

Accepted Manuscript

Title: Ertapenem: Lack of Allergic Reactions in Hospitalised Adults Reporting a History of Penicillin Aallergy

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PII: S0924-8579(13)00316-6

DOI: <http://dx.doi.org/doi:10.1016/j.ijantimicag.2013.08.015>

Reference: ANTAGE 4184



To appear in: *International Journal of Antimicrobial Agents*

Received date: 8-8-2013

Revised date: 27-8-2013

Accepted date: 28-8-2013

Please cite this article as: Cunha BA, Jose A, Hage J, Ertapenem: Lack of Allergic Reactions in Hospitalised Adults Reporting a History of Penicillin Aallergy, *International Journal of Antimicrobial Agents* (2013), <http://dx.doi.org/10.1016/j.ijantimicag.2013.08.015>

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Ertapenem: lack of allergic reactions in hospitalised adults reporting a history of penicillin allergy

Sir,

A common problem in clinical practice is antibiotic selection in patients with a history of penicillin allergy. When cephalosporins were introduced, there was concern regarding penicillin cross-reactivity. For decades, cephalosporins have been safely used in patients with a history of non-anaphylactic reactions, e.g. drug fever and drug rash, to penicillins. Those manifesting allergic reactions to β -lactams experience the same type of reaction with repeated exposures. Structurally, carbapenems are β -lactams, but they differ from β -lactams in their resistance and allergic potential [1,2]. The first carbapenem introduced for widespread use was imipenem/cilastatin, which was widely used with very few allergic reactions (1–3%). The rate of penicillin allergy is difficult to assess in the general population and estimates are usually based on patient surveys or skin testing. Negative skin testing is not always predictive of immediate hypersensitivity reactions [2]. Carbapenems remain an important addition to the infectious diseases armamentarium. Carbapenems are often needed for empirical therapy in critical care settings where skin testing is rarely available on an urgent/around-the-clock basis. Imipenem/cilastatin has been largely replaced by meropenem [2]. It has also been shown that in the rare patient with a penicillin allergic reaction to imipenem/cilastatin, meropenem has been used without incident, which has also been our experience [3].

For years, meropenem has been a mainstay of empirical therapy for serious systemic infections worldwide [1]. Meropenem studies have shown that the incidence of allergic side effects is 0.1% [4]. Furthermore, the largest clinical study on meropenem allergic reactions in 110 patients who reported a history of penicillin allergy (59 with non-anaphylactic reactions and 51 with anaphylactic reactions) has been previously published. The 110 adults reporting a history of either anaphylactic or non-anaphylactic penicillin allergy were given meropenem without an initial test dose or skin testing. Most importantly, none of the 51 patients reporting anaphylactic penicillin reactions had any reaction to meropenem [5].

Ertapenem has become a useful alternative to meropenem in intra-abdominal/soft tissue/bone infections where vancomycin-resistant enterococci or antipseudomonal coverage is not needed. When ertapenem was released, as previously with meropenem, there were concerns about ertapenem cross-reactivity in patients reporting a history of penicillin allergic reactions. We are aware of no published clinical studies on ertapenem in those reporting a history of penicillin allergy. Based on our meropenem experience, it has been our practice to give ertapenem to adult patients reporting a history of non-anaphylactic or anaphylactic reactions to penicillin without a test dose or skin testing. Over the years we have had no allergic reactions to ertapenem. We wanted to report a sample of our experience over a 6-month period. Patients receiving ertapenem plus other antibiotics were excluded. During a 6-month period, 42 patients with a history of penicillin allergy were prospectively treated with ertapenem monotherapy for 1–42 days (mean 8.3 days). None of the 24 patients in the non-

anaphylactic group who received ertapenem monotherapy had any allergic reactions. More importantly, none of the 18 patients reporting history of anaphylactic reactions to penicillin had any reaction to ertapenem (Table 1).

We conclude that although our 6-month data set is small, it is reflective of our considerable non-reported experience over the past few years, i.e. no allergic reactions with ertapenem monotherapy in patients reporting a history of penicillin allergy. These are the only existing data on ertapenem in adult patients reporting a history of penicillin allergy. Our past and ongoing experience suggests that clinicians can use ertapenem monotherapy without a test dose or skin testing, even in those reporting a history of anaphylactic reactions to penicillin.

