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Letters to the Editors

Randomised, double-blinded, placebo-controlled, clinical trial of ozone therapy as treatment of sudden sensorineural hearing loss

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Dear Sirs

We read with interest the paper entitled 'Randomised, double-blinded, placebo-controlled, clinical trial of ozone therapy as treatment of sudden sensorineural hearing loss' by A Ragab, E Shreef, E Behiry, S Zalat and M Noaman. In the past, we too have treated a few patients affected by sudden sensorineural hearing loss with ozone therapy. Our results were mixed and not good enough to report.

The paper by Ragab and colleagues is extensive and well written. However, having ourselves worked on ozone treatment methodology for several years, we found serious pitfalls in the methodology reported.[1,2]

The ozone concentration used per millilitre of blood is never mentioned and this point must be clarified. Moreover, ozonation of blood was performed in bags that are unlikely to be ozone-resistant and which may release phthalates in the blood. The placebo group was also infused with sterile distilled water. This is a serious mistake as it will provoke some haemolysis, and possible upregulation of haem-oxygenase-I, which is a protective enzyme able to alter the clinical outcome.

The authors report that both infusion sets (containing either ozonated blood or sterile distilled water) were 'covered with foil and labelled'; however, was the plastic tubing used for the infusions also covered? It is also reported that the placebo group received back their own blood instead of sterile distilled water in the fifth as well as in the 10th session. This may mean that patients received 500 ml of blood in a single infusion, and this sudden overload may modify the clinical response.

We also feel that the experimental design is basically inappropriate. In order to interpret clinical results, the experimental group must receive ozonated blood of a definite ozone concentration, while the placebo group should receive neither water nor saline but only their own blood which has been simply oxygenated.[3] These serious technical mistakes make the results doubtful and difficult to compare.

We hope that our comments will be useful for further studies.

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Authors' reply

Dear Sirs

I appreciate Prof Bocci and his colleagues' interest in and comments on my and my colleagues' paper.

In the hierarchy of evidence that influences healthcare policy and practice, randomised, controlled, clinical trials (RCTs) are considered the most reliable form of scientific evidence because they eliminate spurious causality and bias.[1] To our knowledge, our study is the first RCT of ozone therapy as treatment of sudden sensorineural hearing loss (SNHL).

Prof Bocci has treated only a few patients, and the references he uses to identify pitfalls in the present RCT were published by his team and represent their personal opinion. None of the references cited contain any data from prospective RCTs.

In response to the specific points regarding ozone concentration, we did report that the concentration used was 5 per cent of the gas mixture ($O_2 + O_3$). European healthcare regulators clearly recognise the role of phthalates. The three European Union directives relating to medical devices stipulate rigorous and exhaustive testing of materials and also govern which materials may be employed. Di-(2-ethylhexyl) phthalate – the member of the phthalate family used in almost all PVC healthcare applications – is actually specified by the European Pharmacopoeia as the plasticiser to be used in blood bags.[2] As this phthalate is chemically inert and does not react in any way, ozonation of blood was performed in such bags in our study. Blood bags are still used in most ozone therapy centres worldwide, and the release of phthalates is not a documented hazard in any of the reported studies using such bags. From a chemical point of view, phthalates could migrate out of plastic in the presence of solubilising lipids, lipoproteins or albumin; however, ozone is a gas.

As regards the covering of plastic tubes, a standard infusion set was used and this was covered with foil, as mentioned in the text.

Undertaking autotransfusion with the same amount of blood as withdrawn previously would not be likely to overload the patient, considering the small amount used, and this would not, we feel, alter the results. We certainly did not encounter any symptoms or signs of volume overload in our patients.

I hope that these replies address the concerns raised.

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