Protein binding of temocillin is lower in plasma from patients in intensive care units compared to healthy subjects: in vitro and in vivo studies

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Background and Aims

Only the unbound concentration of β-lactam antibiotics is considered as potentially active (capable of binding to the bacterial target) [1]. Therapeutic drug monitoring, however, generally measures total plasma concentrations only [2], and extrapolates unbound concentrations from SMPC data that are most often obtained in healthy subjects. In the companion poster (P2220), we study the pharmacokinetics of temocillin (TMO) in healthy volunteers. We show that protein binding is high in this population, as also reported in the SmPC of the product [3].

The present study aims at comparing the protein binding of temocillin in plasma from healthy subjects and critically-ill patients (hospitalized in ICU).

Materials & Methods

- **In-vitro**: Plasma samples from 8 healthy donors (HD) and 10 critically-ill patients donors (PD) spiked with temocillin (8 to 350 mg/L) and incubated for 30 minutes at 37°C.
- **In-vivo**: Plasma samples were collected over 12 h from 8 healthy volunteers (HV) having received 2 g of temocillin as IV infusion over 40 min.

**Protein binding of TMO is measured by HPLC-MS/MS**:

- **In-vitro study**: Plasma samples from 8 healthy donors (HD) and 10 critically-ill patients donors (PD) spiked with temocillin (8 to 350 mg/L) and incubated for 30 minutes at 37°C.

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**Protein concentrations were determined by HPLC-MS/MS for TMO**:

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This study was approved by the ethical committee of the Medisch Universitair Vlaanderen (Ectra 2015-003457-18) and of the cliniques universitaires St Luc, Brussels (B4301216S2939; NCT03440216).

**References**


**Discussion and Conclusions**

We confirm the high plasma protein binding of temocillin but show that it is lower and weaker in vivo (lower binding capacity and affinity) for samples from critically-ill patients than from healthy people.

The reasons for reduced binding in patients' samples probably include lower protein concentration (reducing Bmax) and displacement from binding sites by co-administered drugs (increasing Ki).

A further challenge is similar in vitro and in vivo for healthy people, in vitro testing may be a useful tool to evaluate drug protein binding if using plasma samples from the appropriate population (to be verified with samples from critically-ill patients).

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