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Nasopharyngeal Temperature During Rhinothermy

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Key words: Rhinothermy, Temperature, Airways, Nasopharyngeal

1. Abstract

Purpose/Aim: To investigate the effect of rhinothermy delivering 100% humidified air at 41°C and 30 to 35L/min on nasopharyngeal airspace temperature.

Materials and Methods: In this single-centre, non-blind, non-randomized, parallel arm interventional study, nasopharyngeal airspace temperature was continuously measured during delivery of 100% humidified air via a rhinothermy device at 41°C and 30 to 35L/min (rNHF) (n=6), and at 31°C and 10L/min ('sham' rhinothermy) (n=6). The primary objective was to determine whether the mean nasopharyngeal temperature during delivery of rNHF whilst nose breathing was within 1.5°C of the device's set dew point temperature of 41°C. Change in nasopharyngeal temperature during nose breathing and mouth breathing was also compared for both interventions.

Results: 12 participants aged 18 to 75 years were recruited. The mean (SD) nasopharyngeal airspace temperature during delivery of rNHF at 41°C whilst nose breathing was 37.9°C (1.22), and with 'sham' rhinothermy at 31°C was 36.8°C (0.18). There was no significant difference in nasopharyngeal airspace temperature between nose and mouth breathing for both interventions combined (difference (95% CI) -0.1°C (-0.59 to 0.36), p=0.60).

Conclusions: The mean nasopharyngeal airspace temperature during delivery of rNHF whilst nose breathing was not within 1.5°C of the device's set dew point temperature of 41°C. Dew point temperatures may need to be set considerably higher than the target nasopharyngeal airspace temperature when investigating the effect of rhinothermy on symptom severity or duration of respiratory tract infections caused by viruses with temperature-dependent replication.

2. Introduction

Viral respiratory tract infections such as the common cold and influenza cause significant morbidity and have a substantial economic impact on society [1-4]. Human

rhinoviruses (HRVs) cause up to two-thirds of colds and have temperature-dependent replication.[5] In vitro replication of most HRV strains is optimal between 33°C and 35°C [5], which is within the normal physiological temperature of the upper airways [6], whereas temperatures of 39°C to 45°C have been demonstrated to inhibit viral replication [7-10]. Influenza is one of the most important public health problems globally, causing up to 5 million severe illnesses and 0.5 million deaths annually [11]. Viral replication and the subsequent host inflammatory response also play key roles in the pathogenesis of influenza infection [12] and in vitro studies have demonstrated a reduction in virus replication with exposure to temperatures of 39°C to 41°C for a number of strains of influenza A and C virus [13-15]. Furthermore, disease severity and mortality associated with avian influenza A (H5N1) virus, have been linked to high pharyngeal viral loads [12] and local hyperthermia may enhance antiviral activity [16,17]. The potential clinical significance of these effects is suggested by animal models of experimental influenza infection in which treatment of fever increases mortality [18].

These observations raise the possibility that rhinothermy, which delivers heated, humidified air to the upper airways via the nares, may attenuate the severity and duration of common cold or influenza symptoms through potential inhibition of viral replication. Fisher and Paykel Healthcare Limited (Auckland, New Zealand) have manufactured a rhinothermy device that can deliver 100% humidified air heated to 41°C at 35L/min (rNHF).

We have recently completed a randomized controlled trial (RCT) investigating the effectiveness of rNHF in the treatment of the common cold [19]. A total of 170 participants aged 18 to 75 years were recruited within 48 hours of developing symptoms of the common cold. They were randomized to five days of either rNHF (100% humidified air delivered at 35 L/min and 41°C for two hours daily) or 'sham' rhinothermy (100% humidified air delivered at 10 L/min and 31°C for ten minutes daily) and followed for 14 days. There was no difference between treatment groups for the severity or duration of symptoms overall, or in the subgroups with PCR-confirmed HRV or coronavirus infection [19].