Funding: None.

Competing interests: None declared.

Ethical approval: Not required.

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Table 1

Ertapenem use in adults with a history of penicillin allergy

Patient No.	Age (years)	Sex	History of penicillin allergy	Clinical infection	Ertapenem dose	Ertapenem days
Patients with a history of penicillin allergy and anaphylactic reactions ^a						
1	60	F	Angioedema	Cellulitis	1 g (i.v.) q24h	5
2	61	M	Angioedema	Cellulitis	1 g (i.v.) q24h	5
3	73	M	Angioedema	Diverticular abscess	1 g (i.v.) q24h	27
4	48	M	Laryngospasm	Osteomyelitis	1 g (i.v.) q24h	42
5	59	M	Angioedema	Cellulitis	1 g (i.v.) q24h	7
6	74	F	Hives	Cellulitis	1 g (i.v.) q24h	10
7	56	M	Hives	UTI	1 g (i.v.) q24h	14
8	56	F	Hives	Pneumonia	1 g (i.v.) q24h	2
9	49	F	Hives	Osteomyelitis	1 g (i.v.) q24h	42
10	41	F	Hives	Abscess	1 g (i.v.) q24h	1
11	65	M	Hives	Cellulitis	1 g (i.v.) q24h	4
12	89	M	Hives	Cellulitis	1 g (i.v.) q24h	2

13	82	F	Hives	Cellulitis	1 g (i.v.) q24h	3
14	66	M	Hives	Osteomyelitis	1 g (i.v.) q24h	9
15	80	M	Hives	Pneumonia	500 mg (i.v.) q24h b	2
16	92	M	Hives	Pneumonia	1 g (i.v.) q24h	5
17	56	F	Hives	Osteomyelitis	1 g (i.v.) q24h	3
18	87	F	Urticaria	Cellulitis	1 g (i.v.) q24h	4
Patients with a history of penicillin allergy: non-anaphylactic reactions						
1	83	M	Rash	UTI	1 g (i.v.) q24h	3
2	49	F	Rash	Osteomyelitis	1 g (i.v.) q24h	42
3	42	F	Unknown	Cellulitis	1 g (i.v.) q24h	2
4	64	F	Unknown	Cellulitis	1 g (i.v.) q24h	12
5	84	F	Rash	Cellulitis	1 g (i.v.) q24h	2
6	38	M	Rash	Wound infection	1 g (i.v.) q24h	6
7	87	F	Unknown	UTI	1 g (i.v.) q24h	10
8	87	F	Rash	Cellulitis	1 g (i.v.) q24h	7

9	77	F	Rash	Cellulitis	1 g (i.v.) q24h	9
10	65	F	Rash	Cellulitis	1 g (i.v.) q24h	1
11	26	M	Unknown	Dental abscess	1 g (i.v.) q24h	4
12	82	M	Unknown	Cellulitis	1 g (i.v.) q24h	1
13	83	M	Unknown	Pneumonia	1 g (i.v.) q24h	8
14	75	F	Pruritus	Diverticulitis	1 g (i.v.) q24h	6
15	88	M	Unknown	Cellulitis	1 g (i.v.) q24h	1
16	58	M	Unknown	Pneumonia	1 g (i.v.) q24h	6
17	89	F	Unknown	Osteomyelitis	1 g (i.v.) q24h	5
18	78	F	Unknown	Osteomyelitis	1 g (i.v.) q24h	4
19	39	F	Rash	Wound infection	1 g (i.v.) q24h	3
20	47	F	Unknown	Diabetic foot ulcer	1 g (i.v.) q24h	5
21	71	F	Rash	Intra- abdominal abscesses	1 g (i.v.) q24h	6
22	84	M	Rash	Bronchitis	1 g (i.v.) q24h	2

23	70	F	Unknown	UTI	500 mg (i.v.) q24h ^b	13
24	77	F	Rash	Colitis	1 g (i.v.) q24h	5

i.v., intravenous; q24h, every 24 h; UTI, urinary tract infection.

^a Anaphylactic reaction defined as hypotension, bronchospasm, laryngospasm and acute/severe total body hives/urticaria.

^b Dose adjusted for creatinine clearance of 25 mL/min.