patient was deteriorating, amoxicillin with clavulanic acid was given. Clindamycin was the first choice in the case of β-lactam antibiotic allergy. This study investigated whether the described standard treatment regimen was sufficient or if an alternative newer antibiotic such as moxifloxacin was necessary in any case.

The study was performed in the Department of Oral and Maxillofacial Surgery and the Institute for Infection Medicine at the University of Kiel, Germany. The protocol adhered to the ethical tenets of the Declaration of Helsinki. After appropriate informed consent, each subject signed a declaration to confirm accordance to participate.

A total of 517 bacterial strains were isolated from 94 patients with odontogenic abscesses. Ninety-two of 94 abscesses (98%) were polymicrobial. Three hundred and sixteen (61%) of the isolates were aerobes or facultative aerobes, and 201 (39%) of the isolates were anaerobes. The average number of isolates was 5.5 per patient. The most prevalent bacteria were the viridans streptococci group (170 isolates) representing 53.8% of the aerobic/facultative anaerobic bacteria. Prevotella spp. (106 isolates) comprised 52.7% of the strict anaerobes and were the predominant species in that group. Other bacteria identified were present at significantly lower levels. In no patient were any multiresistant strains such as methicillin-resistant Staphylococcus aureus (MRSA) identified (Table 1).

Susceptibility testing revealed that over 98% of the aerobes/facultative aerobes and 95.5% of the anaerobes were susceptible to moxifloxacin in vitro. Amoxicillin with clavulanic was less effective against aerobes and facultative aerobes with 71.2% found to be susceptible, but showed the greatest efficacy against the anaerobes with 99.5% being susceptible. Doxycycline (69.3%/93.5%) and clindamycin (64.2%/97.0%) demonstrated moderate efficacy against the first-named aerobes and facultative aerobes, but good efficacy against the secondary anaerobes. The corresponding values for penicillin were lowest at 62% and 77.6%, respectively. However, it is important to note that penicillin was effective against more than 80% of the viridans streptococci and ~75% of Prevotella spp., which were identified as the dominant strains in oral abscesses.

In the clinical collective, patients with minor abscesses received surgical treatment but no antibiotics (36.4%). Penicillin was administered to 30.4% of the patients. Amoxicillin with clavulanic acid was given in 18.2% and clindamycin in 15.1%. Ninety-two of the 94 patients showed significant recovery with the described treatment. Only two cases required the use of other antibiotics. An advanced antibiotic such as moxifloxacin was not required in any case.

This study demonstrates that penicillin is not the most potent antibiotic against odontogenic abscesses flora in vitro when compared with amoxicillin with clavulanic acid, clindamycin, doxycycline or the modern moxifloxacin. Moxifloxacin proved the most potent in vitro against isolated aerobic bacteria (>98%) and returned good results for anaerobic bacteria (>95%). However, it also does show that the dominant strains of the majority of oral abscesses are still susceptible to traditional penicillin. These observations are in accordance with our clinical experience. We suggest that in addition to adequate surgical abscess drainage, an additional intravenous penicillin regimen is sufficient for the rapid resolution of clinical symptoms in the majority of patients with severe odontogenic abscesses.

Therefore, we still stick to the long-standing ‘grandmother’ penicillin as our antibiotic of first choice in patients with severe odontogenic abscess even though, through the results of in vitro analyses, it would no longer seem to be in vogue.

**Funding**

This study was supported in part (first 30 patients) by Bayer Vital GmbH, Leverkusen, Germany.

**Transparency declarations**

None to declare.

**References**


Journal of Antimicrobial Chemotherapy
doi:10.1093/jac/dkn009
Advance Access publication 31 January 2008

**Potential for underdosing and emergence of resistance in Acinetobacter baumannii during treatment with colistin**

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Keywords: A. baumannii, antibiotic resistance, therapeutic drug monitoring

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Increasing antibiotic resistance in Gram-negative bacteria and continuous narrowing of antimicrobial therapeutic choices are worrying trends. Colistin remains sometimes the only option in the treatment of Acinetobacter baumannii strains with in vitro resistance to most antibiotics including carbapenems, aminoglycosides, fluoroquinolones and glycolcyclines.

In particular, we wish to highlight the potential for underdosing and the associated risk of emergence of resistance, especially when managing certain groups of patients such as those with extensive burns, when an abnormal creatinine clearance as well as features of immunosuppression may be intrinsically present. We illustrate this with our experience of treating infections caused by such multidrug-resistant A. baumannii with the parenteral preparation of colistin, colistimethate sodium (CMS).

