PHASE 1

'PROOF OF PRINCIPLE', RANDOMISED, CROSS-OVER STUDY OF THE EFFECT OF A NEW THERAPEUTIC DEVICE AND A MARKETED DEVICE ON NASAL AIRFLOW RATES IN NORMAL, HEALTHY ADULTS

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BACKGROUND INFORMATION

Morbidity resulting from nasal obstruction is very common in our community. Nasal obstruction can contribute to headaches, poor concentration and irritability during the day and snoring and obstructive sleep apnoea during the night.

The public health importance of snoring is enormous because its prevalence is so high. Snoring is the audible result of upper airway obstruction whilst sleeping. Studies have indicated that 40% of middle aged man and 20% of middle aged women habitually snore (1,2,3,4) Snoring causes not only social consequences, but has been linked to adverse health outcomes including hypertension, cardio vascular events, daytime sleepiness and accidents (1). Independent risk factors that make an individual more likely to snore include: age, male sex, smoking, body mass index and nasal obstruction (5,6,7,8,and 10). Of these only nasal obstruction is easily amenable to therapy.

Common therapies directed to improve nasal airway airflow include medication, surgery and devices to open the nasal valve. The link between improved nasal breathing and reduction in snoring by medical and surgical means is already well established (9,14,15,and 16). Nasal dilators work by opening the nasal valve, the narrowest portion of the human upper airway. This is the region defined by the septum, upper lateral cartilage and head of the inferior turbinate and is situated approximately 8 mm from the nasal opening.

We know that airflow in a rigid tube like the nasal cavity is proportional to its radius to the power of four; so small changes in the nasal valve would have a dramatic improvement on airflow. Devices have obvious advantage over surgery, are simple to apply, free of morbidity and can work when other therapies fail.

The market-leading device is an externally placed plaster-like device called Breathe Right™ which works by pulling the nasal valve open. Studies have demonstrated some effectiveness of this device in reducing snoring (11,12,13).

ASAP BreatheAssist Pty Ltd has developed a novel device that is placed internally to expand the nasal valves. Each side is independently adjustable for each nostril to maximize the amount of expansion whilst enabling the user to control the amount of pressure produced and comfort. We believe that an internal nasal valve dilator is more effective in increasing the radius of the nasal valves and therefore provide greater airflow than an external dilator. This trial set's out to test this hypothesis.

BreatheAssist™ is made of medium grade polymer approved by the US FDA and European health agencies for human use. The device is compressed to dilate each nasal valve independently and is safe from inhalation by nature of its bridge across the septum. The device is intended to treat nasal obstruction of all causes and in turn benefit sufferers of snoring and possibly Obstructive Sleep Apnoea (OSA). It could also increase airflow for sporting activities and hold the nasal value open after surgery or during dental procedures.

OBJECTIVES

a) To demonstrate that BreatheAssist™ increases nasal airflow rates in normal, healthy adults.
b) To generate flow rate data for both the BreatheAssist™ and BreatheRight™ devices to enable a direct comparison between the two devices.

STUDY DESIGN AND METHODOLOGY

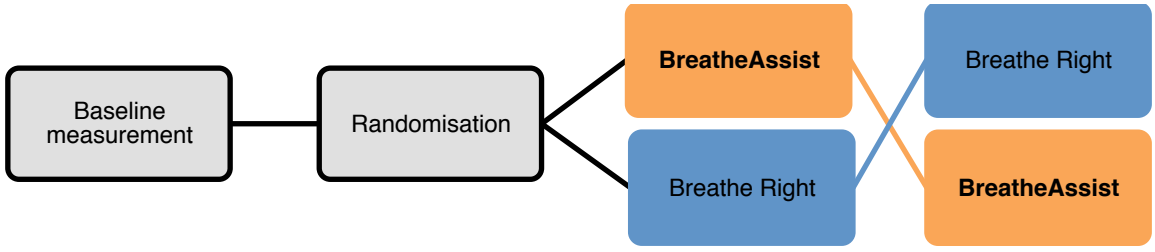
The study was designed as a randomised cross-over study. The principal investigator Mr Simon Braham is a senior nasal surgeon at the Royal Victorian Eye and Ear Hospital, Melbourne Australia who has a special interest in treating problems with the nasal valve. The study was performed under the auspices of the Ethics Committee of the Royal Victorian Eye and Ear hospital using four technician's experienced in using a rhinomanometer, providing mechanically objective measurements of nasal airflow. Statistical analysis was preformed by an independent statistician.

