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Pharmacokinetics and pharmacodynamics of linezolid on Staphylococcus aureus using a dynamic in vitro hollow fiber infection model.

M. Dominique*(1), N.Prébonnaud(2), A.Chauzy(3), S.Marchand(2), C.Dahyot fizelier(1)

(1) Anesthésie Réanimation, CHU de Poitiers, Poitiers, France , (2) Laboratoire de Pharmacocinétique et toxicologie, CHU de Poitiers, Poitiers, France , (3) Université de Poitiers, Inserm, Poitiers, France

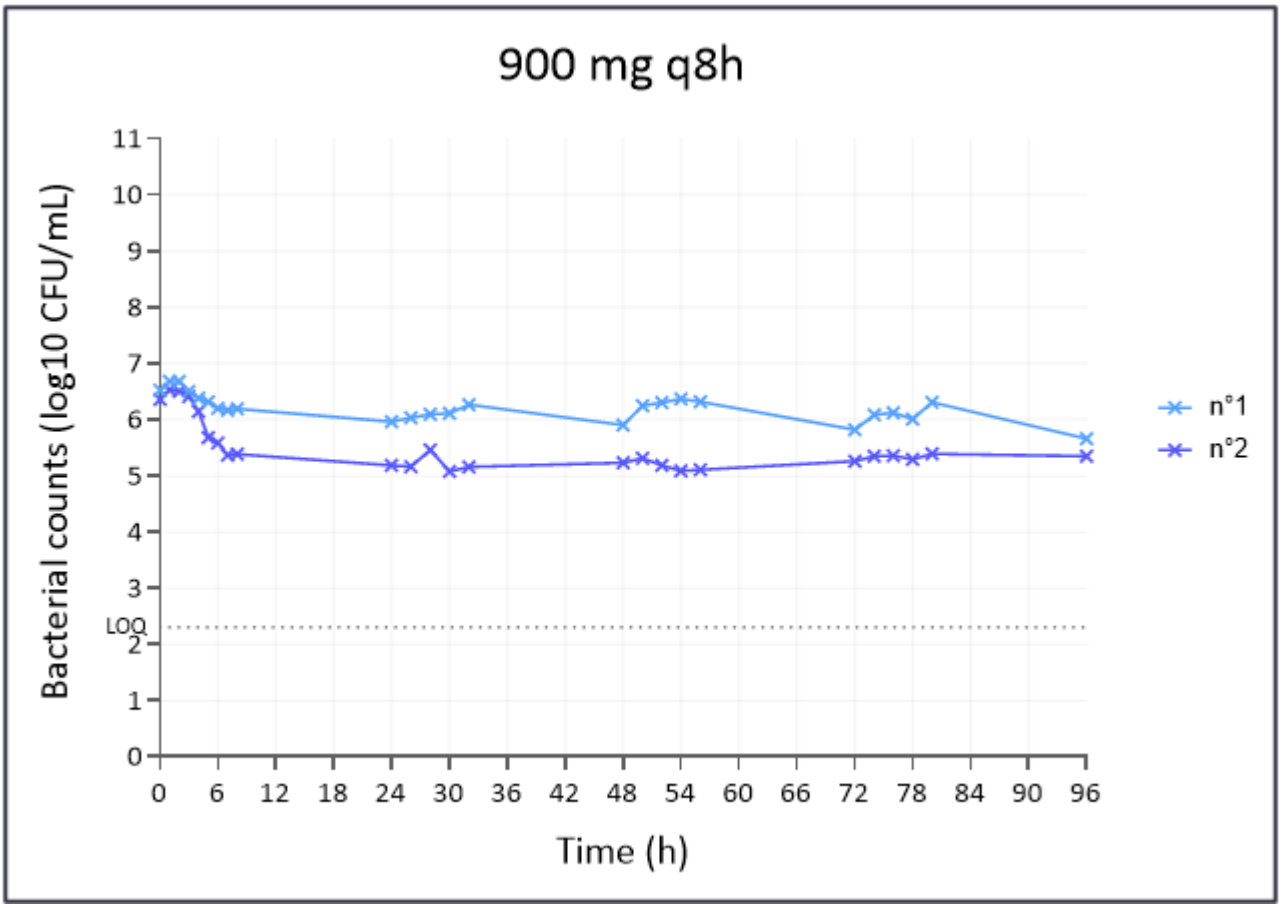
**Auteur présenté comme orateur*

Position du problème et objectif(s) de l'étude:
Infectious complications associated with external ventricular drainage are of bad prognosis. Linezolid (LNZ) is a treatment option. However, the PHRC "PK-POP LCR" showed that probability of reaching the target in the cerebrospinal fluid (CSF) (AUC/CMI>100) was insufficient at usual dosing regimen for LNZ. The objective was to perform a pharmacokinetic/pharmacodynamic (PKPD) evaluation of LNZ on meticillin-susceptible Staphylococcus aureus (MSSA) in vitro hollow fiber infection model (HFIM).

Matériel et méthodes:
A population PK model of LNZ, previously developed in ICU infected patients (PHRCN 16-0501), was first used to simulate LNZ concentrations in plasma and CSF after administration of different dosing regimens (600 mg q12h, 900 mg q12 h and 900 mg q8h). These PK profiles were then reproduced in a dynamic HFIM (n=3) over 96h to evaluate LNZ efficacy against a MSSA strain (ATCC29213, MIC = 4 mg/L) at an inoculum of 106 CFU/mL in Mueller Hinton broth. Serial samples were collected throughout the experiments to quantify the bacteria over time

Résultats & Discussion:
In HFIM experiments, using plasma or CSF concentrations as PK input showed a similar PD effect. After a short stationary phase, regrowth was observed respectively at 6h and 24h for 600 mg q12 h and 900 mg q12h, both reaching bacterial counts around 108-1010 CFU/mL at 96h. At 900 mg q8h, the bacterial growth kept stationary throughout the experiment (about 106 CFU/mL).

Conclusion:
LNZ at 600 mg q12h, had a transient and limited efficacy on MSSA. Increasing the dose showed a limited improvement, even at 900 mg q8h where the bacterial counts remained stationary around the inoculum value throughout the experiment. However, experiments were carried in MHB a rich medium favorable for bacterial growth. These experiments are going to be reproduced in artificial CSF to be closer to in vivo conditions



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