One potential explanation for the lack of effect could be that the nasopharyngeal airspace temperature during rNHF therapy may have been markedly lower than the rNHF device's set dew point temperature of 41°C, and as such not high enough to inhibit viral replication. To better interpret our findings relating to the effect of rNHF on the common cold and to inform future similar studies, we investigated the effect of rNHF on nasopharyngeal airspace temperature. Our hypothesis was that the mean nasopharyngeal temperature (°C) during delivery of rNHF whilst nose breathing would be within 1.5°C of the device's set dew point temperature of 41°C.

3. Material and Methods

3.1 Study design and participants

This was a non-randomized, parallel arm, interventional trial of 12 healthy, adult participants who received one of two possible interventions, either delivery of 100% humidified air via a rhinothermy device either at 41°C and 30 to 35L/min (rNHF), or at 31°C and 10L/min ('sham' rhinothermy). The study was undertaken at a single site in Wellington, New Zealand (the Medical Research Institute of New Zealand (MRINZ)) in accordance with Good Clinical Practice (GCP) guidelines and the Declaration of Helsinki. The trials was registered with the Australian New Zealand Clinical Trials Registry (ANZCTR): ACTRN12620000064909. Ethics approval was given by New Zealand Northern B Health and Disability Ethics Committee (19/NTB/225). All participants provided written informed consent.

The study was advertised to participants who had previously participated in the rhinothermy in the common cold study [19]. Advertisements included contact details for the principal investigator who then sent a study-specific information sheet to potential participants. All participants provided written, informed consent prior to proceeding with the screening and study visit.

3.2 Study aim

The primary aim of the study was to determine whether the mean nasopharyngeal airspace temperature during delivery of rNHF whilst nose breathing was within 1.5°C of the device's set dew point temperature of 41°C. A temperature of "within 1.5°C" was chosen as an appropriate cut-off as a number of studies have found that temperatures of >39°C inhibit viral replication of HRV and some strains of influenza A and C virus.[8-10,13-15] As such, if rNHF with a set dew point temperature of 41°C achieves a minimum nasopharyngeal airspace temperature of 39.5°C, there may be a role for rNHF in the treatment of HRV and influenza infections.

3.3 Eligibility criteria

Eligible participants were healthy adults aged 18 to 75 years who in the investigator's opinion were able and willing to comply with all study requirements.

Exclusion criteria included: a history of an immunocompromising condition or notifiable disease; any respiratory condition including but not limited to

asthma, COPD, bronchiectasis, and pulmonary fibrosis; nasopharyngeal conditions such as deviated septum and chronic rhinosinusitis which the investigator considered could impair nasal breathing; current use of or requirement for oral antibiotics for respiratory tract infection, pneumonia, or infective exacerbation of an underlying respiratory condition; current use of or requirement for parenteral antibiotics; current use of anticoagulation medications; previous sinus surgery; a pre-existing bleeding disorder; an episode of epistaxis during the week prior to the study visit; a neurological or neuromuscular condition that could cause disorders of breathing, swallowing, or posture; previous allergic reaction to local anesthetic.

3.4 Interventions

Following the screening process, enrolled participants were allocated to receive either rNHF (100% humidified air delivered at 30 to 35 L/min and 41°C) or 'sham' rhinothermy (100% humidified air delivered at 10 L/min and 31°C). A total of 12 participants were enrolled in total, with six participants in the rNHF group and six participants in the 'sham' rhinothermy group. Participants were asked to use the interventions whilst nose breathing, mouth breathing, and breathing "normally". Nose breathing and mouth breathing were defined as periods when the participant was asked to breathe exclusively through their nose or mouths respectively and without talking. Breathing "normally" was defined as a period when the participant could choose to breathe through their mouth or nose at any time and were allowed to talk if they chose. Participants were advised not to consume hot or iced drinks for 30 minutes prior to commencing the study visit.

