatment , the parameters of jitter, shimmer and APQ increased significantly, which may be due to the saturation of the hydration film on the surface of vocal cords caused by aerosol treatment, and the vocal cords' pronunciation stability could not be further improved.

In addition, the parameters of jitter, shimmer and APQ in IS group were significantly lower than those in HS and SW group. It shows that IS has obvious advantages in treating vocal cord dehydration caused by dryness. This may be related to the ion concentration in IS. Vocal cord epithelial cells regulate intracellular and extracellular ion concentration through various ion channels, thus regulating intracellular and extracellular water balance. Na-K-2Cl cotransporter, AQP, ENaC and CFTR channel proteins are important channels for regulating ions in vocal cord epithelial cells. These channels are directly or indirectly related to the concentration of Na-K-2Cl cotransporter, AQP, ENaC and CFTR. The change of sodium ion and chloride ion concentration in the chemical solution may also increase the water content of vocal cords, thus reducing the hardness of the vocal cords, making it easier for the vocal cords to form stable mucosal waves and the voice quality to be more stable[21, 22]. The concentration of ions in the nebulized solution can also cause different degrees of hydration on the surface of vocal cords. The effect of vocal cord dehydration on vocal behavior has always been a hot research topic in the field of voice science, because the degree of vocal cord dehydration is a key factor affecting the normal operation of vocal cord function, but due to its complexity, many of these problems need to be further studied.

Conflict of Interest Statement

The authors had no conflicts of interest to declare in relation to this article.

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