Changes in the classification and management of skin and soft tissue infections

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Although skin and soft tissue infections (SSTIs) are extremely common in both primary and secondary care, there is a lack of validated evidence-based schemes for the classification of clinical presentation or severity, and there are few data available on treatment outcomes. The commonly used ‘Eron classification’ is based on the consensus views of an expert panel, while the Clinical Resource Efficiency Support Team (CREST) ‘Guidelines on the Management of Cellulitis in Adults’ have not been validated in clinical trials. In the current issue of JAC, investigators at Ninewells Hospital in Dundee, Scotland, report a retrospective study of patients with SSTIs who were treated with antibiotics. The patients were stratified into four classes of clinical severity, based on the presence or absence of sepsis and co-morbidity, and their standardized early warning score. The empirical treatment received by patients in each class was compared with the recommendations of the CREST guidelines. The findings do not make comfortable reading. Overall, 43% of patients (and 65% at the mildest end of the clinical spectrum) were overtreated, while mortality (at 30 days) and inadequate antimicrobial therapy increased with severity class. Strikingly, 35 different empirical antimicrobial prescribing regimens were noted. These findings, which are likely to reflect the situation in many hospitals, show that SSTIs remain a significant cause of mortality and that empirical therapy is bordering on the haphazard, with significant under treatment of severely ill patients.

Keywords: SSTIs, severity, empirical

Introduction

The diagnosis of a skin and/or soft tissue infection (SSTI) is frequently made in both primary and secondary care. In 2004–05 in the UK alone, 69 576 admissions for such infections were recorded.1 The vast majority of SSTIs are caused by a small spectrum of pathogens, mainly β-haemolytic streptococci of groups A, C and G, and Staphylococcus aureus.

The clinical spectrum of SSTI varies from mild local inflammation at one extreme, to life-threatening necrotizing fasciitis associated with uncontrollable sepsis at the other. The clinical features of SSTIs are readily explained by their underlying pathogenesis. Once the aetiological agent has broken through the skin, which is the primary host defence, there are no anatomical boundaries limiting its spread through the cutaneous and subcutaneous tissue. Further resistance to the spread of infection depends on the innate and adaptive immune responses of the host. Our current understanding suggests that the degree of invasiveness of a given pathogen is very much determined by the number and combination of virulence factors expressed, including those that damage components of the host tissues and those that impede host defence mechanisms, such as phagocytosis by polymorphonuclear leucocytes. Clinical concern that the initial presentation of an SSTI may develop into a life-threatening condition has led to ‘unproven good clinical practice’, in which severe SSTIs are commonly treated in hospital under close clinical monitoring.2

It comes as a surprise that despite the availability of numerous clinical data, such as those from case series, individual case studies and reviews, there is no commonly agreed classification of the clinical presentation of SSTI, or a score for assessing the clinical severity of an SSTI validated by either prospective or retrospective clinical studies.

Recent attempts to classify SSTIs using clinical criteria

Over the last decade, two attempts have been made to establish schemes for the stratification of bacterial SSTIs that would be applicable to their clinical management, although neither has been validated in prospective or retrospective clinical studies. Ki and Rotstein3 proposed an assessment scheme based on the site of primary infection, in particular, involvement of the hands and/or head, while Eron et al.2 proposed a stratification (the ‘Eron classification’) and recommendation on critical

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...decision points in the management of SSTIs. However, application of these recommendations in clinical practice appeared to be cumbersome and difficult to translate into treatment protocols. Nevertheless, under the auspices of the Department of Health of Northern Ireland, the Clinical Resource Efficiency Support Team (CREST) has translated the Eron recommendations into the ‘Guidelines on the Management of Cellulitis in Adults’ (CREST guidelines). Even though the CREST guidelines are much easier to apply in clinical practice, their validity has never been proven by a clinical study.

‘Dundee classification’ of SSTIs

In this issue of JAC, Marwick et al. present both a stratification of SSTIs and a clinical score permitting assessment of their severity and the resulting impact on patient management. They assessed the validity of their proposed criteria by retrospectively analysing a total of 205 patients admitted to hospital with a clinical diagnosis of SSTI. In detail, they: (i) updated the CREST criteria into a classification that can be easily applied in the clinical setting; (ii) used an up-to-date definition of sepsis; (iii) replaced the CREST clinical criteria for categorizing the most severe cases with a standardized early warning score (SEWS) derived from the measurement of physiological parameters, including respiratory rate, oxygen saturation, temperature, systolic blood pressure, heart rate and level of consciousness; and (iv) analysed, retrospectively, patients admitted with an SSTI as identified by ICD codes, by applying their criteria and assessing the appropriateness of the prescribed antibiotic therapy for each patient.

