Common Treatments for Common Colds: A Pilot Study

RESEARCH PROTOCOL

[**S**quirting **N**asal saline solution **O**r **R**outine **T**reatment (SNORT) Study]

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Aims
This project aims to compare the effectiveness of the addition of nasal saline spray to routine care for minimisation of the symptoms of acute URTIs. It also aims to assess the feasibility of conducting a randomised controlled trial for this purpose in general practice and to refine the processes of the trial.

Synopsis
Over the last few years, the National Prescribing Service (NPS) (http://www.nps.org.au/) has conducted regular campaigns aimed at educating the public about appropriate treatments for the common cold. They have continually reinforced the message that common colds are caused by viruses, and therefore antibiotics are likely to have no benefit. The NPS have produced resources to educate the public that treatments such as nasal saline, steam inhalation and decongestants that relieve symptoms are more helpful than antibiotics for common colds and viral upper respiratory tract infections.

However, the effectiveness of isotonic nasal saline spray for relief of common cold or acute rhinosinusitis symptoms has not been adequately evaluated – most studies have been too small or of poor methodological quality. Therefore this pilot study aims to determine the feasibility of conducting a general practice based, randomised controlled trial to assess the efficacy of nasal saline spray on the duration of general unwellness and symptoms associated with the common cold or acute rhinosinusitis.

In this study, consenting patients who have visited their GP because of a common cold or acute rhinosinusitis will be randomised to either nasal saline spray plus usual care or usual care alone. All study participants will be requested to not use steam inhalations, or any nasal decongestants or nasal sprays other than the trial medication for the duration of their participation in this study. The duration of general unwellness, cough, runny or blocked nose and sore throat, as well as the use of other treatments including antibiotics will be compared in both groups. Patients will be followed up until their first day of wellbeing or for 6 weeks, whichever occurs first.

We will assess the willingness of general practice patients to participate in this study (recruitment rate), their ability to comply with the study protocol, withdrawal rate, and any practical issues that arise within the general practice during the recruitment phase. Additionally, we will assess the practicality of and any issues associated with the procedures for following up patients by the research officer.

Research question(s)

- In patients with common cold or acute rhinosinusitus, does application of an isotonic nasal saline spray at least four times per day decrease duration and severity of general unwellness associated with these conditions, compared with usual treatment (excluding any nasal decongestant agents and steam inhalations)?

- In patients with common cold or acute rhinosinusitus, does isotonic nasal saline spray decrease antibiotic use compared with usual treatment (excluding any nasal decongestant agents)?

- In patients with common cold or acute rhinosinusitus, does nasal saline spray decrease severity and duration of malaise, compared with usual care (excluding any nasal decongestive agents)?

P all patients 2 years or older with common cold or acute rhinosinusitus

I nasal saline 4 times per day + usual care (excluding any nasal decongestants)

C usual care (excluding any nasal decongestants)

O duration and severity of nasal stuffiness, cough and rhinorrhea

Secondary research questions:

- What is the feasibility of conducting this randomised controlled trial of isotonic nasal saline solution in general practice?

- What is the acceptability to patients of isotonic nasal saline spray in treatment of nasal stuffiness, cough and rhinorrhea?

Background & Literature review

Troublesome cough, nasal stuffiness and rhinorrhea (runny nose) are common symptoms associated with viral upper respiratory tract infections (URTIs). These symptoms may persist for many weeks, and contribute to a significant percentage of patient visits to GPs each year (estimated to be about 6% of general practice consultations[1]. The diagnosis of post viral cough is highly variable, with poor agreement on the causation being labelled as bronchitis, post nasal drip or sinus problems. Antibiotics are commonly prescribed in this situation, particularly if the patient reports coloured mucus[2], yet the evidence suggests a limited and problematic role for antibiotics for post viral cough. The National Prescribing Service (NPS) has produced patient education resources promoting the benefit of treatments such as nasal saline, steam inhalation and decongestants over antibiotics for viral URTIs.

Nasal saline irrigation is a popular treatment for sinonasal conditions. Its potential mechanism for alleviating upper respiratory symptoms is by clearing excess mucous, reducing congestion and improving breathing.[3] It is reported to increase the frequency of nasal ciliary beating, thereby improving mucociliary clearance.[4] In addition to relieving sinonasal symptoms, nasal saline irrigation may also remove

infectious material from the sinuses and reduce cough associated with post-nasal drip.[5]

The research literature suggests a clinically significant benefit of nasal saline in the treatment of cough associated with chronic rhinosinusitis and established sinus infections, and for assisting mucociliary clearance.[3] However, studies investigating the clinical benefit of nasal saline in acute URTIs are predominantly small and methodologically flawed, although they do suggest some benefit.[6] No studies on the benefit of saline nasal spray when post viral cough was the presenting symptom were identified, and none that documented the reduction in antibiotic usage by the adoption of this treatment strategy.

This project explores these issues through an open label, randomised clinical trial which aims to compare the effectiveness of the addition of nasal saline spray to usual treatment. The duration of cough as well as the use of other treatments, including antibiotics, will be documented in both groups.

Methods

Research Design – randomised controlled open label trial.

