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Optimization of beta-lactam antibiotics exposure in pediatric intensive care unit: protocolization of continuous infusion

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Position du problème et objectif(s) de l'étude:
Beta-lactam continuous infusion (BLCI) is currently recommended in adult intensive care units to achieve target concentrations (TC). In children, a few studies suggest the value of BLCI to achieve TC and BLCI was protocolized in pediatric intensive care unit (PICU) of our hospital in February 2022. The objective of this study was to determine the impact of BLCI on the achievement of TC, the length of hospitalization (LH), and duration of antibiotic treatment (DA) in PICU population.

Matériel et méthodes:
A monocentric retrospective study was conducted in PICU, concerned children with beta-lactam treatment greater than 2 days and at least one sample for therapeutic drug monitoring (TDM). From January 2018 to February 2022 (P1), beta-lactam were administrated in discontinuous infusion with TDM upon clinical pharmacist request. From February to September 2022 (P2), BLCI were mostly used and TDM were performed at day 1 and after dosage adjustment. The data collected included demographic, clinical, biological, pharmacological, and antibiotic treatment prescriptions. The primary endpoint concerned the achievement of 4 times the minimum inhibitory concentration (MIC); the secondary endpoint concerned clinical impact of BLCI. Differences between the two dosing regimens were tested using the Student t test and the Chi2 test. Linear mixed models with random intercepts and subjects were used to explore the association between clinical and biological parameters and achievement of TC or LH or DA.

Résultats & Discussion:
Populations from both periods were comparable: sex ratio 1.38, ages from 0 to 19 years, and mean weight of 13,04 kg (standard deviation (SD): 17,4 kg). In P1, 214 assays involved 103 patients; in P2, 199 assays involved 72 patients. 48 samples were uninterpretable (P1=17.3%, P2=5.5%, $p<0.001$) and excluded from the primary endpoint. In P2 more samples were higher than 4 times MIC (P1=29.14% vs P2=73.68, $p<0.001$), and less samples were lower than 4 times MIC (P1=70.86% vs P2=26.32%, $p<0.001$). BLCI was associated with decreased LH: 38 vs 19.6 days (SD: P1=41.9, P2=16.2; $p<0.001$). BLCI reduced DA: 12 vs 8 days (SD: P1=7.27, P2=6.71; $p<0.001$). Moreover, BLCI was associated with a greater decrease in c-reactive protein between day 1 and day 5/6 after initiation of the antibiotic (P1=7.38 mg/ml vs P2= 52.85 mg/ml; $p<0.001$). The multivariate model confirmed the impact of BLCI on TC ($p<0.001$), LH ($p<0.001$) and DA($p<0.001$).

Conclusion:
BLCI in PICU significantly achieved TC, decreased LH by about half, reduce DA, and CRP at day 5/6. These results encourage the maintenance of BLCI in PICU and should be confirmed by a prospective randomized study.

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