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Voice bubbling therapy for vocal cord dysfunction in difficult-to-treat asthma – a pilot study

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ABSTRACT

Objective: Dysfunctional breathing often coexists with asthma and complicates asthma control, especially in difficult-to-treat asthma. Voice bubbling therapy (VBT) by a specialized speech therapist may influence the breathing pattern. This pilot study investigated the effect of voice bubbling therapy (VBT) in participants with difficult-to-treat asthma, who fulfilled criteria for dysfunctional breathing pattern.

Method: Twenty-four patients were randomized between VBT and usual care (UC). VBT is blowing into a glass (resonance) tube (28 cm in length, 0.9 cm inner diameter) which ends in a bowl of water (1.5 litre). Lung function, capillary blood gas and questionnaires were measured at baseline, at 6 and 18 weeks of follow up.

Results: No difference in ACQ and quality of life was found after VBT compared to UC group. However, after six weeks of bubbling therapy, pCO₂ levels measured in capillary blood gas were higher (baseline median (IQR) pCO₂ = 33.00 (17.25 – 38.6) mmHg; week 6 pCO₂ = 36.00 (29.00 – 42.3) mmHg) $p = 0.01$. Moreover, Δ pCO₂ (baseline – 18 weeks of follow up) was significantly correlated with Δ AAQLQ ($r_s = 0.78$, $p = 0.02$).

Conclusion: VBT in participants with difficult-to-treat asthma resulted in a higher average pCO₂ level, indicating the treatment may improve hyperventilation. However, this did not improve asthma control or quality of life. VBT may have value for a better management of asthma related symptoms.

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Introduction

Dysfunctional breathing often coexists with asthma and complicates asthma control, especially in difficult-to-treat asthma (1). Difficult-to-treat asthma is defined as persistent uncontrolled asthma despite the use of high dose inhalation corticosteroids (ICS) and long acting beta-agonist (LABA). This may be due to severity of the underlying asthma, but often results from other causative factors such as non-adherence, persistent exposure to allergens or toxins, chronic rhinosinusitis, gastro-oesophageal reflux (GERD), obstructive sleep apnea syndrome (OSAS) or serious psychosocial comorbidity (2). Vocal cord dysfunction (VCD) is also a co-morbid condition in difficult-to-treat asthma and is characterized by abnormal adduction of the vocal cords during respiration causing intermittent airway obstruction.

Voice bubbling therapy (VBT) by a specialized speech therapist may influence the breathing pattern (3). VBT involves blowing through a glass straw in water. By forming bubbles, low-frequency vibrations are created in the hypopharynx area. This could result in relaxation of the soft tissue around the vocal cords and lead to improvement of airway symptoms.

This pilot study investigated whether VBT is an effective treatment to improve asthma control in patients with difficult-to-treat asthma, who fulfilled criteria for dysfunctional breathing pattern.

Methods and materials

Case definition

The study was conducted in three medical centers in the Netherlands from April 2016 to September 2018.

Patients with uncontrolled asthma despite optimal treatment (ICS and LABA), with an asthma control questionnaire (ACQ) score of ≥ 1.5 and signs of dysfunctional breathing were included. The diagnosis of dysfunctional breathing pattern was made on a combination of clinical signs of dysfunction breathing (according the Pittsburgh vocal cord dysfunction index (PVCDI) ≥ 4) and chronic hypoxemia with a $p\text{CO}_2 < 35 \text{ mmHg}$ (4.7 kPa) and/or $\text{HCO}_3^- < 23 \text{ mEq/L}$ (4). PVCDI is a four point scoring list which includes the following items: presence of hoarseness/dysphonia, presence of wheezing, throat tightness and fragrances/perfume as a trigger for complaints. All participants were under surveillance of a pulmonologist and checked for the right diagnosis of asthma before inclusion, according to the GINA guidelines (<https://ginasthma.org/>). Other causative factors of uncontrolled asthma such as non-adherence, persistent exposure to allergens or toxins, chronic rhinosinusitis, GERD, OSAS and serious psychosocial comorbidity were excluded or treated adequately before inclusion. Exclusion criteria were active smoking or a history of more than 10 packyears, exacerbation of asthma or airway infection in the past 6 weeks, if participants were not able to perform a reproducible lung function, an $\text{FEV}_1 < 80\%$ or $\text{FeNO} > 50 \text{ ppb}$. All patients were referred to the ear, nose and throat specialist for laryngoscopy to exclude anatomical/mechanical abnormalities. Written informed consent was obtained from all participants. Approval of the study was obtained from the local Medical Ethical and Institutional Review Board of Rotterdam (TWOR) in the Netherlands.

