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 hemodynamic alterations, endothelial damage, apoptosis and 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 do not also adsorb drugs, including antibiotics, in particular those whose blood concentration must be kept constant over time to be effective.
The purpose of the study is to determine, *in vitro*, the amount of vancomycin necessary to saturate all bonds available within the Jafron HA380 adsorbent cartridge.

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). 500 ml of saline solution spiked with different amount of Vancomycin were circulated.
Repeated boluses of 100mg of Vancomycin were administered in the saline solution reservoir. Samples were collected after 5 min of Vancomycin equilibration (no circulation) and then after 20 min of HP to determine the adsorption of each dose.
Secondly, we performed two circulation containing extremely high quantity of Vancomycin (5,000 mg in 500ml and 10,000 mg in 1000ml) for 300 minutes. Samples were collected every 20 minutes.
Removal ratio (RR) was calculated as the concentration reduction compared to baseline in percentage.

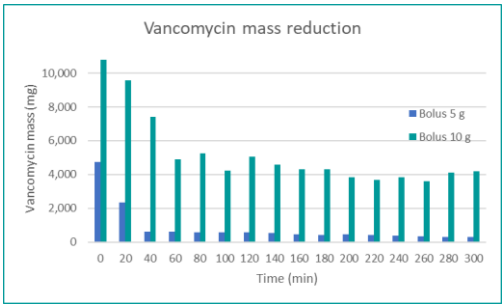

Figure 1. *Vancomycin mass variation in the reservoir during HP simulation with HA380 mini-modules. Circulating solutions were enriched with 5,000 mg and 10,000 mg of Vancomycin.*

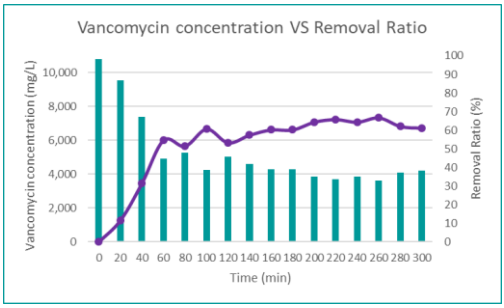

Figure 2. *Vancomycin concentrations decrease (vertical bars) compared to the Removal Ratio curve (data referred to 10 g of Vancomycin in 1 L of saline solution).*

Results

A total amount of 700 mg and 900 mg of Vancomycin was injected in two different experiments with repeated boluses of 100 mg. At the end of the two experiments the total masses adsorbed were 650 mg on 700 mg and 840 mg on 900 mg, the RRs were 92% and 94%, respectively.
In the second experimental approach, 4,500 mg of the 5,000 mg were adsorbed in the end of the experiment (RR=94%). In the experiment with 10,000 mg, 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 6,100 mg towards 10,000 mg injected, on average. This amount saturated the mini-module binding sites.

Conclusions

The application of HA380 mini-modules allowed to determine the amount of Vancomycin necessary to reach the saturation of the sorbent material. Based on the obtained results, we estimated that the cartridge HA380 could retain more than 24 g of Vancomycin during HP circulation. Further investigation is needed to validate our results and to better understand HA380 performance in clinical practice.

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