Cephalexin—a new oral antibiotic

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Summary

The pharmacology, antimicrobial activity and clinical uses of cephalexin, a semi-synthetic derivative of cephalosporin C, are described.

Cephalexin is active, when taken by mouth, against Gram-positive cocci, including penicillinase-producing staphylococci, and against many Gram-negative organisms including Gram-negative rods.

There is a low incidence of side effects.

Introduction

The value of parenteral cephaloridine is so universally established that it highlights the need for a form which is active by mouth. This is now available as cephalexin monohydrate (Wick, 1967; Muggleton *et al.*, 1968), a semi-synthetic derivative of cephalosporin C. It is broad-spectrum, bactericidal, well-absorbed after oral administration, not significantly bound to serum protein, and mainly excreted by the kidneys. The combined experience of laboratory and clinical workers was reviewed on 2 and 3 June 1969 at a symposium in the Royal Society of Medicine, London.

Pharmacology

Following a single dose, peak blood levels are noted at 1 hr in fasting subjects. Food causes a delay in onset, a lower peak and prolongation of the blood levels. Most of it is excreted unchanged by glomerular filtration and tubular secretion in the urine during the first 8 hr after absorption. Probenecid causes retention and delay in excretion (Braun *et al.*, 1968). Serum protein binding is of the low order of 25%. Studies at the Michael Reese Hospital, Chicago (Kabins *et al.*, 1969) relate serum and urinary levels of cephalexin following its oral administration to thirty-five adult patients with creatinine clearances ranging from 174 ml/min down to 0.2.5. The mean serum half-life was 1.2 hr, rising to 22 hr in those with the poorest creatinine clearances; haemodialysis reduced this prolonged serum half-life to 4–5 hr. Mean urinary excretion after single doses was 75% at 8 hr in those with fairly good renal function, and 3.6% at 24 hr in those with the poorest creatinine clearances.

Antimicrobial activity

Cephalexin is active against most Gram-positive cocci including penicillinase-producing staphylococci; *C. diphtheriae*; Gram-negative cocci, especially *N. gonorrhoeae*; and a range of Gram-negative bacilli including *Esch. coli*, *Proteus mirabilis*, *K. pneumoniae*, *Salmonellae*, *Shigella* and some strains of *H. influenzae* (Foord *et al.*, 1969). It is not active against *Proteus morgani* or *Proteus vulgaris*, which produce a cephalexin-destructive β -lactamase, nor is it active against *Pseudomonas* or *Mycobacteria*.

Therapeutic dose

Cephalexin is available as 250- and 500-mg capsules, which should be given in a dose of 1–4 g daily for a week. It is a large capsule to swallow and has an unpleasant taste, which needs to be disguised by an aperitif of the patient's choice. It is best absorbed from an empty stomach, and the blood level is prolonged by probenecid.

Clinical infections

Urinary tract infections

Faiers, Leigh & Brumfitt (1969) found a 90% cure rate in eighty-nine urinary tract infections, comprising antenatal, hospital or domiciliary infections. Although they were impressed by this overall high-level efficacy, they were deterred by a 35% incidence of side-effects, which included gastro-intestinal symptoms (in nineteen), vulval irritation in eleven and a skin eruption in one patient.

We have found it to be effective in seven of ten (70%) patients with chronic urinary tract infections (Bailey, Walker & James, 1970) but did not find such an alarming incidence of side-effects. Speirs *et al.* (1969) claim an 80% success rate with urinary tract infections, and toxic effects have not been troublesome in their series. However, their subsequent follow-up rate has not been so promising. Richards & O'Grady (1969) likewise noted that the urine was sterilized by the initial course of treatment, but infection recurred within 7 days of withdrawing the drug in 60% of their series.

This may partly be due to the fact that strains of *Esch. coli* change into filamentous forms when treated with cephalixin. Most are dead, but some revert to normal by cultivation in a cephalixin-free liquid medium (Fujii, Konno & Ubukata, 1969).

Gonorrhoea

Cephalixin in a single oral dose of 2 g was well-tolerated and successful in a series of Bradford patients (Oller & Smith, 1969), and was an acceptable alternative when penicillin was contra-indicated in Birmingham (Fowler, 1969).

Respiratory tract infections

In Johannesburg, Seftel *et al.* (1969) obtained an overall cure rate of 80% when cephalixin was given in doses of 1 g 6-hourly for 5–10 days to patients with lobar pneumonia (twenty-five), bronchopneumonia (two), acute or chronic chest disease (six), acute follicular tonsillitis (ten) and tonsillar diphtheria (one).

We have likewise found a good response in twelve of fifteen (80%) patients with lower respiratory tract infections, when using only 500 mg four times daily for 7 days (Bailey *et al.*, 1970).

Toxicity

It is a safe oral antibiotic with a relatively low incidence of side-effects when given in doses of 500 mg four times per 24 hr. Reported side-effects include gastrointestinal symptoms, including sore mouth, and pruritus of pregnancy. Its lack of toxicity makes it a particularly welcome new antibiotic for use in patients with poor renal function (Kabins *et al.*, 1969).

Indications for oral cephalixin

A new oral antibiotic is always welcome in domiciliary practice. Indications for its use are currently as follows:

(1) *Penicillinase-producing staphylococcal infections* in penicillin-allergic individuals, as an alternative to parenteral cephaloridine or instead of erythromycin. Marietti, Carlisle & Saslaw (1969) compared and found cephalixin to be as effective as the semi-synthetic penicillins when given by twice-daily intragastric administration to monkeys with penicillinase-producing staphylococcal septicaemia.

(2) *Streptococcal septicaemia*. The same workers also found intragastric cephalixin to be life-saving when administered to monkeys with haemolytic streptococcal septicaemia.

(3) *Gonorrhoea* which has failed to respond to penicillin or to Septrin, or when the patient is allergic to penicillin and to sulphonamides. In these

circumstances the alternatives are parenteral cephaloridine or kanamycin.

(4) *Chronic urinary tract infections* as an alternative to ampicillin, Septrin, nitrofurantoin, cephaloridine and the tetracyclines. It is active against *Proteus mirabilis*. It is non-toxic in the presence of the poorest renal function (Kabins *et al.*, 1969).

(5) *Gram-negative infections* in general and *Klebsiella pneumoniae* infection in particular, for they are stubborn to treat by all available means.

(6) *Upper respiratory tract infections* including streptococcal sore throat and scarlet fever.

(7) *Lower respiratory tract infections* as an alternative to ampicillin, Septrin and the tetracyclines.

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