Study design

Patients were randomized 1:1 between usual care (UC) and VBT. The study was a two-armed randomized controlled trial. Participants were randomized to either the two groups in a 1:1 ratio. Randomization was not stratified. There was no blinding for the treatment. Allocation took place by an independent researcher after collection of the baseline data. The method of allocation was concealed in sequentially numbered, sealed, opaque envelopes. Patients in the UC group received standard care with optimal treatment of asthma. Patients randomized to VBT received standard care with optimal treatment of asthma and bubbling therapy in four sessions (1 hourly session per week with the speech therapist) and instructions to practice at home minimum three times a day and maximum five times a day for five to ten minutes.

VBT is performed by blowing into a glass (resonance) tube (28 cm in length, 0.9 cm inner diameter) which ends in a bowl of water (1.5 litre) (Picture I). A speech therapist is required at the beginning of therapy for the correct implementation of the technique and to provide information about the nature and circumstances of dysfunctional breathing. In multiple session the participant will learn different exercises and will receive instructions on the performance of the exercises.

Measurements

The Asthma Control Questionnaire-6 (ACQ) was used to assess asthma control, the total score ranges from 0 to 6, a reduction of > 0.5 was considered clinically relevant (5). The Mini Asthma Quality of Life Questionnaire (miniAQLQ) was used to assess quality of life (6). The total score ranges from 1 to 7, a change of score of > 0.5 can be considered clinically important. The Nijmegen hyperventilation scale (NHS) was used to quantify the symptoms of hyperventilation. The total score ranges from 0 to 64, a score ≥ 19 denotes the presence of respiratory distress and dysfunction. The higher the score the more distress is present (8). To quantify the psychosocial consequences of their voice in daily life, the voice handicap index (VHI) was used (7). The total score ranges from 0–120, which can be divided into 4 class (total score < 20 : your voice does not cause limitations, total score 20–40: your voice is the cause of a number of psychosocial limitations, total score 40–60: your voice significantly limits your options in several areas, total score > 60 : your voice problem is beginning to form a handicap).

Lung function was measured at baseline, at 6 and 18 weeks of follow up, including spirometry (FEV_1 , FVC, FEV_1/FVC , $\text{FEF}_{25-75\%}$) and FeNO . Participants were allowed to continue their inhalation medication prior to the lung function. Also, a capillary blood gas was taken at baseline, at 6 and 18 weeks of follow up.

Statistical analysis

The data of the randomized subjects are analyzed according to the intention to treat principle. The primary outcome is the comparison of proportions of patients with a change of 0.5 in ACQ (before/after) at week 6 between VBT and UC group. Difference in these proportions between the groups were tested with the Fisher's Exact test. Secondary outcomes were differences in ACQ, FEV_1 , miniAQLQ, NHS, VHI,

Table 1. Baseline characteristics of the study population.

