Drotrecogin alfa (activated): is there room for improvement?

doi:10.1017/S0265021508004572

EDITOR:

We read with interest Ridley's paper presenting an audit on the clinical impact of the use of drotrecogin alfa (activated) outside clinical trials [1]. He and his colleagues report reduced mortality in patients treated with drotrecogin alfa (activated) when compared with expected mortality derived from APACHE II score and organ dysfunction score [1]. In a similar audit that we performed recently, there was one particular finding that we think should be emphasized.

Although we were not among the five largest users of drotrecogin alfa (activated) in England, as a large teaching hospital with tertiary referral specialities, a total of 60 of our patients received drotrecogin alfa (activated) from January 2002 to June 2007. Data for all patients were collected from the Intensive Care National Audit and Research Centre (ICNARC) database [2], patients' notes and drotrecogin alfa (activated) prescription charts.

Our data are comparable with those in Ridley's paper with respect to patient age (65 yr vs. 29/60 patients were in the 50–70 yr age group), median organ dysfunction (3 vs. 2.8) and average APACHE II score (median within range 18–22 vs. 24/60 patients in the 21–30 APACHE II score group). The site of sepsis was lung in 55% of patients, abdomen (peritonitis, pancreatitis, ruptured oesophagus) in 35% and 'other' (neutropenic sepsis, meningitis) in 11.6%.

All patients receiving drotrecogin alfa (activated) (APC) had two or more dysfunctional organs and were already receiving optimal ICU care. However, although overall mortality in our unit is lower than the national average according to ICNARC data, mortality 4 weeks after initiation of drotrecogin alfa (activated) was higher than in Ridley's audit (64% vs. 43%).

When we looked at the time lapse between prescription and administration of APC, we found that among the 60 patients, only 13 received APC within 1 h of it being prescribed, 22 between 1 and 8 h, and 25 after 8 h. When this was compared to outcome, we noted that mortality was significantly (Fisher's exact test, $P = 0.343$; www.quantitativeskills.com/sisa/statistics/fisher.htm) higher (19/25; 76%) among patients who received drotrecogin alfa (activated) 8 h after prescription than among those who received it within 8 h (18/35; 51%).

APC is licensed for application within 24 h. The ENHANCE study has shown that earlier APC administration is better [3]. It is difficult to establish the zero point and the delay in APC administration because there is often a long time interval between the first symptoms of sepsis and ICU admission. Another 8 h delay in drug supply in a patient with multiorgan failure can be crucial. Our audit revealed that delayed administration of APC can jeopardize its therapeutic effect. This audit exposes a disparity between clinical practice and current recommendations and can serve as a basis for improving clinical practice. Following this audit we implemented changes in drug administration, shortening the time interval between prescription and administration to less than 1 h. We have obviously traversed a learning curve on the use of drotrecogin alfa (activated) and we hope that this report can help other, less-experienced units to overcome this problem.

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Accepted for publication 1 May 2008 EJA 5098
First published online 5 June 2008