# Preliminary results of antibiotics pharmacokinetics in critically ill children with septic shock treated with CKRT and Cytosorb hemoperfusion

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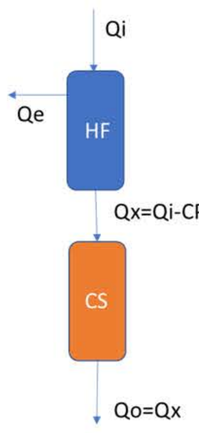
## BACKGROUND

Extracorporeal hemadsorption (HA) techniques are increasingly used as adjuvant therapeutic strategies in septic shock with severe hyperinflammatory response. Although treatment seems to be most effective to remove pro-inflammatory mediators, its influence on antimicrobials pharmacokinetic should not neglect with potentially clinical impact. In addition, critically ill children and newborn have different drugs pharmacokinetics than adults, due to different volume distribution and body composition, furthermore using cartridge with high priming volume can expose pediatric patients to unsuccessfully therapies. We report preliminary results the impact of Cytosorb pharmacokinetics of different antibacterial agents commonly used in pediatric patients.

## METHODS

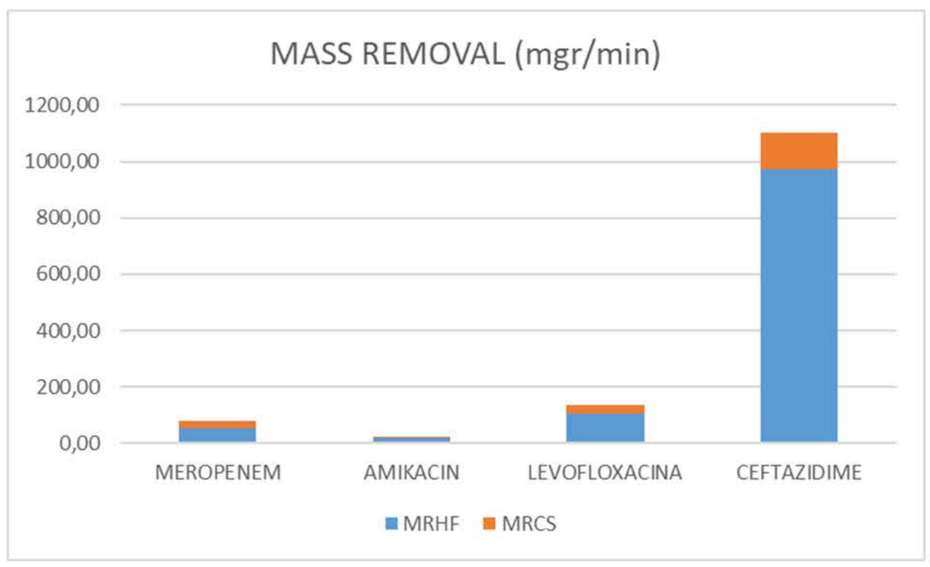
We performed therapeutic drug monitoring in 5 critically ill children with septic shock. treated with CKRT and Cytosorb in post-hemofilter position. Three molecules (**Meropenem, Levofloxacin, Ceftazidime**) with a time dependent mechanism of action were tested at trough for 3 consecutive days by the start of the hemoperfusion and 1 molecule (**Amikacine**) with concentration dependent mechanism of action was tested at peak and trough for 2 consecutive days by the start of the hemoperfusion. Drugs concentrations were monitored in 4 sites: pre-hemofilter ($P_{PRE}$), post-hemofilter ($P_{POST}$), post-cartridge ($P_{CY}$) and in the waste bag ($P_{EFF}$).

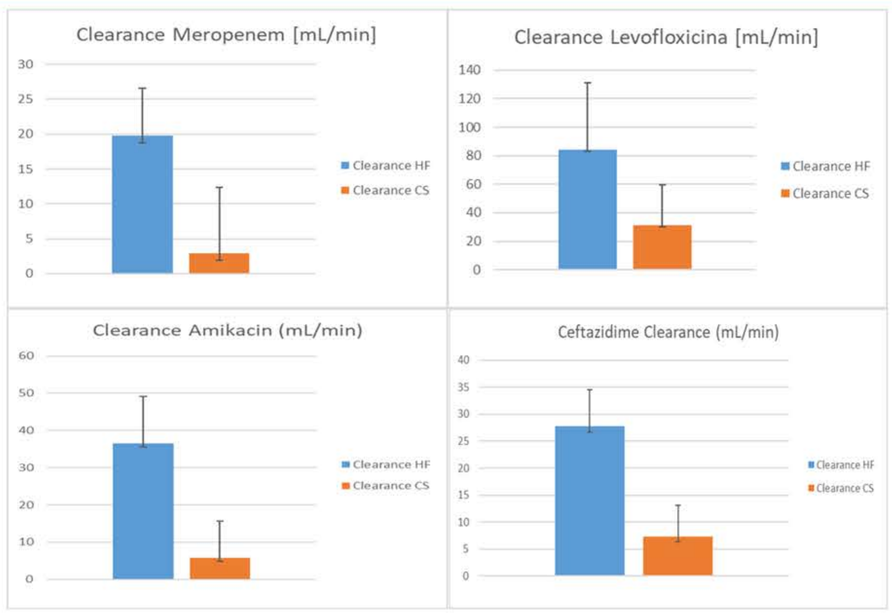



HF= Hemofilter/CKRT
CS = CytoSorb
Qi = HF blood inflow [mL/min]; Ci = HF inflow drug concentration [mgr/mL];
Qe = Effluent flow [mL/min]; Ce = Effluent concentration [mgr/mL];
Qx = HF blood outflow [mL/min]; Cx = HF outflow drug concentration [mgr/mL];
CP = weight loss [mL/min];
Qo = CS blood outflow [mL/min]; Co = CS outflow drug concentration [mgr/min];

| REMOVAL RATIO (%) | | % of Drug Removal Concentration-dependent |
|---|---|---|
| $RR\%_{HF} = [(Ci-Cx)/Ci]*100$ | $RR\%_{CS} = [(Cx-Co)/Cx]*100$ | |
| **MASS REMOVAL (mgr/min)** | | mgr of Drug Removed per minute Concentration-Dependent |
| $MR_{HF} = Qx*Cx-Qi*Ci$ | $MR_{cs} = (Co-Cx)*Qo$ | |
| **Clearance (mL/min)** | | mL of blood completely purified of a Target molecule Concentration-indipendent |
| $MR_{HF} = Qe*Ce/Ci*(Qi/(Qi+Qe-CP)$ | $MR_{cs} = Qx*(Cx-Co)/Cx$ | |

## RESULTS




**CKRT showed higher clearance levels for all antibiotics considered. The highest clearance levels were observed, for both, CKRT and Cytosorb, in Levofloxacin (CKRT 103,6 ml/min; Cytosorb 30,9 ml/min). No CytoSorb removal was observed in Amikacin.**

## CONCLUSIONS

This preliminary report shows a minimal impact of Cytosorb on the target drugs removal. Highest MR and Clearance were observed in CKRT as compared to CytoSorb.

Average mass removal (mg/min) of all the drugs considered is higher in CKRT (> 60% of the total mass removal).

To the best of our knowledge this is the first report about pharmacokinetics dynamic in critically il children treated with CKRT and Cytosorb for septic shock.