Amoxicillin/Clavulanic Acid
An Update of its Antibacterial Activity, Pharmacokinetic Properties and Therapeutic Use

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Summary

Clavulanic acid enhances the antibacterial spectrum of amoxicillin by rendering most \(\beta\)-lactamase-producing isolates susceptible to the drug. In clinical trials amoxicillin/clavulanic acid is clinically and bacteriologically superior to amoxicillin alone and at least as effective as numerous other comparative agents, such as orally administered cephalosporins, cotrimoxazole, doxycycline and bacampicillin, in the treatment of adults and children with the most common forms of infection encountered in general practice, i.e. urinary tract infections, upper and lower respiratory tract infections, otorhinolaryngological infections, and skin and soft tissue infections. It may also provide effective treatment for uncomplicated gonorrhoea, chancroid and gynaecological infections as well as acting as a prophylactic agent against surgical infection.

Thus, in general practice environments where \(\beta\)-lactamase production has restricted the effectiveness of amoxicillin, the combination of clavulanic acid with amoxicillin has clearly extended the usefulness of a tried and proven first-line antibacterial agent.

Clavulanic acid is an irreversible ‘suicide’ inhibitor of intracellular and extracellular \(\beta\)-lactamases, effective against a wide variety of these enzymes including those of Richmond and Sykes classes II to V (but not class I cephalosporinases), staphylococcal \(\beta\)-lactamase, and \(\beta\)-lactamase produced by \textit{Bacteroides fragilis}. Clavulanic acid, therefore, protects amoxicillin from inactivation by many \(\beta\)-lactamases. As a consequence the antibacterial activity of amoxicillin has been restored at a time when the spread of resistance due to \(\beta\)-lactamase production severely threatened its usefulness.

Clavulanic acid alone possesses only weak antibacterial activity, except against \textit{Legionella} spp., and certain strains of \textit{Branhamella catarrhalis}, \textit{B. fragilis} and \textit{Neisseria gonorrhoeae}. However, the addition of clavulanic acid to amoxicillin increases the susceptibility to amoxicillin of amoxicillin-resistant strains of Gram-negative and Gram-positive aerobic and anaerobic bacteria where resistance is caused by \(\beta\)-lactamase production. These include \textit{Staphylococcus aureus} (but not methicillin-resistant strains), \textit{Haemophilus} spp., \textit{Branhamella catarrhalis}, \textit{Neisseria gonorrhoeae}, \textit{Escherichia coli}, \textit{Proteus} spp., \textit{Klebsiella pneumoniae}, \textit{Citrobacter} diversus, \textit{Salmonella} and \textit{Shigella} spp., \textit{Campylobacter jejuni}, \textit{Bacteroides} spp., and \textit{Mycobacterium} spp. The susceptibility of amoxicillin-sensitive strains is not generally affected by the addition of clavulanic acid.

Amoxicillin/clavulanic acid is bactericidal \textit{in vitro}, usually at concentrations no more