Letter to the Editors

Important details to be clarified about the effect of rectal ozone on the portal vein oxygenation

Velio Bocci, Iacopo Zanardi & Valter Travagli

Università degli Studi di Siena, Dipartimento di Fisiologia (VB) and Dipartimento Farmaco Chimico Tecnologico (IZ, VT), Viale Aldo Moro, 2 53100 Siena, Italy

We read with interest the paper by Zaky *et al.* [1]. In this study, the results of the propranolol pharmacokinetics in cirrhotic patients show that after 14 rectal administrations of oxygen-ozone (300 ml of 40% ozone/oxygen mixture), all parameters of the drug's metabolism improve. However, in our opinion there are a few important details to be clarified: firstly, what is the real ozone dose, because the reported sentence 'rectal ozone insufflation at a dose of 300 ml of 40% ozone/oxygen mixture' means only that 120 ml ozone were in gas mixture, but unless the ozone concentration (usually expressed as $\mu\text{g ml}^{-1}$) is defined, the actual dose remains unknown. Secondly, an increased oxygen tension and saturation in the portal vein have been found. Such a result agrees also with our experimental data previously performed in rabbits [2]. Nevertheless, gaseous ozone cannot be present as such in the portal vein because ozone is never absorbed after rectal administration by the colo-rectal mucosa, contrary to what happens to oxygen [2, 3].

What then is the role of ozone? Does ozone improve oxygen absorption by the mucosa or are the compounds generated by ozone reaction in the luminal content and mucosal surface to have a relevance in modifying the propranolol parameters? Indeed, the control experiment performed by the administration of either 180 ml or 300 ml oxygen only is critically missing. We have clarified that oxygen is the natural carrier but the reactive gas is ozone, which inside the rectal lumen very rapidly generates hydrogen peroxide and a variety of lipohydroperoxides and alkenals [4]. They are highly reactive and rather than oxygen, may well be responsible for the modified propranolol pharmacokinetics, but they have been neither mentioned nor apparently measured. In our experiments these compounds were significantly present in portal blood and far less, as expected, in the jugular vein.

To date, on the basis of our knowledge, rectal insufflation of 200–300 ml of an oxygen-ozone mixture (maximum ozone concentration $35 \mu\text{g ml}^{-1}$, hence an

ozone dose of 7–10 mg per treatment) in liver cirrhosis may be a little helpful but cannot modify the prognosis.

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

Competing Interests

There are no competing interests to declare.

REFERENCES

- 1 Zaky S, Kotb H, Fouad E. The effect of rectal ozone on the portal vein oxygenation and pharmacokinetics of propranolol in liver cirrhosis (a preliminary human study). *Br J Clin Pharmacol* 2011; 71: 411–5.
- 2 Bocci V, Borrelli E, Corradeschi F, Valacchi G. Systemic effects after colorectal insufflation of oxygen/ozone in rabbit. *Int J Med Biol Environ* 2000; 28: 109–13.
- 3 Bocci V. *Ozone. A New Medical Drug*, 2nd edn. Dordrecht, The Netherlands: Springer, 2011.
- 4 Bocci V, Borrelli E, Travagli V, Zanardi I. The ozone paradox: ozone is a strong oxidant as well as a medical drug. *Med Res Rev* 2009; 29: 646–82.

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CORRESPONDENCE

Emeritus Professor Velio Bocci, Department of Physiology,
University of Siena, Viale Aldo Moro 2, 53100 Siena,
Italy.

Tel.: +39 05 7723 4226

Fax: +39 05 7723 4219

E-mail: bocci@unisi.it

or

Professor Valter Travagli, Chief of the Post-graduate School of
Hospital Pharmacy, University of Siena, Viale Aldo Moro 2, 53100
Siena, Italy.

Tel.: +39 05 7723 4317

Fax: +39 05 7723 4333

E-mail: travagli@unisi.it