

Combating mortality from severe sepsis

Thousands of patients suffering from severe sepsis are set to benefit from the publication of the National Institute for Clinical Excellence (NICE) guidelines recommending the use of Xigris (drotrecogin alfa (activated), Eli Lilly & Company Ltd, Basingstoke). Drotrecogin alfa (activated) is the only drug specifically designed to treat severe sepsis and has been recommended for use in adult patients who have severe sepsis that has resulted in multiple organ failure and who are being provided with optimum intensive care support (NICE, 2004).

Severe sepsis affects 21 000 people a year, accounting for nearly 27% of all critical care admissions in England, Wales and Northern Ireland (Padkin et al, 2001; NICE, 2004). The body's response to overwhelming infection commonly leads to multiple organ failure and death. Despite advances in critical care medicine, severe sepsis still kills almost half the patients affected and even those who survive often suffer permanent organ damage and disability (Young et al, 2001).

Traditionally, the management of severe sepsis has been limited to antibiotics, eradication of underlying infection and general supportive care. Drotrecogin alfa (activated) is most efficacious when treating the most severely ill patients (i.e. those with two or more organs failing). Drotrecogin alfa (activated) can help reduce mortality rates by as much as 6.1%, saving over 1000 lives per year (Bernard et al, 2001).

Drotrecogin alfa (activated) is recombinant activated protein C, which is an essential modulator of the coagulation system in health. In patients with severe sepsis, levels of protein C are depleted and correlate with increasing mortality. Drotrecogin alfa (activated) promotes both anticoagulation and fibrinolysis. However, in severe sepsis, its main mechanism of action appears to be via its anti-inflammatory properties.

NICE RECOMMENDATIONS

The NICE guidance states:

- Drotrecogin alfa (activated) is recommended as a suitable treatment option for patients with severe sepsis who have two or more organs failing and who are receiving optimum intensive care support
- The use of drotrecogin alfa (activated) should only be initiated and supervised by a specialist consultant with intensive care skills and experience in the care of patients with sepsis
- Drotrecogin alfa (activated) is therefore recommended as a suitable treatment option for 12% of patients with severe sepsis (NICE, 2004).

IDENTIFYING SEVERE SEPSIS

Unfortunately, the diagnosis of severe sepsis can be imprecise. Consequently, initial treatment is often delayed. Early identification and treatment of severe sepsis can improve the patient's chance of survival. All health-care professionals should identify suspected cases of severe sepsis as quickly as possible (Kleinpell, 2003b). Risk factors for severe sepsis include:

- Extremes of age
- Surgical or invasive procedures
- Malnutrition
- Chronic illness
- Immune deficiency (Kleinpell, 2003a,b).

Changes in vital signs (especially pyrexia, increased respiratory rate and hypotension) are important signs which need to be recognized as such. Evidence has shown that the most successful management of sepsis occurs when an aggressive approach to treatment is pursued (Vincent et al, 2003). If a septic patient does not improve early in his/her treatment, his/her chances of survival are deteriorating. Therefore all suspected cases of severe sepsis should be referred to the critical care team if the patient does not respond positively to initial resuscitation. Once reviewed by the critical care team, the best treatment option will be ascertained.

Guidelines for the management of a septic patient have been produced (Dellinger et al, 2004) and form the main therapeutic thrust of the Surviving Sepsis Campaign, which hopes to reduce deaths from sepsis by 25%. The Surviving Sepsis Campaign guidelines describe the main treatment principles for septic patients and emphasize the importance of initial resuscitation, diagnosis, antibiotic therapy, infection control, fluids and nutrition, vasopressors, steroid replacement, drotrecogin alfa (activated), respiratory support, transfusion and glucose control. These guidelines are unique because they have been endorsed by critical care societies worldwide and so

KEY POINTS

- Severe sepsis affects 21 000 people a year.
- Early identification and treatment of severe sepsis can improve the patient's chance of survival.
- The National Institute for Clinical Excellence has recommended the use of Xigris (drotrecogin alfa (activated)) in the treatment of adult patients with severe sepsis resulting in two or more organ failures, when combined with optimum intensive care support.
- These guidelines will broaden access to this life-saving treatment.
- Doctors and primary care trusts need to respond positively to this guidance in order to help save lives.

will standardize and optimize treatment for sepsis throughout the world.

CONCLUSIONS

The publication of the NICE guidance is set to widen access to this potentially life-saving treatment. Many primary care trusts are already providing funding for drotrecogin alfa (activated) but these numbers are likely to rise.

Doctors and primary care trusts need to respond positively to this guidance by reviewing current practices, defining clinical circumstances in which drotrecogin alfa (activated) should be used and implementing training to ensure effective identification of severe sepsis. Ensuring this should help to

reduce the number of people dying from severe sepsis and guarantee the best standard of care for patients. **HM**

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