Use of therapeutic drug monitoring for continuous ampicillin therapy of critically ill patients Weber L[1], Stephani C[2], Wieditz J[2,3]., Streit F[4], Scheithauer S[5], Moerer O[2]

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Background: Therapeutic drug monitoring (TDM) of beta-lactam antibiotics is recommended to account for pharmacokinetic variability particularly in critical illness. However, the impact of TDM-guided dosing on clinical outcomes remains unknown. Systematic reviews and meta-analyses of TDM-guided dosing call for further studies to better assess the benefit of beta-lactam TDM in critically ill patients.

Methods: Ampicillin plasma levels (collected three times a week around 5 am) of patients who were treated for various serious illnesses in the anesthesiological-surgical intensive care unit of the University Hospital Göttingen (UMG) between 2015 and 2022 were retrospectively evaluated. The parenteral administration of ampicillin was initially always carried out continuously after a short infusion of 2 g ampicillin with 1 g sulbactam (primary standard daily dose 9 g ampicillin/sulbactam). Plasma levels between 30 and 60 mg/l were considered to be in the therapeutic range. Doses were adjusted according to TDM results analyzed with a Multiparametric Antibiotic LCMS-Assay on CLAM2030-LCMS8050 (Shimadzu Corporation).

Results: We analyzed data of 225 patients, who had been treated with ampicillin/sulbactam and monitored with 466 ampicillin plasma-level measurements. With regular dose adjustments based on plasma-level values the percentage of those ampicillin plasma-levels that were within the therapeutic range increased over the course of therapy from 30% (n=206) at the first to 70% (n=15) at the fifth consecutive sampling, with subtherapeutic values constantly declining accordingly, while the percentage of supratherapeutic dosing remained unchanged until the fourth measurement.

Conclusions: Our data demonstrate that TDM helps in achieving therapeutic plasma levels in continuous ampicillin therapy of critically ill patients. Further studies need to assess if this indeed benefits clinical outcome.

Key Words: ampicillin; therapeutic drug monitoring; drug concentration; critical illness.