	Usual care <i>N</i> = 11 (45.8%)	Voice bubbel therapy <i>N</i> = 13 (54.2%)	<i>P</i> -value
Gender			
• Female	11 (100)	11 (85)	0.48
• Male	–	2 (15)	
Age (y)	40 (30 – 45)	43 (33 – 52.5)	0.31
Body mass index (kg/m ²)	28.2 (21.7 – 30.9)	28.0 (25.6 – 34.0)	0.55
Smoking history			
• Never	6 (54.5)	7 (53.8)	0.86
• Stop > 6 months ago	5 (45.5)	5 (38.5)	
• Unknown	–	1 (7.7)	
Medication			
• ICS	1 (9.1)	1 (7.7)	0.64
• ICS/LABA	2 (18.2)	6 (46.2)	0.18
• ICS/LAMA	1 (9.1)	2 (15.3)	0.56
• ICS/LABA/LAMA	7 (63.6)	3 (23.1)	0.11
• Unknown	–	1 (7.7)	
Steroid use in the last 3 months	6 (54.5)	3 (23.1)	0.21
FEV1, post %-predicted	100 (83 – 109)	85 (78 – 106)	0.37
pCO ₂ (mmHg)	33.75 (32.0 – 34.0)	33.0 (29 – 35.6)	0.35
FeNO (ppb)	18 (10.2 – 27.5)	15.5 (11.3 – 29.3)	0.95
ACQ	2.17 (2.00 – 2.50)	2.00 (1.65 – 2.50)	0.49
miniAQLQ	4.6 (3.79 – 5.4)	4.77 (3.7 – 5.06)	0.87
NHS	23 (16 – 33)	25 (16 – 36)	0.96
VHI	15.5 (10.5 – 23)	11 (4 – 29)	0.92

All variables are presented as median with the IQR or as number (%). BMI body mass index (weight (kg)/height² (cm)), FEV1 forced expiratory volume in 1 s, FeNO fractional exhaled nitric oxide (ppm), ACQ-6 asthma control questionnaire, AQLQ asthma quality of life questionnaire, NHS Nijmegen hyper-ventilation score, VHI Voice Handicap Index.

tested with the Wilcoxon signed rank test comparing baseline with 6 weeks of follow up and baseline with 18 weeks of follow up. A *p* values (two-sided) < 0.05 is considered to indicate a statistically significant difference in all comparisons. All statistics were conducted using SPSS (IBM SPSS statistics version 26).

There is no data available about the effect of voice bubbling therapy on asthma control in patients with asthma. Therefore, an accurate sample size calculation was not possible prior to the study. *Post hoc*, we performed a sample size calculation using the median ACQ of both groups at 6 weeks of follow up. Based on the median of group A (UC median = 1.92) and group B (VBT median = 1.5), with a standard deviation of 0.7, at least 2 × 45 (2-sided) patients have to be included (type I error: 0.05, 2-sided; type II error: 0.20 or power = 80%; randomization ratio 1:1).

Results

Twenty-four patients were included in this study: 22 female and 2 male patients. Eleven patients were randomized to UC and 13 patients were referred for VBT. There was no difference in baseline characteristics between the two groups (Table 1). Four patients were lost to follow up during the study period. The median ACQ at baseline was 2.17 for the UC group and 2.00 for the VBT group. At 6 weeks, the median ACQ for the UC group was 1.83 and 1.50 for the VBT group and resp. 2.0 and 1.83 at 18 weeks. An

ACQ reduction of > 0.5 was considered clinically relevant and was achieved by 3 out of 10 patients in the UC group vs 4 out of 11 in the VBT group at week 6 (*p* = 0.99). A significant increase in pCO₂ in the capillary blood gas was found after six weeks of VBT (baseline median (IQR) pCO₂ = 33.00 (17.25 – 38.6) mmHg; week 6 pCO₂ = 36.00 (29.00 – 42.3) mmHg, *p* = 0.01) (Table 2 and Figure 1). A change of > 0.5 points in miniAQLQ is considered clinically important. Both, the UC group as the VBT group showed a decrease of the median score of >0.5 points at 18 weeks, however this did not reach significance (UC group baseline median (IQR) miniAQLQ = 4.60 (2.33–6.33); week 18 miniAQLQ = 3.90 (3.60–6.13); VBT group baseline miniAQLQ = 4.77 (2.93–5.80); week 18 mini AQLQ = 4.13(1.7–5.6)). The VBT group showed a decrease of the median score of the NHS from 25 to 17 after 6 weeks of follow up, were values ≤19 are considered within normal and functional domain (*p* = 0.13). The UC group also showed a decrease in median score of the NHS, but to a lesser extent. All the values of the VHI are below 20, which implicated the voice does not cause limitations for the participants (Table 2).

