A Study of the Effects of Sodium Citrate on Olfactory Thresholds

Research Protocol

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Summary
The aim of this study is to look at the human effect of sodium citrate on the sense of smell. If there is shown to be an improvement on olfactory thresholds this may have a profound impact on the way anosmia or hyposmia is treated and managed.

Introduction
Previous research has suggested that sodium citrate improves hyposmia by decreasing mucus calcium levels in the nose\(^1\). This was supported by an animal study that found prolonged olfactory stimulation in frog olfactory receptor cells when creating a similar environment\(^2\). The theory behind these effects relates to calcium ions (Ca\(^{2+}\)) and their role on olfactory receptor neurons. A reduction in free Ca\(^{2+}\) ions is likely to increase the excitability of olfactory neurons, thus improving the sense of smell. A sodium citrate solution douched in the nose should have the effect of binding free calcium ions in the nasal mucus, thus reducing mucosal calcium.

Aims and Objectives
To identify if there is an influence on an individual’s sense of smell with the use of sodium citrate.

Study Design and Methods
The study will be undertaken at the ENT department of the Leicester Royal Infirmary and in a research laboratory at the University of Leicester and also at the ENT departments of the
James Paget Hospital (Great Yarmouth) and Norfolk & Norwich Hospital. Fifty subjects will be recruited. Basic demographic data will be collected and the subjects will be asked to complete a questionnaire about their sense of smell. Subjects will be invited to undergo a series of smell tests using graded concentrations of 4 odours in 250ml bottles. This test has been described and validated by our previous work. The test will be fully explained to the subject beforehand by the researcher who will test the patient. The subject will be started with the smallest concentration of each odour and will ascend through the bottles until they detect 2 in a row, at which point the weaker concentration of the odour will be taken as their threshold. They will have a threshold levels determined for the odours phenethyl alcohol (roses), 1-butanol (pear), acetic acid (vinegar) and eucalyptol (menthol).

Then, the subject will then have their nose sprayed with either sodium citrate (9% concentration) or with sterile water (control). Patients will be randomly allocated to either of the two groups using a coded bottle system. Both patient and tester will be blinded to the solution used as these will be made in the pharmacy and coded for anonymity – the code will be broken at the end of the trial. Subjects will then be retested with the odour bottles and threshold levels established at 15-minute intervals for 2 hours. The purpose of the repeated tests is to determine the length of the effect (if present) of the citrate on the olfactory ability of the patients.

(N.B. Sodium citrate is a licensed product for use in body cavities (e.g. stomach, bladder) and can be found in the British National Formulary – the concentrations proposed do not exceed those used elsewhere.)

Inclusion criteria:
- All patients with an objective reduction in their ability to smell

Exclusion criteria:
- Patients who are proven to have a normal sense of smell
- Patients with nasal polyps
- Patients with any allergies
- Patients with asthma
- Age less than 16 or greater than 60
Data Collection, Management and Analysis
The data collection will be recorded by hand using a threshold graph. Information recorded will include age, sex, race, temperature, humidity, and nasal PIFR. The data will be stored on computer anonymously after assigning a number to each subject. The results will be analysed by the researchers and by a statistician (Allan Clark, University of East Anglia).

References

Methodology Flow Chart:

50 Subjects are recruited to volunteer from ENT clinic if symptoms of olfactory disturbance are reported

Subjects are offered participation in the study and given a PIS to read – they can opt to return another day if they prefer to have more time to consider participation

Examination of nose and then proforma completed for epidemiological data

1st olfactory test performed

Patients sprayed into both nostrils with anonymous (coded) solution

25 patients with 9% citrate

25 patients with Sterile water

Series of olfactory tests performed at 15-minute intervals for 2 hours

End of participation in study