3.5 Rationale for interventions

rNHF and 'sham' rhinothermy treatment groups were selected as they directly correlate with the interventions investigated in the common cold study and would help with the interpretation of this study's findings. Furthermore, establishing the mean nasopharyngeal airspace temperature achieved during rNHF treatment will guide future similar studies of rhinothermy.

Nose and mouth breathing were compared as these may cause fluctuations in nasopharyngeal airspace temperature [20] and any findings may inform the methodology of future studies.

3.6 Intervention allocation and blinding

This was a non-blind, non-randomized study. A study investigator allocated the interventions to each participant on the day of the study and split the allocation of interventions to ensure six participants were in each intervention group. The allocation procedure was determined by whether participants had previously participated in the randomized controlled trial of the same device in an RCT of rhinothermy for the common cold [19], N=4, where they used the rNHF or Sham depending on that randomization; or whether they were not part of that trial, N=8, where they received simple allocation to one of the two treatments, to ensure that there were a total of six participants in each group.

3.7 Study procedures

A list of the study equipment used can be found in Supplementary Appendix 1. For the remainder of the methods, results, and discussion sections, "nasopharyngeal temperature" denotes nasopharyngeal airspace temperature. The order of study interventions is shown in Figure 1.

3.8 Baseline temperature rhinothermy device

An "AB" thermistor (Amphenol Corporation, Connecticut, USA) was inserted into one of the nasal prongs attached to the interventional device to allow temperature measurement of the delivered air for five minutes.

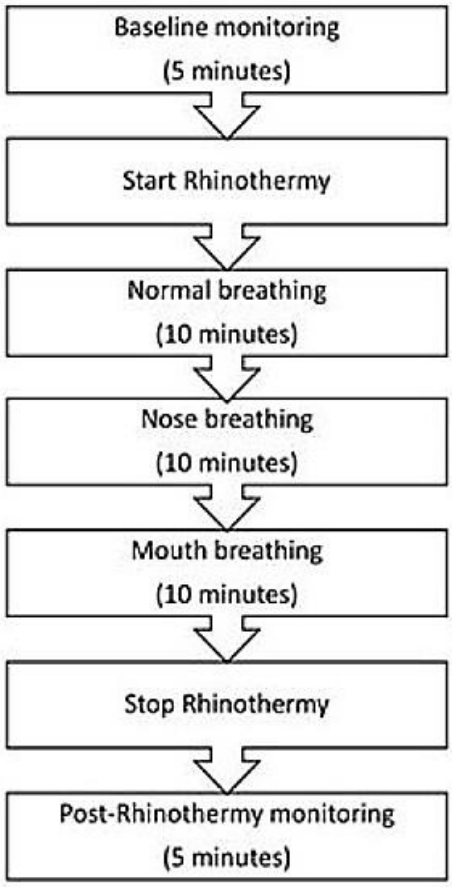


Figure 1: Order of study interventions.

3.9 Baseline nasopharyngeal measurements

Nasopharyngeal temperature was continuously measured using an "AB" thermistor nasopharyngeal temperature probe. Local anesthetic and vasoconstrictor nasal spray were administered to the participant's nostrils and nasopharynx. Once anesthetized, a doctor trained and competent in nasal endoscopy placed the nasopharyngeal temperature probe via the nares into the participant's nasopharynx under direct visualization using a flexible nasoendoscope [Olympus ENF-VH Rhino-Laryngo videoscope, Sony medical grade monitor, and Olympus CV-170 video system center]. The final position of the temperature probe was photographed. All photographs were stored electronically and only in association with the participant's study ID. Once the temperature probe position was confirmed in the nasopharynx, there was a minimum five-minute period of monitoring to confirm stable read outs from the temperature probe and to obtain the baseline (pre-intervention) nasopharyngeal temperature.

