Cost-Effective Use of Once-Daily Ceftriaxone in the Treatment of Moderate to Severe Infections: Introduction to a Symposium

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Ceftriaxone is the first cephalosporin with a very long serum half-life (approximately 8 h) which gives it a wide range of clinical utility. A great deal of clinical experience with this third-generation cephalosporin has been gathered over the years. Some of these data will be consolidated by the papers presented here.

This workshop, held in Montreal, Canada, on July 18, 1990, will examine various aspects of the clinical usefulness of ceftriaxone. In particular, its once-daily administration in the treatment of moderate to severe bacterial infections will be discussed.

An important aspect of ceftriaxone is its highly favourable pharmacokinetics. When used intravenously at concentrations between 1 and 2 g over a reasonable period of time, ceftriaxone gives plasma levels which exceed the minimum inhibitory concentrations of a wide range of pathogenic organisms.

Tissue concentrations of unbound ceftriaxone also reach bactericidal levels after intravenous administration of clinically appropriate amounts (between 1 and 3 g). Pharmacokinetics are an important consideration when examining the use of ceftriaxone in any infection among the geriatric population. Age-related changes in urinary clearance, as indicated by creatinine clearance levels, and volume of distribution become increasingly relevant and may have an impact on the dosing levels of ceftriaxone in this population.

Paediatric infections in general respond well to ceftriaxone intervention. Successful bacteriological responses have been documented in children diagnosed with sepsis and infections of skin and soft tissues, bone and joints, and abdomen and lower respiratory tract. A good overall response has been achieved in a variety of conditions ranging from serious infections of the central nervous system to less severe urinary tract infections.

Outpatient use of parenteral antibiotics is gaining favour among many infectious 2 Andriole
disease physicians, especially for patients who have infections not serious enough to merit initial hospitalization or those eligible to receive the latter part of their therapy as outpatients. A variety of (3-lactam antibiotics, as well as aminoglycosides and glycopeptides, have been tried as parenteral outpatient therapy for patients with moderate to severe bacterial infections. Their use frees hospital beds and allows a more appropriate use of hospital space.

Amongst the third-generation cephalosporins, ceftriaxone appears to be particularly suited to this role, since once-daily administration provides ease of administration which is necessary for outpatient acceptance of any therapy. A reduction in health care expenditure often results as a consequence of the decrease in time and personnel needed to administer the drug.

The difficulties of treating community-acquired infections for which there is often no specific defined causative agent are well known. A broad in vitro spectrum of activity is of great importance for an antibiotic likely to be used as empiric therapy. Ceftriaxone is one agent considered suitable as monotherapy for the majority of pneumonial pathogens and in addition is suitable for use in non-hospital settings including nursing homes and long-term care facilities. The choice of a third-generation cephalosporin for routine use in hospitals is determined by similar considerations. A relative lack of side-effects and low therapy cost are additional factors used to differentiate between a group of very similar drugs. Changing formulary drugs can be hard to achieve in large hospitals. Successful interventions need to be managed using a combination of regulations and persuasion followed by continuous and long-term monitoring.

In recent years, the anti-infective field has begun implementing policy designed to reduce unnecessary health care expenditure by recommending the correct therapy, at an appropriate level of dosage, for each condition. A continuously monitored policy that uses the most appropriate antibiotics administered on the basis of their pharmacological parameters can result in more appropriate and cost-effective patient care. The trend is for the preferential use of drugs that perform well at greater dosage intervals and thus towards once-daily regimens.

In summary, the pharmacokinetics of ceftriaxone which enable its effective 24-hour delivery make a major contribution towards its suitability for use as an outpatient therapy. Once-daily delivery of ceftriaxone appears effective for the empiric treatment of bacterial infections due to susceptible organisms. The results presented at this symposium and published here give additional insight into the role that antimicrobial agents such as ceftriaxone can play in reducing health care costs when used on an outpatient basis or as a hospital formulary antibiotic.