A Spearman's rank-order correlation was run to determine the relationship between the delta of the secondary outcomes. There was a positive correlation between ΔpCO₂ (baseline – 18 weeks of follow up) and ΔminiAQLQ (baseline – 18 weeks of follow up) of the VBT group, which was statistically significant (*r*_s = 0.78, *p* = 0.02) (Figure 2).

Table 2. Effect of Voice Bubbling Therapy on participants with difficult-to-treat asthma and dysfunctional breathing pattern.

	Baseline Usual care N = 11	Voice bubbling therapy N = 13	6 weeks follow up Usual care N = 11	Voice bubbling therapy N = 12	18 weeks follow up Usual care N = 10	Voice bubbling therapy N = 10
ACQ	2.17 (0.33 – 3.50)	2.00 (0.33 – 3.00)	1.92 (0.17 – 2.83)*	1.50 (0.66 – 3.67)	2.17 (1.17 – 3.00)	2.08 (0.33 – 4.67)
FEV1 (post %-predicted)	100 (69 – 113)	85 (71 – 115)	97 (77 – 107)*	89.50 (71 – 109)	88.5 (49 – 112)	93 (71 – 108)
pCO2 (mmHG)	33.75 (30.75 – 35.00)	33.00 (17.25 – 38.6)	33.00 (30.5 – 39.6)	36.00 (29.00 – 42.3)*	35.00 (29.0 – 37.0)	34.80 (27.0 – 38.0)
miniAQLQ	4.60 (2.33 – 6.33)	4.77 (2.93 – 5.80)	4.40 (3.67 – 6.67)	4.93 (3.40 – 5.80)	3.90 (3.60 – 6.13)	4.13 (1.7 – 5.6)
NHS	23 (8 – 46)	25 (5 – 45)	20 (8 – 30)	17 (2 – 38)	25 (14 – 29)	25.5 (0 – 37)
VHI	15.50 (10.50 – 23)	11 (4 – 29)	10 (4 – 12)*	14 (0.75 – 16)	7.5 (3.0 – 19.25)*	7.5 (3.0 – 19.25)

Data are presented as median (IQR). FEV1 forced expiratory volume in 1 s, ACQ-6 asthma control questionnaire, AQLQ asthma quality of life questionnaire, NHS Nijmegen hyperventilation score, VHI voice handicap index.

*p values < 0.05 Wilcoxon signed rank test comparing baseline with 6 weeks of follow up and baseline with 18 weeks of follow up.

Discussion

This pilot study investigated whether VBT was effective to improve asthma control in patients with a difficult-to-treat asthma and dysfunctional breathing pattern. Although the primary outcome measure was not met, we found an increase in pCO₂ level in the intervention group after 6 weeks of VBT indicating that there may be some effect of the treatment on dysfunctional breathing. Moreover, Δ pCO₂ was significantly correlated with Δ miniAQLQ suggesting that it is clinically meaningful.

Previous literature described several potential therapies to treat VCD, for example therapy performed by speech pathologist, education about VCD, helium oxygen therapy, mild sedatives like benzodiazepines and botulinum toxin injection (9–11). Bruton et al. described the effect of physiotherapy breathing retraining in patients with incompletely controlled asthma, which showed improvement in quality of life despite having little effect on lung function or airway inflammation (12). Multiple studies showed the Buteyko breathing technique resulted in improved quality of life in asthma patients, however no effect on lung function was found as well (13,14). In recent years, VBT has been applied in the Netherlands to treat problems of the voice and vocal cords. VBT could result in relaxation of the soft tissue around the vocal cords and lead to improvement of symptoms in these patients.

