Vancomycin adsorption during *in vitro* model of hemoperfusion with mini-module of HA380 cartridge

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Background

Septic shock is one of the most frequent causes in Intensive Care Unit (ICU) admission and is related to a very high risk of mortality. About one third of patients with sepsis develops AKI which contributes to a worsening prognosis. AKI due to sepsis is the result of a dysregulated host immune response to infection, with the production of inflammatory mediators and cytokines that cause haemodynamic alterations, endothelial damage, apoptosis and, finally, immunoparalysis. The new Jafron HA380 cartridge has been specifically designed for use in clinical conditions characterized by cytokine storm such as sepsis. Given the growing application of these devices in cases of septic AKI in ICU, an unsolved problem is whether these polymers adsorb drugs, including antibiotics. In vitro experiments were conducted to determine its adsorption capacity towards Vancomycin antibiotic and to establish possible strategies to maintain effective plasma level in critically ill patients undergoing extracorporeal therapies.

Methods

In vitro circulation was performed using a dedicated testing platform Galileo and a scaled closed-loop hemoperfusion (HP) circuit set-up. A customized cartridge was built assembling mini-module components scaled in dimension towards HA380 and filled with 75 g of HA380 beads (25% of the regular size content). In vitro experiments with incremental concentrations of vancomycin in the test solution were carried out in a recirculation circuit until sorbent saturation was observed. Samples were collected every 20 minutes from the reservoir.
Removal ratio (RR) was calculated as the concentration reduction compared to baseline in percentage.
The Langmuir isotherm model has been applied:

$$\eta_{end} = \frac{Q_0 \cdot b \cdot m_o}{1 + b \cdot m_0}$$

where Q_0 and b are always constants, m_0 represents the initial amount of Vancomycin load (mg) and η_{end} is the final load adsorbed onto the solid beads (mg/g).

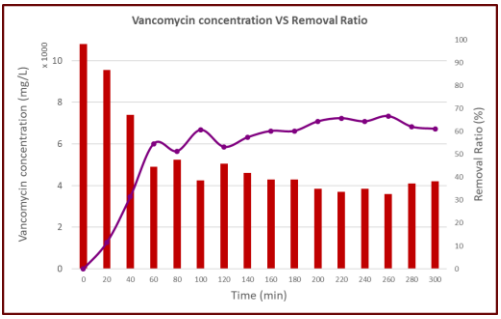

Figure 1. *Vancomycin concentrations decrease (vertical bars) compared to the Removal Ratio curve (data referred to 10 g of Vancomycin in 1 L of saline solution).*

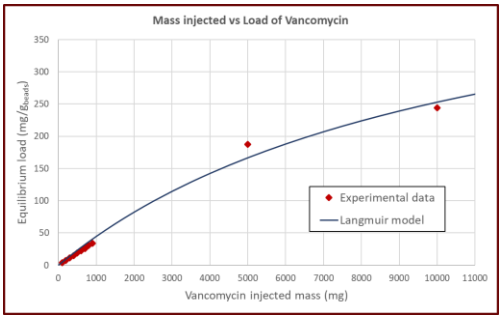

Figure 2. Vancomycin on solid beads adsorption experimental data and best fit with a Langmuir isotherm.

Results

In vitro circulation confirms the affinity of beads material in binding Vancomycin molecules. The kinetics of vancomycin adsorption shows a rapid decay of the concentration in the first part of the experiments, after this period the curve became flat and the adsorption phenomenon negligible. In the experiment with 10 g, after 60 minutes of rapid adsorption (RR=55%), the curve reached a plateau converging to a RR higher than 60%. The sorbent beads were able to bind 6.1 g towards 10 g injected. In different experiments with various concentration of vancomycin, a maximum amount of 244mg/g of sorbent was adsorbed. The kinetics appears to be governed by a Langmuir-like isotherm with maximal removal speed in the early minutes and a plateau after 60 minutes.

Conclusions

HA380 adsorbs significant amounts of vancomycin. Adjusting the achieved results with the experimental minimodule to a full-scale cartridge, a total of 25grams of antibiotic can be removed. This might have affected outcome results in clinical trials. This suggests to prescribe administration to critically ill patients requiring HP, immediately after or in the inter-session time window. In case of administration during HP, adequate adjustment and plasma level monitoring is strongly recommended.

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