A previously healthy 22-year-old lady sustained 80% burns requiring admission to the intensive care unit. During her prolonged hospital stay, the wounds became colonized with an A. baumannii strain susceptible only to colistin. The isolate’s resistance to gentamicin, amikacin, tobramycin, imipenem, meropenem, piperacillin/tazobactam, sulbactam and ciprofloxacin was confirmed by the Antibiotic Resistance Monitoring and Reference Laboratory (ARMRL), Health Protection Agency Centre for Infections, Colindale, London, UK. The MIC of colistin as determined by agar dilution was ≤0.5 mg/L, well within the susceptible range. When the patient became septicemic and A. baumannii was isolated from blood culture, she was prescribed initially 1 million units of CMS (Colomycin®) three times a day; a suboptimal clinical response with persistence of pyrexia, on a background of normal renal function, prompted an increase in the dose to 2 million units three times a day. However, because of new onset of seizures of unknown aetiology, thought to possibly represent neurotoxic side effects, 24 h later the CMS dose was reduced back to 1 million units three times a day.

After an initial clinical improvement and resolution of the acute infective episode, a blood culture collected during a recurrent septic event again grew A. baumannii and thus CMS (Colomycin®) was recommenced at gradually increasing doses from 1 million units twice a day to 1.5 million units three times a day. Pre- and post-dose drug levels measured by bioassay at the Regional Antimicrobial Reference Laboratory (RARL), Bristol, were 3.7 and 5.4 mg/L, respectively (target levels: 4 mg/L). It is known that clinical efficacy usually reduces as the MIC approaches the breakpoint and that isolates with such an MIC may produce subpopulations with an MIC just over the breakpoint. In our case, suboptimal colistin serum concentrations may have contributed to the selection of a population with higher MIC.

When tested by ARMRL, the MIC of colistin for the second isolate was found to have increased to the breakpoint level of 4 mg/L. It is known that clinical efficacy usually reduces as the MIC approaches the breakpoint and that isolates with such an MIC may produce subpopulations with an MIC just over the breakpoint. In our case, suboptimal colistin serum concentrations may have contributed to the selection of a population with higher MIC.

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We have treated with colistin since then several patients (including other burns patients), using a starting dose of 2 million units three times a day if the baseline urea and electrolytes (U&Es) are normal. Pre- and post-dose levels would normally be checked 3–5 days after commencement of therapy; if colistin concentrations are outside the therapeutic range, taking also into consideration the overall clinical picture, doses are adjusted accordingly.

It is our belief that therapeutic drug monitoring may have a role in managing colistin therapy. The British National Formulary (BNF) recommends serum colistin concentration monitoring especially in renal impairment, cystic fibrosis and neonates; the target ‘peak’ plasma concentration (~30 min after intravenous injection or infusion) is 10–15 mg/L (125–200 U/mL), a range with a lower limit even higher than that proposed by the RARL. However, measuring by bioassay the serum level of the active component (colistin) while it co-circulates with its intravenously administered prodrug (CMS) is not straightforward because of uncertainties regarding the rate of both in vivo and in vitro hydrolysis of CMS to colistin. Employing HPLC as an alternative method for determining the concentration of these components may partially but not completely resolve these issues.

Furthermore, there is little information on the pharmacokinetics of colistin at infection sites after intravenous administration and in particular there are no such studies in burns patients. It is generally acknowledged that in this group, an apparently ‘normal’ renal function may in fact conceal an elevated glomerular filtration rate (GFR) which potentially may reflect an accelerated clearance of certain antibiotics. Under these circumstances, it is advisable that such groups of antibiotics are used at least at their maximum recommended dose; preferably drug levels should be monitored.

The ideal dose of intravenous colistin is not clearly established. Although the BNF recommends 1–2 million units every 8 h for adults over 60 kg, some authors advise up to 3 million units every 8 h for life-threatening infections. In our experience, there is a general reluctance among clinicians and Medical Microbiologists to use high doses of colistin because of perceived risk of significant toxicity. However, in a recent review, Falagas and Kasiakou concluded that the incidence of nephrotoxicity in recently published experience with polymixins in general is less common and severe compared with older reports. Furthermore, the neurotoxic side effects are much less common than the nephrotoxic ones, they are usually mild and resolve shortly after therapy is discontinued.

In conclusion, in burns patients we advocate prescribing intravenous colistin at the maximum recommended dose in order to ensure best chance of therapeutic success and prevention of resistance. It is of course mandatory that renal function is taken into account and closely monitored, preferably by measurement of more sensitive parameters such as the GFR. In addition, therapeutic drug monitoring is valuable, especially in critically ill patients, as well as in those in other categories of patients with abnormally high or low drug clearance. Further studies are needed on the pharmacokinetics of CMS and colistin, particularly in burns patients.

Transparency declarations
None to declare.

References