3.10 Order of temperature measurements

After the five-minute baseline measurement period, the nasal cannulae were placed on the participant and the rNHF (Fisher and Paykel Healthcare, Auckland, New Zealand) or 'sham' rhinothermy (MyAIRVO2, Fisher and Paykel Healthcare, Auckland, New Zealand) intervention started. Nasopharyngeal temperatures were measured for a minimum of 10 minutes each whilst:

- Breathing "normally"
- Nose breathing
- Mouth breathing

Each 10-minute period included a minimum of five minutes "run-in" and five minutes "recording". The nasopharyngeal temperature readings measured during the "recording" period, were the readings included in the analysis. Participants were advised not to eat and drink while the nasopharyngeal temperature probe was in situ.

3.11 Post-intervention measurements

Following the above measurements, the intervention was stopped, and nasopharyngeal temperature measurements continued for a minimum of five minutes. On completion of all temperature measurements, the nasopharyngeal temperature probe was removed, and the study visit was concluded.

3.12 Data collection

Output from the nasopharyngeal temperature probes were logged using custom software and hardware produced by FPH and exported into Microsoft Excel. Data were collected and managed using REDCap (Research Electronic Data Capture) tools hosted at MRINZ [21]. REDCap is a secure, web-based software platform designed to support data capture for research studies, providing an intuitive interface for validated data capture; audit trails for tracking data manipulation and export procedures; automated export procedures for seamless data downloads to common statistical packages; and procedures for data integration and interoperability with external sources.

3.13 Outcomes

The primary outcome for this study was the mean nasopharyngeal temperature during delivery of rNHF whilst nose breathing. Secondary outcomes were the difference in mean nasopharyngeal temperature whilst nose breathing and mouth breathing. Other outcomes were the mean nasopharyngeal temperature whilst nose breathing, mouth breathing, and breathing "normally"; the mean baseline nasopharyngeal temperature; and the mean temperature of the air emitted from the nasal prongs.

3.14 Statistical analysis

Statistical analysis was by intention to treat. Temperatures are reported in degrees centigrade (°C). Data descriptions are by mean and standard deviation (SD), median and 25th to 75th percentiles as the inter-quartile range (IQR), and minimum (min) to maximum (max) values. Categorical variables are described by counts and proportions expressed as percentages. Mean estimates are compared to set values by a t-test and confidence intervals for means by a t-test. A mixed linear model was used to compare nose versus mouth breathing and incorporate a comparison of rNHF versus 'sham' rhinothermy with participants as a random effect. SAS version 9.4 (SAS Institute Inc., Cary, USA) was used for all analyses.

4. Results

A flow diagram outlining participant study progress is shown in Figure 2. There were 12 participants enrolled in the study, mean (SD) age 27.8 (9.6), nine females and three male (Table 1). There were six participants in each group. The mean (SD) baseline nasopharyngeal temperature pre-intervention for all participants was 34.4°C (1.29), and the mean (SD) nasopharyngeal temperature post-intervention was 35.4°C (0.89) in the rNHF group and 35.3°C (0.52) in the 'sham' rhinothermy group (Table 2).