Key findings of the ‘Dundee study’

The study by Marwick et al. addressed three key aspects of the current approach to managing SSTIs. Firstly, they investigated co-morbidities that may complicate or delay the resolution of SSTIs. Both the Eron and CREST guidelines recommend intravenous (iv) antibiotic therapy in patients with certain specified co-morbidities, such as obesity or peripheral vascular disease. Marwick et al. did not find any evidence supporting this assumption, which is based on conclusions drawn by expert panels when extrapolating from data found in the literature. Jorup-Ronstrom et al. came to the same conclusion when investigating the management of cellulitis. This leads to the conclusion that Dundee classes 1 (no significant co-morbidity, no sepsis, SEWS ≤4) and 2 (one or more significant co-morbidities, no sepsis, SEWS <4), in fact, can be merged and that most of these patients can be managed in the community with oral antibiotic therapy. Extrapolating from this study would mean that >70% of this cohort could have been managed in the community. Secondly, Marwick et al. investigated the impact of sepsis as a complication of a primary SSTI and noted that even in the absence of more severe physiological manifestations, patients in severity class 3 (sepsis, but SEWS <4) had worse clinical outcomes than patients not having sepsis (severity classes 1 and 2). This observation clearly raises the issue of whether patients with SSTI accompanied by sepsis should be managed in a high-dependency/intensive care setting rather than on a standard ward. Thirdly, Marwick et al. evaluated the importance of using a SEWS (primarily developed as an early indicator of serious illness) and showed it to be a powerful means for identifying high-risk patients presenting with an SSTI. As the application of SEWS is now accepted good clinical practice in the UK for both acute presentation in the emergency setting as well as monitoring of inpatients, it should not prove difficult to change the relevant protocols accordingly.

Marwick et al. made another rather disturbing observation, namely the uncertainty amongst doctors about the appropriate antimicrobial therapy for SSTI. In their cohort of 205 patients, they found no less than 35 different antibiotic regimens, some of which were not appropriate for the respective condition. Apparently, this is not limited to the UK, as demonstrated by Edelsberg et al. in the USA.

Impact of the ‘Dundee study’

It would be desirable to have the Dundee stratification of the severity of SSTIs validated in a prospective cohort study. However, until such prospective data become available, the authors believe that the evidence of the ‘Dundee study’ is sufficiently robust to encourage the medical community in the UK to review its current approach to the management of SSTIs. Application of the ‘Dundee criteria’ should identify patients who can safely be managed with oral antibiotic therapy in the community, leading to a reduction of the bed pressure in UK hospitals. However, where oral therapy is deemed inappropriate, outpatient parenteral antibiotic therapy (OPAT) is a safe and cost-effective option. There is no unequivocal evidence, as yet, that any of the new therapies for SSTIs are superior to existing treatments in terms of clinical effectiveness. However, one recently published review summarizes evidence that daptomycin, which is specifically licensed for the treatment of severe SSTIs, elicited a more rapid clinical response compared with standard antibiotics. If this potentially important observation is confirmed in future clinical trials, an initial short course of iv daptomycin may lead to either an early switch to oral antibiotics or cessation of therapy and subsequent discharge from hospital. Lastly, the development of new dosing regimens for old antibiotics by applying pharmacokinetic/pharmacodynamic concepts may well permit iv administration of these antibiotics in the community, abrogating the current need for admission to hospital for iv administration. One such example would be the Danish OPAT regimen for teicoplanin, which has been shown to be cost-effective in relation to SSTIs.

As referred to above, the uncertainty amongst doctors regarding which antibiotics are indicated for the treatment of SSTIs is of grave concern. As the vast majority of SSTIs are caused by a small number of pathogens (mainly \(\beta\)-haemolytic streptococci of groups A, C and G, and \(S.\) aureus), and the potential involvement of other relatively uncommon pathogens such as Pasteurella multocida can be established by a well-taken clinical history, the observation of 35 different antibiotic prescribing regimens among a cohort of patients with SSTIs is alarming. This further highlights the urgent need for training doctors in developing a rational approach to the prescribing of appropriate antimicrobial chemotherapy. In Dundee, in light of the findings by Marwick et al., a simple protocol that is regularly reviewed and supported by clinician education has been implemented to reduce variation.
With the rapid increase of widespread resistance to antimicrobial agents, it is imperative that the British General Medical Council explicitly include antimicrobial prescribing in the training of medical students well beyond what is stated in ‘Tomorrow’s Doctors’.14

**Transparency declarations**
None to declare.

**References**