Author’s response to reviews

Title: Paranasal sinus air suction for the treatment of acute migraine – A randomized, double blind, pilot Study

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Thank you for the reviews

Please mention if you obtained IRB approval for this study from your institution.

Ethical clearance was taken from Medical Research Institute ethical committee, Colombo. Registration No: 38/2016

Clinical Trial Registration number = SLCTR/ 2017/018

Sri Lanka Clinical Trials Registry

Date of Registration = 29 Jun 2017

Universal Trail Number = U1111-1190-2358

I didn't understand exactly how you enrolled subjects in the study. I assume that there was a baseline visit for enrollment and then another visit during a migraine attack. What were the criteria for a qualifying migraine attack? Was this an outpatient study? How long was their
migraine present? Were the subjects allowed to treat prior to the treatment? What about rescue treatment for treatment failures?

The subjects were patients in the age group of 16–19 years, diagnosed with migraine according to the International Headache Society (IHS) criteria. Patients with more than 3 migraine attacks but not more than 15 attacks per month, were selected. The participants were selected from two stage randomization process with stage 1 being selection of schools randomly from Kandy district (an administrative unit) in Sri Lanka and stage 2 being selection of subjects randomly within the selected schools. This was carried out as an outpatient study. When these patients presented with typical migranous attack (throbbing or pulsatile quality with nausea, vomiting, photophobia or phonophobia with or without aura) for more than one hour they were randomized into treatment (paranasal suction) or placebo (placebo suction) group. All subjects were studied only once, after a single migraine headache. All participants were advised to come to hospital when they get an acute migranous episode and not to take abortive (symptomatic) therapy before the therapy. So subjects were not allowed to treat prior to the treatment and if so they were excluded. The treason was that then this treatment effect is confounded with other treatment effect.

We did not collect information regarding rescue treatment for treatment failures.

The trial measured response at 60 seconds. This is interesting as a proof of concept but given that migraine typically lasts much longer I'm not sure it's clinically meaningful. What about responses after the treatment at 30, 60, 120 minutes and sustained pain response/freedom? Did you measure associated symptoms such as nausea and their response to treatment?

This was conducted as a pilot study. Here we did not measure 30, 60, 120 minutes respond or associated symptoms such as nausea and their response to treatment. This was conducted mainly to proof of concept. Second research is ongoing to measure long term response, other symptoms and side effects.

How was the person applying pressure to the supraorbital area blinded to the treatment?

Same person did this examination and he was not aware whether that patient underwent treatment or placebo.
I was not familiar with the procedure of applying sinus pressure during the treatment. What was the reason for performing this procedure? What about subjects without significant frontal headache?

Applying pressure in the supraorbital area is part of the routine examination of headache especially for sinusitis. But this can be suggested to check migraine headache (reference -21 ). In this research it was found that suborbital tenderness also significantly dropped in the treated group compared to the control group. In addition it was found that almost all patients had suborbital tenderness (98% - left side and 100% - right side). Therefore this examination finding can be suggested to be used as a symptom to diagnose migraine headache . However the number of subjects in this research was small and so more research is needed to confirm this finding before using this as a diagnostic tool of migraine.

I didn't understand the first paragraph on page 4 which discussed the sinus-nitric oxide link. Certainly NO is one of many molecules (CGRP, PACAP, prostaglandin E2) which reliably trigger migraine. But nobody thinks any single molecule is the cause of migraine. If NO was the main cause of migraine, wouldn't high flow oxygen work much better than it does? Rewrite to state that NO may play an important role in migraine and cluster pathophysiology, but that treatment with oral non-selective NO inhibitors has yet to be proven safe or effective.

The content of that is based on references below

I agree to NO is one of many molecules (CGRP, PACAP, prostaglandin E2) which reliably trigger migraine and corrected. Please kind to go through these reference that Dr Rathnasiri (principal investigator ) written and published that will clear your understanding of this hypothesis and NO relationship with CGRP, PACAP, prostaglandin E2 and many other molecules .

01. Paranasal Sinus Nitric Oxide and Migraine(Medical Hypnosis : www.jouernla elsievr.com(Medical hypotheses,80(2013),329-340).


03. Migraine and neurological disorders disorder explained by Sinus hypoxic nitric oxide theory(Biomedical journal ,September 24(2014) ).

I rewrote stating that NO may play an important role in migraine and cluster pathophysiology, but that treatment with oral non-selective NO inhibitors has yet to be proven safe or
effective. Please read the following references as well. I agree that that treatment with oral non-selective NO inhibitors has yet to be proven safe or effective. But our procedure is to removal of causative molecule without change or systemic effect is taken by a drug


I object to using a case series from a surgeon of his own patients without a control as "proven" evidence that sinus surgery can "cure migraine headache." I was not able to find the Novak full reference online as the journal is no longer in publication. Perhaps I am biased, but in my 16 years of practice seeing dozens of patients who have had sinus surgeries for various reasons - including congestion, breathing problems or headache - I have never once seen a patient with migraine cured by sinus surgery.

We have quoted this from published work. (Reference 17) it is not used to prove our hypothesis

In the discussion avoid making exaggerated claims without evidence such as "This treatment modality is the probably the most economic and effective method to treat acute migraine…", or that "this examination finding can be suggested … to diagnose migraine.." or that the study results teach us about the pathophysiology of migraine aura.

Thanks for comment we added it in other way to reduce exaggeration

Minor concerns:

Some of the triptans, particularly non-oral triptans, demonstrate significant differences at < 30 minutes.

In this research we did not try to compare this with drugs. However, our hypothesis is that this paranasal suction is used to remove causative molecule mechanically. Thus it is less time duration to get relief than most of the drug treatments available that act chemically
What is "natural nasal cycle"

The nasal cycle is the often unnoticed alternating partial congestion and decongestion of the nasal cavities in humans and other animals. It is a physiological congestion of the nasal conchae, also called the nasal turbinates, due to selective activation of one half of the autonomic nervous system by the hypothalamus.

Please follow A reference is there regarding the phenomenon


How about a picture of the device?

This is just a common air sucker used in hospitals. The air pressure of these can be adjusted.