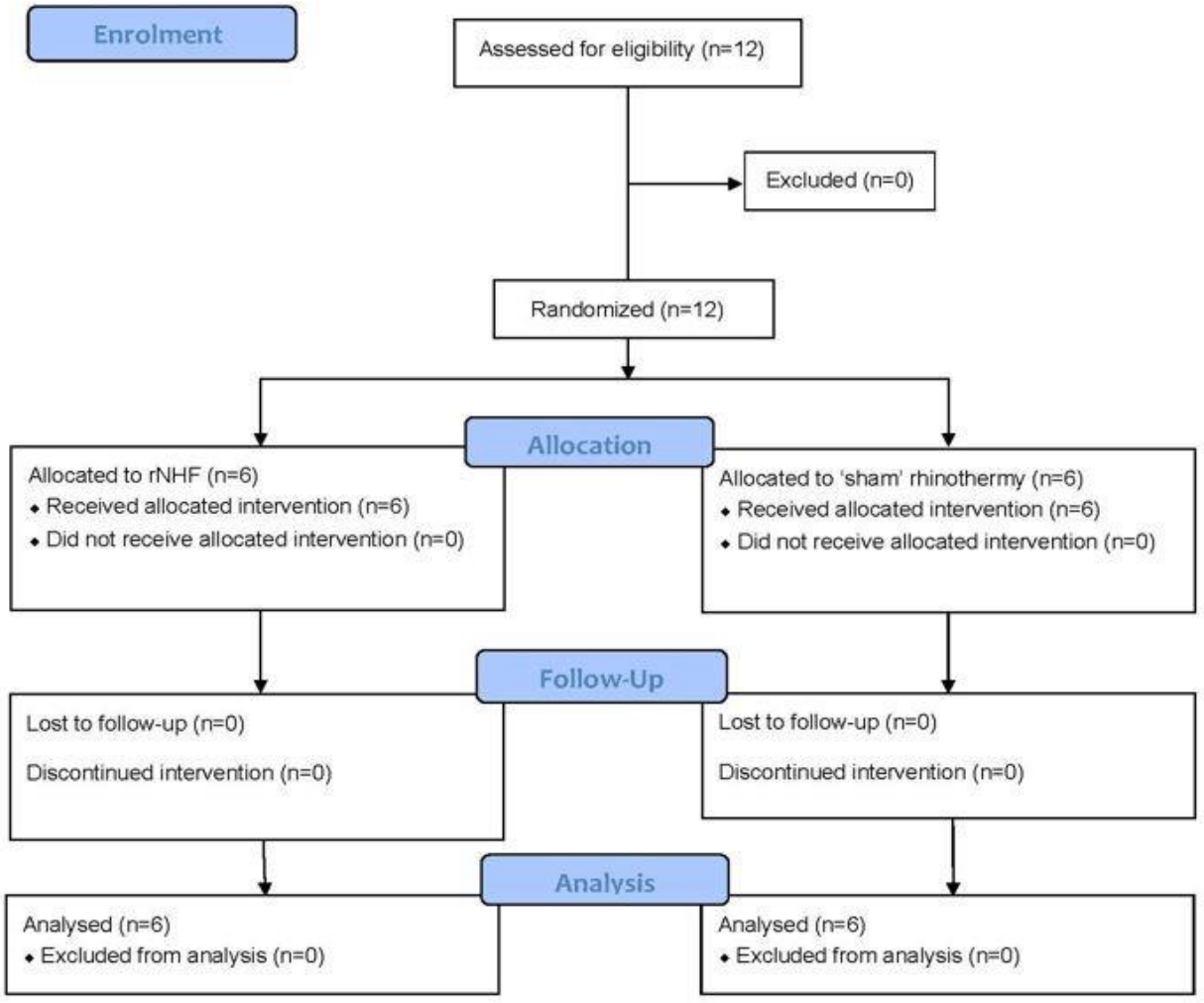


Figure 2: Flow diagram outlining participant study progress.

Table 1: Participant characteristics.

Age (years)	**rNHF n=6**	**'sham' rhinothermy n=6**	**All n=12**
Mean (SD)	23.4 (3.1)	32.3 (12.0)	27.8 (9.6)
Median (IQR)	23.1 (21.9 to 25.5)	30.1 (22.9 to 35.8)	24.4 (22.4 to 31.4)
Min to Max	18.9 to 28.1	21.2 to 53.5	18.9 to 53.5
	Randomization n/n (%)		
Sex			
Female	4 (66.7)	5 (83.3)	9 (75)
Ethnicity			
Asian	1 (16.7)	2 (33.3)	3 (25)
European	2 (33.3)	3 (50)	5 (41.7)
MELAA	0 (0)	1 (16.7)	1 (8.3)
Maori	2 (33.3)	0 (0)	2 (16.7)
Pacific	1 (16.7)	0 (0)	1 (8.3)

4.1 Primary outcome

The mean (SD; 95% CI) nasopharyngeal temperature during delivery of rNHF whilst nose breathing was 37.9°C (1.22; 36.6 to 39.1) (Table 3).