20 volunteers who met the inclusion and exclusion criteria (see Table 1) were recruited to undergo baseline assessment of their nasal flow rate and were then be randomised to either BreatheAssist™ or Breathe Right™. There was at least a 10-minute rest period between testing each device with a rest period of 10 minutes between devices. Volunteers were then crossed over to the alternative device to that originally tested, (See Figure 1)

Table 1. Selection Criteria

Inclusion Criteria	Exclusion Criteria
Male or Female	Do not suffer from symptomatic nasal disease
Age 18 years +	Do not have a current Upper Respiratory Tract Infection
Are in good health as gauged by medical examination	Do not have a current Lower Respiratory Tract Infection
	Use of nasal decongestants, anti-allergens or inhalants on the day of the test
	Do not have a severely deviated septum as gauged by physical examination
	Do not have severely collapsed nasal walls/valves as gauged by physical examination

Fig. 1. Study Design



RESULTS

Comparison of Device BreatheAssist (BA) to baseline

VARIABLE	MEAN	95% C OF . INTERVAL
BREATHEASSIST	642.8	586.5541 to 699.0459
BASELINE	467.15	395.5034 to 538.7966
DIFFERENCE	175.65	111.4525 to 239.8475

p=0.0000

Comparison of Device Breathe Right (BR) to baseline

VARIABLE	MEAN	95% C OF . INTERVAL
BREATHERIGHT	450.75	400.3831 to 501.1169
BASELINE	467.15	395.5034 to 538.7966
DIFFERENCE	-16.4	-73.57149 to 40.77149

p=0.5553

Comparison of Device BR to Device BA

VARIABLE	MEAN	95% C OF . INTERVAL
BREATHEASSIST	642.8	586.5541 to 699.0459
BREATHERIGHT	450.75	400.3831 to 501.1169
DIFFERENCE	192.05	138.6928 to 245.4072

p=0.0000

STATISTICAL CONCLUSIONS:

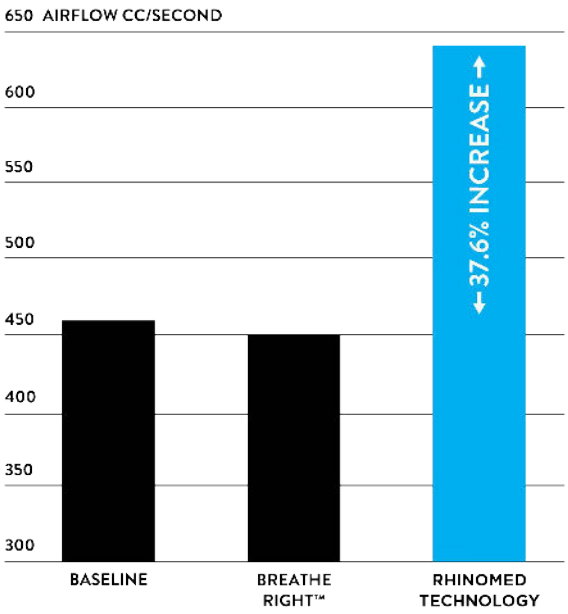
1. Device BA is significantly different to the baseline.
   Mean difference is 175.65 (95% CI 111.4525 to 239.8475) (p=0.0000).

2. Device BR is not significantly different to baseline.
   Mean difference is -16.4 (95% CI -73.57149 to 40.77149) (p=0.5553).

3. Device BA is significantly different to Device BR.
   Mean difference is 192.05 (95% CI 138.6928 to 245.4072) (p=0.0000).

Data were analysed using paired t-tests to calculate the differences in airflow for the two devices. Mean differences, confidence intervals and p values were calculated by comparing the airflow between each device and baseline as well as between devices.

In this instance the number of zeros of the p value is not relevant. What is important for determining significance is the size of the difference, which can be ascertained by the mean difference and the width of the confidence intervals. The p value represents the probability of obtaining the point estimate given that the null hypothesis is true. Given the p values, the probability of there being no difference between devices or device BA with baseline is so little that the number of zeros could go on indefinitely.



MEDICAL CONCLUSION

We conclude that:

A. Dilating the nasal valves using an internal dilator BreatheAssist™ significantly improves airflow (mean increase in airflow +175.65 cc/second).

B. Dilating the nasal valves using an external dilator (Breath Right™) does not significantly alter airflow.

C. BreatheAssist™ is significantly better than Breathe Right™ at improving airflow thus proving our hypothesis that internal dilation is a superior method of nasal dilation.

It should be noted that these results were obtained on normal healthy individuals and we would expect even greater increases in individuals with pre-existing breathing difficulties.

Given the above results and our knowledge of the relationship between improved nasal airflow and reduced snoring, we believe that the BreatheAssist™ nasal dilator technology will be effective in increasing airflow, may in many cases reduce or eliminate snoring and consequently improve the quality of sleep in those who suffer from upper airway obstruction.

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