VBT is an easily executable therapy, which can be carried out with limited resources and in the patient's own time. No side effects were noticed. In comparison with other therapies for severe asthma, such as medication, VBT is an inexpensive therapy and can easily be added as a step-up therapy. However, it does require perseverance and commitment of the patient. We believe a speech therapist is required at the beginning of therapy for the correct implementation of the

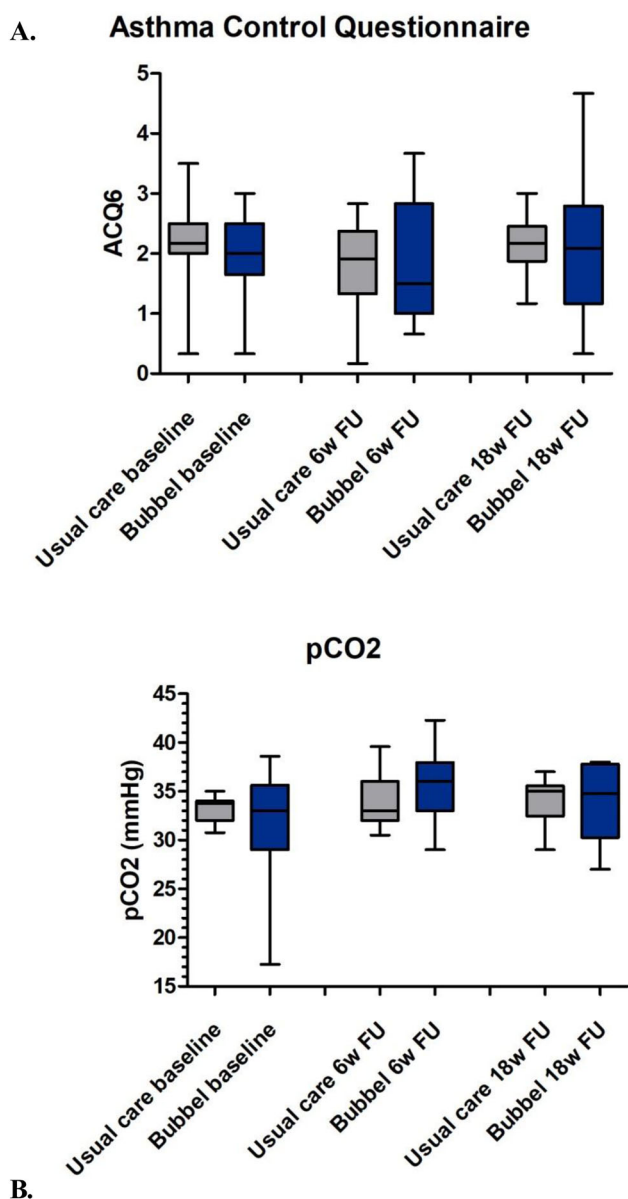


Figure 1. A. Scores of the Asthma Control Questionnaire (ACQ) range from 0 to 6, B. Scores of pCO₂ in mmHg. Data presented as median and IQR.