Table 2: Nasopharyngeal temperature at baseline pre-intervention, and post-intervention.

rNHF			Nasopharyngeal Temperature (˚C)		
Time type	**Measurement**	**N**	**Mean (SD)**	**Median (IQR)**	**Min to Max**
Baseline	Max	6	35.5 (1.64)	34.8 (34.4 to 35.9)	34.3 to 38.6
Baseline	Mean	6	34.7 (1.50)	33.9 (33.6 to 35.7)	33.6 to 37.3
Baseline	Min	6	33.3 (2.27)	33.1 (31.1 to 35.6)	30.7 to 36.2
5 minutes post-intervention	Max	6	36.3 (0.83)	36.4 (36.3 to 36.8)	34.8 to 37.2
5 minutes post-intervention	Mean	6	35.4 (0.89)	35.7 (35.4 to 35.9)	33.6 to 35.9
5 minutes post-intervention	Min	6	33.1 (2.73)	33.8 (31.6 to 35.3)	28.6 to 35.5
'Sham' rhinothermy					
Baseline	Max	6	35.2 (0.75)	35.1 (34.5 to 36.0)	34.4 to 36.0
Baseline	Mean	6	34.2 (1.14)	33.8 (33.2 to 35.3)	33.1 to 35.9
Baseline	Min	6	32.3 (2.45)	31.8 (30.4 to 34.4)	29.5 to 35.8
5 minutes post-intervention	Max	6	36.1 (0.34)	36 (35.9 to 36.4)	35.7 to 36.6
5 minutes post-intervention	Mean	6	35.3 (0.52)	35.2 (34.9 to 35.5)	34.9 to 36.3
5 minutes post-intervention	Min	6	33.6 (2.05)	34.1 (32.9 to 34.5)	30.0 to 36.1
Both groups					
Baseline	Max	12	35.3 (1.22)	34.8 (34.8 to 35.9)	34.3 to 38.6
Baseline	Mean	12	34.4 (1.29)	33.9 (33.6 to 35.5)	33.1 to 37.3
Baseline	Min	12	32.8 (2.31)	32.6 (30.8 to 35.0)	29.5 to 36.2

Table 3: Nasopharyngeal temperature during 'normal', nose, and mouth breathing.

rNHF			Nasopharyngeal Temperature (˚C)		
Breathing mode	**Measurement**	**N**	**Mean (SD)**	**Median (IQR)**	**Min to Max**
Normal	Max	5	39.1 (1.69)	38.9 (38.1 to 40.5)	36.9 to 41.0
Normal	Mean	5	38.5 (1.76)	37.9 (37.4 to 40.2)	36.5 to 40.5
Normal	Min	5	38.0 (1.76)	37.1 (37.1 to 39.7)	36.1 to 40.0
Nose	Max	6	38.5 (1.26)	38.2 (37.8 to 38.9)	36.9 to 40.6
Nose	Mean	6	37.9 (1.22)	37.6 (36.9 to 38.2)	36.8 to 40.1
Nose	Min	6	37.3 (1.17)	37.2 (36.6 to 37.8)	35.9 to 39.3
Mouth	Max	6	38.4 (1.44)	38.3 (37.5 to 40.0)	36.4 to 40.2
Mouth	Mean	6	38.0 (1.48)	37.8 (37.5 to 39.6)	35.8 to 39.7
Mouth	Min	6	38.4 (1.44)	38.3 (37.5 to 40.0)	36.4 to 40.2
'Sham' rhinothermy					
Normal	Max	6	37.3 (0.82)	37.0 (36.9 to 37.1)	36.6 to 38.9
Normal	Mean	6	37.0 (0.68)	36.8 (36.6 to 37.0)	36.5 to 38.4
Normal	Min	6	36.4 (1.03)	36.6 (36.4 to 36.8)	34.4 to 37.4
Nose	Max	6	37.0 (0.21)	37.0 (37.0 to 37.2)	36.6 to 37.2
Nose	Mean	6	36.8 (0.18)	36.8 (36.7 to 36.9)	36.6 to 37.1
Nose	Min	6	36.3 (0.61)	36.6 (35.7 to 36.8)	35.5 to 37.0
Mouth	Max	6	37.0 (0.36)	37.0 (36.8 to 37.1)	36.6 to 37.6
Mouth	Mean	6	36.9 (0.28)	36.8 (36.7 to 37.0)	36.6 to 37.3
Mouth	Min	6	37.0 (0.36)	37.0 (36.8 to 37.1)	36.6 to 37.6

