Penicillin G treatment in infective endocarditis patients – does standars dosing result in therapeutic plasma concentrations?

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Background

Infective endocarditis (IE) results from bacterial or fungal infection of the endocardial heart surfaces and is associated with significant mortality and morbidity. The majority of IE is caused by *streptococci*, *staphylococci* and *enterococci* which are often treated with β-lactam antibiotics, e.g. Penicillin G. For Penicillin G, *f* T>MIC of 40-50% is associated with maximum efficacy as well as resistance suppression. The aim of this study was to determine if Penicillin G 3 grams (g) every 6 hour (q6h) results in therapeutic plasma-concentrations in patients with IE and to assess possible factors that influence inter- and intra-individual variability.

Materials and Methods

Patients diagnosed with IE, who were treated with intravenously Penicillin G, had plasma (p) concentrations determined once weekly, using ultra high performance liquid chromatography. Each patient had two blood samples drawn during a single dosing interval; one sample halfway through the dosing interval (sample A), and one sample at the end of the dosing interval, prior to the next dose (sample B). Penicillin G p-concentrations were interpretated in relation to the known MIC of the microorganism isolated in the blood cultures. A random coefficient model (RCM) was developed to describe the variation in Penicillin G concentration over time.

Table 1. Microorganisms cultured in blood (n = 44)

Microorganism	n (%)	MIC* (range)
Staphylococci	8 (18%)	(0.012 - 0.23)
Streptococci	28 (62%)	(0.016 - 0.25)
Enterococci	7 (16%)	(1 - 8)
Propionibacterum acnes	2 (4%)	(0.016)

*mg/L

Results

46 patients were included in the study. Penicillin G p-concentrations varied considerably between patients and the variation over time was significantly correlated with age, weight, estimated creatinine clearance (eCLcr) and p-albumine (Figure 1). 98% of the patients had Penicillin G p-concentrations that resulted in PK/PD target achievement for blood sample A the first week of treatment (50% *f*T>MIC). 73% of the patients had Penicillin G p-concentrations that resulted in PK/PD target achievement for blood sample B the first week of treatment (100% *f*T>MIC) (Figure 2). The majority of patients who did not achieve pre-defined PK/PD targets had *enterococci* isolated in blood cultures.

Figure 1. Regression coefficients for log p-Penicillin G concentrations versus days plotted against age (a); estimated creatinine clearance (eCLcr) (b); albumin (c); and weight (d).

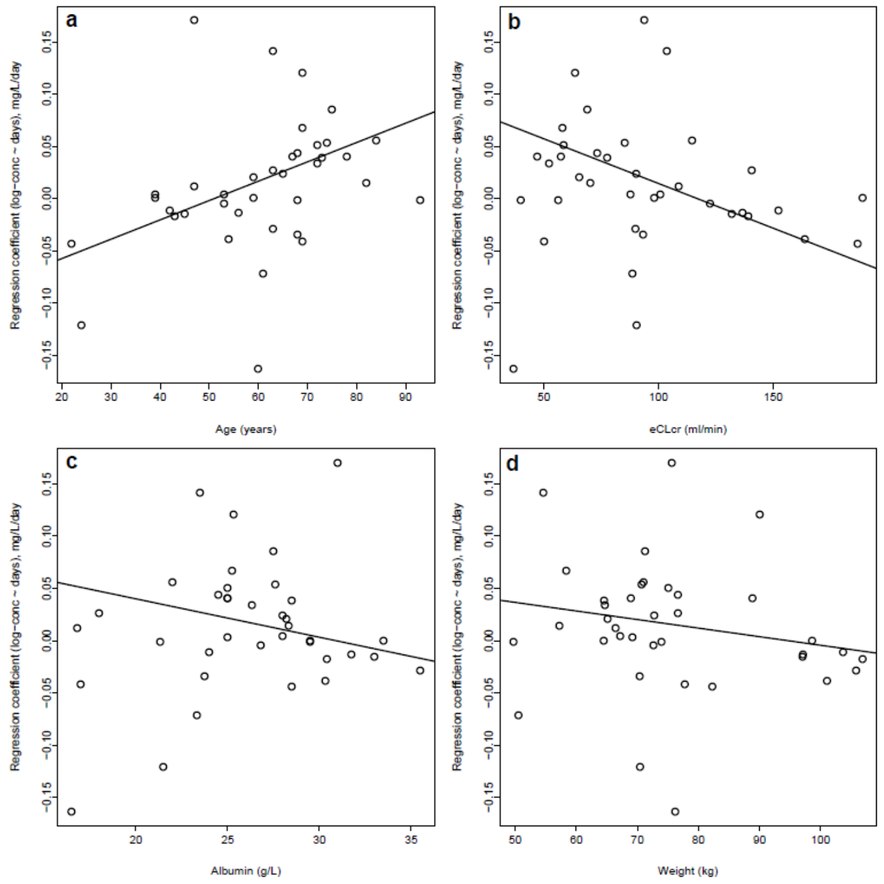
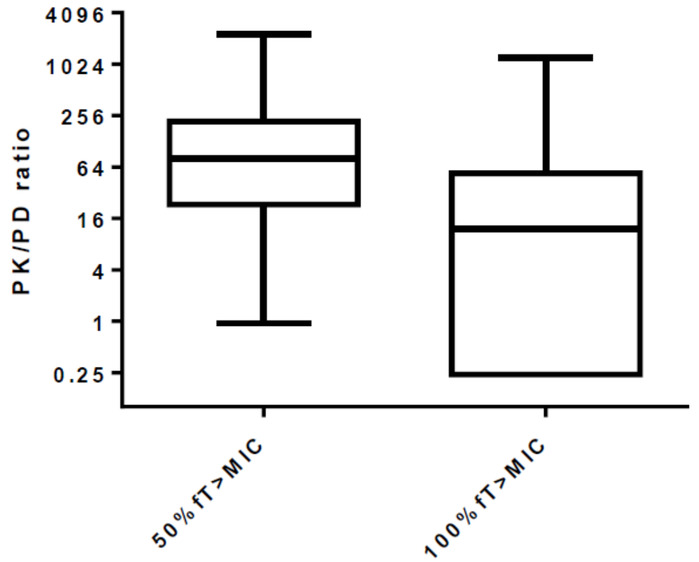


Figure 2. A ratio ≥ 1 means the PK/PD target was achieved.



Conclusions

- Penicillin p-concentrations vary considerably in IE patients and are associated with age, weight, eCLcr and p-albumine.
- In patients with IE caused by streptococci and staphylococci, penicillin 3g q6h results in therapeutic concentrations far above PK/PD targets commonly used.
- For microorganisms with a MIC above 1 mg/L, such as enterococci, Penicillin G 3g q6h may result in subtherapeutic concentrations.

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