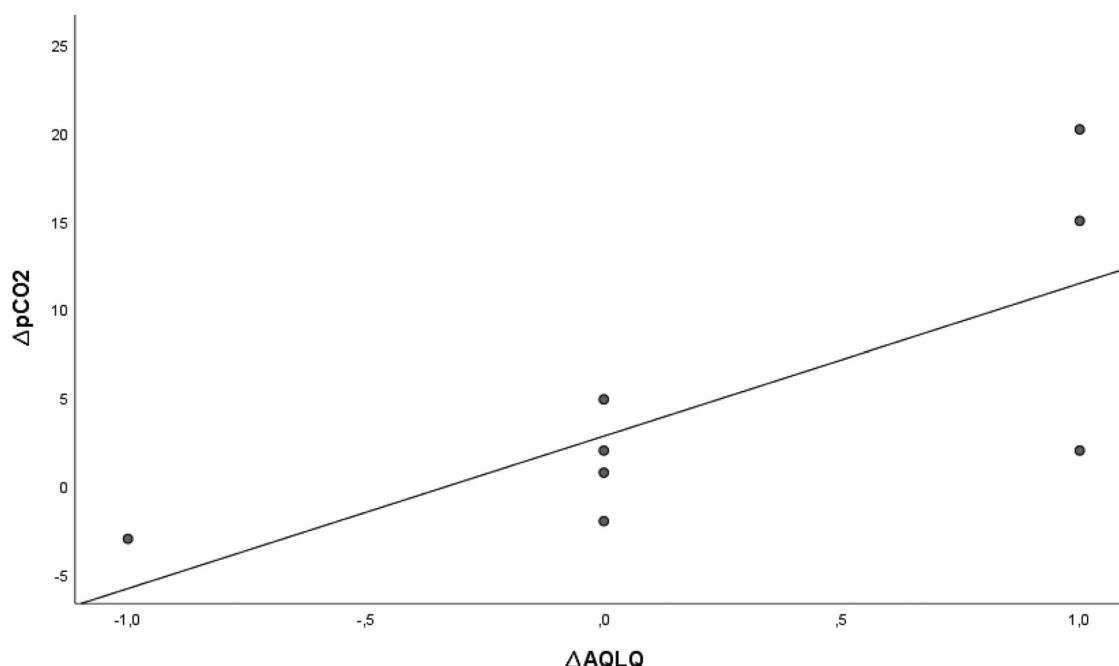


Figure 2. Plot showing the correlation between delta pCO₂ (baseline – 18 weeks of follow up) and delta AQLQ (baseline – 18 weeks of follow up) of the Voice Bubbling therapy group. The correlation was tested by the Spearman's rank-order correlation test. The delta AQLQ was divided into groups; delta AQLQ > -0.5, -0.5 – 0.5 and > 0.5.

technique and also to provide information about nature and circumstances of dysfunctional breathing. Alternatively, a specialized respiratory nurse or lung function technician could be trained to guide and coach the patients with this technique.

The strengths of this study were the randomized design and the strict inclusion criteria. This study also had some limitations. First of all, the study population was of small sample size, so this may be the explanation that the primary outcome was not met. It was difficult to find participants fitting all the inclusion criteria and who were willing to fully commit to the study. A post-study sample size calculation revealed we needed a sample size of $n = 45$ patients per group. A second limitation was the unblinded study design, the intervention made it impossible to perform a double-blinded randomized control trial. A third limitation was the short length of the therapy and the commitment of the participants to practice at home daily. Treatment effects may not last for long after discontinuation of VBT. Adherence of participants to daily practice at home would be essential for long-term benefit. Fourth, the increase in pCO₂ level seen in the intervention group after 6 weeks may be an increase due to regression to the mean. However, the increase is only seen in the intervention group, not in the control group, which makes it less likely to be an effect due to regression to the mean. Finally, the fifth limitation is the potential of attention bias by the

speech therapist as the intervention group received 4 h of speech therapist attention, but the UC group did not. Including a control group receiving a sham treatment could probably prevent this kind of bias in a larger future study.

Conclusion

In conclusion, this is the first study investigating the effect of VBT in participants with difficult-to-treat asthma and dysfunctional breathing pattern. VBT in participants with difficult-to-treat asthma resulted in a higher average pCO₂ level, indicating the treatment may improve hyperventilation. However, this did not improve asthma control or quality of life. VBT may have value for a better management of asthma related symptoms. This is a pilot study with a small sample size, further research studying a greater population is needed to investigate effects of VBT in patients with the combination of difficult-to-treat asthma and dysfunctional breathing pattern.

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SE contributed to data-collection, data analysis and writing of the draft of the manuscript. Y.T. was involved in writing the study design and METC approval. T.V., M.O., B.G., J.K., S.B. contributed to data-collection and revision of the manuscript. J.W.A., T.H.v.H. and H.V. contributed to the initial study design and revision of the manuscript. G.B.

initiated, designed and supervised all aspects of the study. He contributed to all versions of the manuscript. All authors approved the final version of the manuscript.

Declaration of interest

The authors report no conflict of interest

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