4.2 Secondary outcomes

The mean (SD; 95% CI) nasopharyngeal temperature during delivery of 'sham' rhinothermy whilst nose breathing was 36.8°C (0.18; 36.6 to 37.1) (Table 3). The estimated difference (95% CI) in mean nasopharyngeal temperature whilst nose breathing and mouth breathing for both interventions combined was -0.1°C (-0.59 to 0.36), p=0.60. A post-hoc interaction analysis found no evidence of a difference between nose and mouth breathing for each treatment group (P-interaction 0.82).

4.3 Other outcomes

For the rNHF group, the mean (SD) nasopharyngeal temperatures were 37.9°C (1.22) whilst nose breathing, 38.0°C (1.48) whilst mouth breathing, and 38.5°C (1.76) whilst breathing "normally". For the 'sham' rhinothermy group, the mean (SD) nasopharyngeal temperatures were 36.8°C (0.18) whilst nose breathing, 36.9°C (0.28) whilst mouth breathing, and 37.0°C (0.68) whilst breathing "normally" (Table 3). The mean (SD) baseline nasopharyngeal temperature was 34.7°C (1.50) for the rNHF group and 34.2°C (1.14) for the 'sham' rhinothermy group (Table 2). The temperature measurements of the air emitted from the nasal prongs were unreliably recorded and the data was incomplete, therefore the results of this outcome are not reported.

4.4 Adverse events

There were no serious adverse events during this study.

5. Discussion

This study has shown that the mean nasopharyngeal temperature during delivery of rNHF whilst nose breathing is not within 1.5°C of the device's set dew point temperature of 41°C. The mean nasopharyngeal temperature of 37.9°C recorded during delivery of rNHF at 41°C would not be expected to result in inhibition of HRV or influenza replication for which temperatures of at least 39°C are required.[8-10,13-15] The possibility of increasing the nasopharyngeal temperature through nose compared with mouth breathing was not supported by our observation that there was no significant difference in nasopharyngeal temperature between nose and mouth breathing.

A potential explanation for the mean nasopharyngeal temperature results during rNHF, despite a device set dew point temperature of 41°C, is that the inspired air has been 'cooled' by the heat and moisture exchange mechanisms of the upper airway [22,23], although at 100% humidification evaporative cooling of the upper airway mucosa during inspiration is limited [24]. In addition, alveolar air gradually decreases in temperature as it travels back out of the respiratory tract [24], as heat and water returns to the mucosa. As such, the subsequent mixing of the inspired heated and humidified air from the device with the cooler expired air, could result in a lower-than-expected temperature in the nasopharynx. Of note, the relative cooling effect of this mixing may be limited if the expired air is warmer than occurs when inspiring ambient air, as the usual mechanism of heat loss to a mucosa that has been cooled by inspired air at ambient temperatures, is altered [22,24].

The increase in mean nasopharyngeal temperature from baseline with delivery of 'sham' rhinothermy may be a result of the isothermal saturation boundary (ISB) moving towards the upper airway when inspiring air that is warmer and of a greater relative humidity than ambient air. The ISB is the point where inspired air reaches alveoli-like temperature and humidity, i.e. 37°C and 100% humidity, and this moves further into the lung with lower inspired air temperatures [22,23].

