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1 Elution and antibacterial activity of meropenem from
2 implanted acrylic bone cement

3

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16

17 Sir,

18

19 Meropenem has good tissue penetration and broad-spectrum bactericidal activity. Often
20 employed to treat multi-resistant Gram-negative organisms, meropenem was active against
21 98.7% of 1657 clinical surveillance Enterobacteriaceae isolates collected in the United
22 States in 2005.¹ Its stability permits combination with polymethylmethacrylate (PMMA) bone
23 cement. We present here the first published account of the use of meropenem-loaded
24 PMMA in human prosthetic joint infection.

25

26 The patient, a 66 year-old with insulin-requiring type 2 diabetes, polymyalgia rheumatica
27 (treated with 10mg prednisolone daily) and nodular prurigo, kindly gave written informed
28 consent to publication. She was 170cm tall and weighed 102kg. She had had her left hip
29 replaced for osteoarthritis at another institution in 1996. This prosthesis had functioned
30 excellently for over 10 years before becoming unstable; cup revision in September 2006 was
31 complicated by formation of an infected haematoma. The joint was replaced again in
32 October 2006 and the patient put on a long antibiotic course. Recurrent dislocation led to
33 further socket revision in July 2007. The patient was referred to our specialist hip revision
34 service with continuing instability in late 2008. On 17th February 2009, both components
35 were revised. Seven operative tissue specimens were sterile. Antibiotic prophylaxis was
36 with 48 hours of vancomycin and gentamicin.

37

38 Post-operatively she developed a wound haematoma. The wound started to discharge and
39 she returned to theatre on 10th March for a washout; the components were retained and the
40 wound closed. Five of five tissue specimens grew *Klebsiella pneumoniae* susceptible to co-
41 amoxiclav, cefotaxime, piptazobactam, carbapenems, ciprofloxacin, amikacin and
42 trimethoprim, but resistant to amoxicillin and gentamicin. Intravenous co-amoxiclav 1.2g
43 thrice daily was administered from 10th to 27th March, followed by oral co-amoxiclav 625mg
44 thrice daily until 20th April.

45

46 Infection persisted, and extensive osteomyelitis developed in the proximal femur. A decision
47 was made to proceed to one-stage revision. Both joint components and the proximal femur
48 were replaced on 21st April. One of three acetabular specimens grew *K. pneumoniae*
49 (susceptibilities as above), while two of three grew *Morganella morganii* susceptible to the
50 cephalosporins, piptazobactam, carbapenems, ciprofloxacin, amikacin and gentamicin, and
51 resistant to co-amoxiclav, colistin and trimethoprim. From 24th April through 12th May the
52 patient received 1.2g co-amoxiclav intravenously thrice daily.

53

54 On 12th May, a large abscess connected superficial and deep tissues. This was washed out.
55 The acetabular component was removed. 10g meropenem was crushed in a sterile vacuum
56 mixing bowl (Optivac® Fusion™, Biomet, Bridgend); two 40g mixes of sterile orthopaedic
57 bone cement (Palacos, Biomet; each mix containing 1.8g gentamicin and 1.8g clindamycin
58 preloaded by the manufacturer) were added. The resulting cement was used to fix the
59 replacement acetabular prosthesis. A third cement mix combined with 5g meropenem was
60 used to coat the stem. Intravenous meropenem and amikacin and serial vac dressings were
61 initiated. Samples of pus, fluid and hip tissue each grew scant *K. pneumoniae* susceptible to
62 ciprofloxacin, cephalosporins, ertapenem and meropenem but resistant to co-amoxiclav,
63 piptazobactam, gentamicin and amikacin.

64

65 On 13th May, drain fluid was collected. An ISO susceptibility test agar plate was seeded with
66 the patient's *K. pneumoniae* isolate; a second plate was seeded with fully susceptible
67 *Escherichia coli* strain ATCC 25922. 20µL of drain fluid was placed at the centre of each
68 plate. Plates were incubated aerobically at 36°C for 18 hours. Inhibition zones suggested
69 that antibacterial activity in the vicinity of the prosthesis was sufficient to inhibit growth of the
70 patient's *K. pneumoniae* (and therefore also her more susceptible *M. morganii*).

71

72 An aliquot of 13th May drain fluid was sent to the UK Antimicrobial Reference Laboratory,
73 Bristol, where its meropenem concentration was measured (by high performance liquid
74 chromatography) at 73.5mg/L. Drug levels in pre- and post-meropenem-dose serum
75 samples (also collected on 13th May) were considerably lower (9.3mg/L and 12.5mg/L
76 respectively), suggesting that meropenem was eluting from the cement. The accepted
77 meropenem susceptibility breakpoint is 4mg/L.²

78

79 The patient received intravenous meropenem 1g thrice daily until 30th July, with intravenous
80 amikacin 1g daily for the first two postoperative weeks. By 30th July, she was well and
81 mobilising, and was discharged home off antibiotics.

82

83 Antibiotic loading of PMMA is routine practice in joints with suspected or proven infection.
84 The aim is to achieve high antibiotic levels at the site of infection while minimising systemic
85 toxicity. The antibiotic used must be heat stable (since cement polymerisation is strongly
86 exothermic) and water soluble (to allow diffusion from cement to tissues). The most
87 common antibiotics used are gentamicin, vancomycin, and cefazolin, either alone or in
88 combination.³ Unfortunately, this patient's *Klebsiella* isolate was gentamicin-resistant,
89 cefazolin is not available in the UK, and other cephalosporins are not heat stable. Previous
90 studies have suggested that meropenem elutes from small PMMA discs *in vitro*,⁴⁻⁵ but the
91 present report is the first to provide useful *in vivo* data. Meropenem should be considered
92 for inclusion in bone cement in patients with difficult-to-treat prosthetic joint infections.

93

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97

98 **Transparency declarations**

99 None to declare.

100

101 **References**

- 102 1. Rhomberg PR, Jones RN. Contemporary activity of meropenem and comparator
103 broad-spectrum agents: MYSTIC program report from the United States component (2005).
104 *Diagn Microbiol Infect Dis* 2007; **57**: 207-15.
- 105 2. Clinical and Laboratory Standards Institute. *Performance standards for antimicrobial*
106 *susceptibility testing: 16th informational supplement (M100-S16)*. Wayne, PA: CLSI, 2006.
- 107 3. Cui Q, Mihalko WM, Shields JS et al. Antibiotic-impregnated cement spacers for the
108 treatment of infection associated with total hip or knee arthroplasty. *J Bone Joint Surg Am*
109 2007; **89**: 871-82.
- 110 4. Andollina A, Bertoni G, Zolezzi C et al. Vancomycin and meropenem in acrylic
111 cement: elution kinetics of in vitro bactericidal action. *Chir Organi Mov* 2008; **91**: 153-8.
- 112 5. Baleani M, Persson C, Zolezzi C et al. Biological and biomechanical effects of
113 vancomycin and meropenem in acrylic bone cement. *J Arthroplasty* 2008; **23**: 1232-8.

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