Letter

Hemorrhagic shock, drag-reducing polymers and 'spherical cows'

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See related commentary by Gutierrez and Fuller, http://ccforum.com/content/8/6/406

It was a pleasure to read the elegant and witty commentary by Gutierrez and Fuller [1] regarding our paper published in *Shock* [2] on resuscitation of rats using our aloe-derived drag-reducing polymer (DRP) solution. However, we disagree with the statement that, 'the application of physical principles to complex living organisms often requires assumptions *ad absurdum*.' There is always physics behind every natural process, including physiological processes in living organisms and hemodynamics. This is a well established and widely recognized philosophical and methodological principle. The physical explanation of systems characterized by extreme complexity is a very difficult task that requires many levels of approximation.

Concerning the effects of DRPs on blood circulation in general, and the hypoperfusion associated with hemorrhagic shock in particular, several synthetic (polyethylene oxides, polyacrylamides) and natural (polysaccharides, DNA) DRPs with completely different chemical structures were found to produce exactly the same hemodynamic effects when injected in blood at minute concentrations. The similarity in effects observed with chemically distinct classes of compounds with DRP-like activity supports the notion that the beneficial effects are due to shared physical properties of these agents.

We hope that readers of this journal will find time to examine another report on the treatment of hemorrhagic shock in rats using two high molecular weight polymers, which was published in February 2004 in *Biorheology* [3]. The polymers were synthetic polyethylene oxide (or polyethylene glycol [PEG]) with a molecular mass of 3500 kDa (PEG-3500) and the aloe-based DRP with a molecular mass of about 4000 kDa. In addition, we used PEG with a much lower molecular mass of 200 kDa (PEG-200) in these experiments. PEG-3500 and the aloe vera derived agent are DRPs. PEG-200 possesses the same chemistry and structure of the higher molecular weight PEG, but it has no drag-reducing ability (the drag-reducing property was found in linear polymers with molecular masses >1000 kDa). The major findings were that the nanomolar concentrations of both DRPs added to the resuscitation fluid prevented death in rats from severe hemorrhage. However, PEG-200 did not produce any beneficial effects when it was added to the resuscitation fluid at 15 times the concentration. Thus, drag-reducing or related viscoelastic properties of the applied polymers were the most important factors in the improved survival from severe hemorrhage. Incidentally, we did not 'attribute systemic hemodynamic changes to decreases in vascular frictional forces' in our analysis of the obtained results. On the contrary, we suggested that the major beneficial effect of the polymers in hemorrhagic shock was their effect on the red blood cell concentration in the microvessel near-wall space (an increase in a microvessel hematocrit) and attenuation of the plasma-skimming effect, which, in fact, would increase the local viscosity and microvessel wall shear stresses, potentially causing a release of shear-dependent vasodilators selectively in microvessels.

Although the exact mechanisms of the intravascular effects of DRPs are yet to be discovered, this extraordinary physical phenomenon has great biomedical potential and warrants further investigation.

Competing interests

The author(s) declare that they have no competing interests.

DRP = drag-reducing polymer; PEG = polyethylene glycol.

Authors' response

Guillermo Gutierrez and Stephanie Fuller

We read with great interest the letter written by Kameneva and Fink in response to our recent commentary [1] on the circulatory effects of DRPs. We directed our comments to the possibility that the salutary effects of aloe-derived DRPs may have resulted from the well known antioxidant properties of aloe vera. As pointed out by Kameneva and Fink in their letter, posthemorrhage rats also exhibit improved survival when infused with a DRP not derived from aloe vera [3]. This finding supports their hypothesis that the beneficial effects of DRP are related to alterations in blood rheology and not just to the scavenging of oxygen free radical species.

A great deal of ground remains to be covered as we begin to understand the *in vivo* rheological properties of DRPs. It may be that the 'spherical cows' alluded to in our commentary may be slimmer than originally thought!

Competing interests

The author(s) declare that they have no competing interests.

References

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