Participant recruitment – Participating GPs will opportunistically identify potentially eligible patients as they present for a consultation for treatment of the common cold or acute rhinosinusitis, and initiate discussion to gauge interest and determine eligibility. Following this consultation, the Practice Nurse (or another suitable staff member) will continue discussions with potentially interested patients, answer their questions, and obtain informed consent.

Inclusion criteria

- Patient is aged 2+ years and has had symptoms of cold (runny nose, sore throat, sneezing, cough lethargy etc), or acute rhinosinusitus for at least 5 days and up to but not more than 3 weeks.

Exclusion criteria

Patients who:

- wish to use any treatment involving a volume of liquid going into the nose (e.g. steam inhalations, nasal sprays, nasal decongestant agents nasal douches, neti pot etc). Participants who have previously been using these may be included, provided they agree to discontinue use for the duration of their participation in the study

OR who have:

- known or suspected Chronic Obstructive Pulmonary Disease (COPD)
- suspected pertussis infection
- facial anatomical abnormalities
- cognitive impairment preventing informed consent
- physical impairment preventing compliance with the study protocol

Recruitment of participating GPs – there is a core group of GPs & associated general practices who have been involved in the development of this project – UQ Health Services (David King, John Bennett, Anita Green), Inala Indigenous Health (Geoff Spurling) and Inala Primary Care. It is expected that additional GPs will be recruited through the South East Queensland Research Network (a network of GPs who have participated in general practice based, clinical research) and the UQ General Practices of Research Excellence (GPs who have lead clinical research in their own practices).

Sample Size – 60 participants, 30 in each group.

Randomisation and allocation to study groups – patients will be randomised to either the intervention or control group. Randomising will be done at the Discipline of General Practice using computer generated random sequences in blocks of ten patients. A set of sealed, opaque, sequentially numbered study packs will be delivered to each participating general practice. Once a patient has consented to participate in the study, they will be allocated a study identifier, and will be given a study pack. The study pack will contain the first fortnight's patient diary, and sufficient study medication for a fortnight. Study packs for the control group will contain 3 packs of Vicks Vapor Drops or similar, of comparable size to the nasal saline spray. This will be a 'thank you' to control group participants and will ensure that all study packs look similar such that practice staff and patients remain blinded to group allocation.

Intervention – the intervention is a nasal saline solution which will be used for a minimum of 4 times per day.

Control – patients allocated to the control group will use usual care treatments only.

Primary outcome measure is the return of wellness, indicated by the patients' assessment of the first day of wellbeing.

Secondary outcome measures include:

1. severity and duration of troublesome nasal stuffiness
2. severity and duration of troublesome cough
3. severity and duration of rhinorrhea
4. severity and duration of malaise
5. antibiotic use
6. adverse effects of treatment
7. patient compliance
8. patient satisfaction.

Data collection – The data will be collected through patient diaries. Patients will be completed on a daily basis until general wellbeing is restored or for 6 weeks, whichever occurs first. Answers will be an indicator of the patients' subjective assessment of the severity of the symptoms each day. Restoration of general wellbeing is defined as when the patient answers 'yes' to the question 'Are you well

again?'. The diary has been adapted from one used by general practice researchers in the UK.[7]

A patient enrolment form will be used to gather basic demographic information, the duration of unwellness prior to attending the GP, and the patient's belief about the effectiveness of antibiotics for treating common cold or acute rhinosinusitis.

Patients' satisfaction with their involvement in the study and, for the nasal saline group, use of the study medication, will be assessed at the time of the final follow-up phone call by asking for patient feedback.

Follow-up – All study patients will be contacted by telephone by the Research Assistant (RA) within 2-3 days of recruitment to ensure understanding and willingness to comply with the study protocol. The RA will contact the patients again 7-9 days after recruitment to determine if symptoms have resolved or whether the patient requires another study pack. A third follow-up call will occur at about day 20, and a third study pack sent out as required. Any patients continuing the treatment / diary at the third call will receive a final follow up telephone call at 6 weeks post enrolment into the study to remind them to send back the symptom diary. The RA will remain blinded to the group to which the patient has been allocated throughout the follow-up period. Another member of staff will make up additional study packs as required.

Analysis – Data will be analysed according to the intention-to-treat principle, comparing the intervention group with the control group. Baseline characteristics and symptoms will be compared using either Student's t-test (for continuous data) or Fisher's Exact Test (for categorical data). We will analyse first day of well-being using Cox regression survival analysis, and will adjust for baseline symptom severity, and duration of illness before visiting the GP. We shall investigate the severity of illness using a symptom score collected on day 3 after enrolment. We will use a multivariate linear regression, adjusting for baseline symptom severity, and duration of illness before visiting the GP. A P-value<0.05 will be considered statistically significant. There will be no adjustment for multiple comparisons.

Dissemination of results – The outcomes of this study will be disseminated through presentations at relevant conferences, and publication in international peer reviewed journals.

Potential Benefit of Findings

Nasal saline spray, if effective, could reduce the duration of the symptoms of the common cold or acute rhinosinusitis thereby improving patient wellbeing. It could also reduce the use of antibiotics and the economic costs associated with disruptions to normal activities. This pilot study will provide important information about the feasibility of conducting an appropriately powered study to determine the effectiveness of this readily available, over-the-counter treatment.

References

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