

Letter

Patience and change: a conflict of interests?

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Published: 19 September 2006

This article is online at <http://ccforum.com/content/10/5/422>

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Critical Care 2006, **10**:422 (doi:10.1186/cc5034)

See related commentary by Friedrich *et al.*, <http://ccforum.com/content/10/3/145>

While we must applaud industry and the Recombinant Human Protein C Worldwide Evaluation in Severe Sepsis (PROWESS) investigators [1] for the tremendous effort and time expended in their multicentre, international study, caution needs to be exercised before deciding to make the intervention of activated protein C (APC) a standard of treatment [2].

We, like many others, have chosen to introduce APC into our practice in the treatment of severe sepsis, despite having an awareness of the progress of associated controversies [3-5]. By choosing to change our practice we may have exposed patients to occult harm or to benefit. Alternatively, patient outcome may have remained unchanged but time, money and clinical effort have been expended (and wasted) in the necessary activities to affect the change. These activities are a significant burden on the multidisciplinary team that carry out intensive therapy, and their effects should not be underestimated.

What impels us to change, then? Why do we not have more patience and either wait for, agitate or participate in the need for more data? Perhaps we feel a desire to demonstrate that we are up to date, that we are dynamic and that we can implement change quickly and effectively locally? We may assume that this is what colleagues as well as the public expect of us. Guidelines from 'learned bodies' [6] may also influence us. In a world that is apparently 'moving forward' rapidly, we do not want to feel that we are being left behind, unchanging and old-fashioned. We need to belong to the group that is dynamic and contemporary.

Having become part of our practice, we now feel ambivalent to the prescription of APC. Notwithstanding the efficacy debate, the resource implications for the prescription of recombinant therapies are considerable. The question of global equitable availability is an additional issue that receives

scant attention. Some days we prescribe the intervention, worrying about the possible side effects and resource implications. Other days we may defend our right not to prescribe them, concerned that we are swimming against the dominant tide of contemporary practice. We agree wholeheartedly with the comments of Friedrich and colleagues in a recent issue of *Critical Care* [2] that we need further new data regarding APC to clarify its treatment effect in sepsis.

Smith and Roberts [7] in their recently published seminal paper give clear contemporary guidance on conducting and publishing clinical trials. They state that a single randomised clinical trial needs to be evaluated in the context of all the information available, and thus needs to be understood in the context of a systematic review. If there is uncertainty despite this, and if the research question posed is deemed important, a further trial is necessary. Is now the time for national academic groups to build on the industry-sponsored PROWESS study and to coordinate and design a further randomised clinical trial – a study that is independent and addresses the issue of the treatment effect of APC in sepsis? We think so. We should also learn from this evolving narrative the lesson that patience remains a virtue and change should not be undertaken lightly.

Competing interests

The authors declare that they have no competing interests.

Acknowledgements

PJDA was sponsored by Chest Heart and Stroke Scotland (CHSS Research Award, R2002/A65) and the Chief Scientist Office (Grant CZG/4/1/37).

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