The optimum temperature for isolation of rhinovirus type 2 is 33°C, with a 400-fold lower yield after incubation at 39°C [9,10]. Replication is significantly reduced for some influenza virus strains after prolonged exposure to temperatures of 39°C and 40°C [13], and intracellular HRV replication is reduced by 90% after a brief exposure to 45°C temperatures.[8] The observation that the mean maximum temperature recorded when nose breathing was 38.5°C suggests that in our previous RCT, the lack of efficacy with the delivery of rNHF at 41°C for 2 hours a day may be due to the inability to reach a sufficiently high temperature to inhibit replication of the HRV identified in 61% of the participants enrolled in the common cold study [19]. Studies assessing safety, tolerability and nasopharyngeal airspace temperatures at higher set dew point temperatures of rNHF should be considered.

5.1 Limitations

There are several study limitations. Firstly, due to the unique nature of this study, there was no previous literature that could inform a sample size calculation to ensure adequate power. Despite this, the upper 95% confidence interval of the point estimate for the mean nasopharyngeal temperature achieved while nose breathing (39.1°C) was below our proposed temperature of 39.5°C. Secondly, different nasal cannula sizes were used for participants based on nares size which may affect delivered air pressure, and flow rates in the rNHF group varied between 30 and 35L/min. Both factors may have an unquantified effect on

nasopharyngeal temperature. Future larger studies may find it useful to assess the effect of these variations in delivery on the temperature of the nasopharynx. Thirdly, although sited under direct vizualization into the nasopharyngeal airspace, the nasopharyngeal temperature probe may subsequently have moved or come in to contact with the nasopharyngeal mucosa which may also affect measured temperatures. Finally, as we did not directly measure at this site, our results may not reflect the temperature specifically of the upper respiratory tract mucosa where viral replication occurs. Indeed, higher respiratory mucosal temperatures may be expected than those recorded within the nasopharyngeal airspace as heat is transferred to the mucosa from the heated inspired air, and the release of latent heat from the water vapor as it condenses on mucosal surface [24].

6. Conclusion

This study shows that delivery of rNHF whilst nose breathing does not increase nasopharyngeal airspace temperature to within 1.5°C of the device's set dew point temperature of 41°C and is unlikely to reach high enough temperatures to significantly inhibit replication of the common respiratory viruses. As such, rNHF with a set dew point temperature greater than 41°C may be needed when investigating whether rhinothermy affects symptom severity or duration of respiratory tract infections caused by viruses with temperature-dependent replication.

7. Competing Interests

The MRINZ has received research funding from Fisher & Paykel Healthcare Limited. The authors have no other conflicts of interest.

8. Funding

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Supplementary Data

STUDY EQUIPMENT

NASAL ENDOSCOPY

- Olympus ENF-VH Rhino-Laryngo Videoscope [REF]
- Olympus CV-170 Video System Center [REF]
- Sony LCD Monitor [REF]

TEMPERATURE PROBES (THERMISTORS)

"AB" thermistors produced by Amphenol ® (Amphenol Corporation, Connecticut, U.S.) were used as the temperature probes for this study. These are glass encapsulated thermistors intended for use in healthcare applications including internal body temperature measurement.

The thermistors were calibrated by Fisher and Paykel Healthcare engineers to within ± 0.2 °C against a dry block temperature. The dry block used is the Venus 2200 produced by Isotech (Isothermal Technology Ltd, Southport, UK). The dry block was calibrated externally by Teltherm Instruments Ltd (Auckland, New Zealand) which is an IANZ (International Accreditation New Zealand) accredited calibration laboratory. Fisher and Paykel Healthcare provided calibration certificates for both the thermistors and the dry block.

RHINOTHERMY DEVICES

Fisher and Paykel Healthcare provided the study intervention devices:

- F&P AIRVO ™ 2 nasal high flow device ('sham' rhinothermy)
- rNHF device