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## ABSTRACT

**Background.** Sepsis is one of the most common causes of hospitalizations and deaths in the world and defined as life-threatening organ dysfunction caused by a dysregulated host response to infections. The final event of this dysregulated and intense inflammatory response is a cytokine storm mainly, which leads to multiple organ dysfunction if it cannot be controlled and stopped by the medical management. **Material and Methods.** New therapeutic resources are under investigations in order to further improve the prognosis of the most severe patients affected with sepsis. One of those therapies is the extracorporeal blood purification therapy with hemoadsorption device HA330 (Jafron Biomedical Co., Ltd, China), which aims to eliminate endo- and exotoxins from the blood during the most severe inflammatory conditions. So far this therapeutic approach was successfully used in a few adult septic patients. Here, we describe and discuss three ALL children who developed severe sepsis and underwent extracorporeal blood purification using HA330 filter. **Results and Conclusion.** We applied the HA330 hemoadsorption in a three pediatric patients hospitalized in the PICU and diagnosed with septic shock. The treatment was associated with hemodynamic stabilization and a reduction of procalcitonin, IL6, C-reactive protein. In one case due to "second hit" episode another session with HA330 was run. We also noted that early initiation of therapy leads to faster and more sustainable results. Further studies needs to demonstrate its safety and efficacy in a large number of pediatric patients

## INTRODUCTION

Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infections. In general, sepsis treatment is mainly based on the broad-spectrum antibiotic administration to fight the ongoing infection, but additional and supportive therapies are usually and variably required according to sepsis severity and clinical background. Unfortunately, patients with severe sepsis may not respond to the usual antimicrobial and supportive therapies. Therefore, new therapeutic resources are under investigations in order to further improve the prognosis of the most severe patients affected with sepsis. One of those therapies is the extracorporeal blood purification therapy with hemoadsorption device HA330 (Jafron Biomedical Co., Ltd, China), which aims to eliminate toxins from the blood during the most severe inflammatory conditions [1]. So far this therapeutic approach was successfully used in a few adult septic patients. Here, we describe and three ALL children who developed severe sepsis and underwent extracorporeal blood purification using HA330 filter.

## MATERIAL AND METHODS

**Case 1:** is a 6 months old girl with confirmed diagnosis of pure red aplasia, presented with fever, general weakness, malaise, anuria, progressive dense maroon-purple spots on anterior abdominal wall, back, inguinal and buttock areas, with areas of necrosis on the left buttock. Due to drastic increase in azotemia (BUN, creatinine) and inflammatory markers (CRP, procalcitonin, IL6) the decision was made to perform continuous veno-venous hemodiafiltration (CVVHDF), Prismaflex, M60, Baxter, USA) with disposable hemoperfusion cartridge HA 330 (Jafron Biomedical Co., Ltd, China) for 4 hrs.

After the 1st session there was drastic improvement in all investigated parameters. Patient's respiratory system required much less oxygen (FiO2 decrease from 60% to 30%), breathing spontaneously. Catecholamines were gradually discontinued. Similarly, inflammatory markers dropped significantly (CRP 517.09 to 138.62 mg/ml; PRC 20.28 to 4.27ng/ml; IL6 839.00 to 67.74 pg/ml). Patient also improved her metabolic status (pH 7.053 to 7.349; pCO2 106 to 45.30; HCO3 16.9 to 23.6) and renal function (creatinine 92.59 to 32.27 μmol/L; BUN 36.14 to 11.67 mmol/l; diuresis 0.6 to 3 ml/kg/hr). However, on the 5th day after the 1st session patient's condition worsened due to progression of sepsis, which required 2nd session of the hemodiafiltration for 4 hrs. The results after 2nd session were similar to those after the 1st session.

**Case2:** is 14 years old boy with confirmed diagnosis of acute lymphoblastic leukemia FAB L2, B II, resistant to all previous chemotherapies (AIOEP ALL-AIOEP-BFM-2009 and ALL-AIOPE-2009-HR block I. On 18th day of hospitalization, patient developed polyorgan insufficiency, sepsis, and was transmitted to PICU.

Despite antibacterial treatment patient did not show any improvement. Patient was febrile for a week in PICU, with high levels of inflammatory markers (CRP 378 mg/l and PRC 103.04 ng/ml), his hemodynamics were unstable even on dopamine (BP – 85/50). Patient's diuresis is only responsive to furosemide (3 mg/kg/day), with constantly high azotemia. The decision was made to perform CRRT (CVVHDF mode) with HA 330 adsorber for 4 hrs.

At the end of procedure patient's inflammation, azotemia and respiratory function improved significantly. All of inflammatory markers decreased significantly. Patient was weaned from mechanical ventilation and was able to maintain normal blood pressure (95/60) without use of any catecholamines.

**Case 3.** 2.5 year old patient with ALL, FAB L2, B-II, who was admitted to the hospital for chemotherapy based on AIEOP-BFM ALL 2009 protocol II. After treatment with HDMTX (5 mg/m<sup>2</sup>), despite the continuous monitoring of methotrexate level in the blood, patient developed side effects, such as toxic dermatitis, toxic enteritis, toxic hepatitis and ulcerative stomatitis and was transferred to PICU. On the 4th day of PICU stay, patient developed sepsis, acute kidney injury and pneumonia. Procalcitonin and CRP levels were as high as 848.00 ng/L and 259.40 mg/L, respectively. Combination of antibacterial treatment didn't show any result. In order to decrease the inflammatory markers in the blood the decision was made to perform CVVHDF with hemoperfusion cartridge HA 330 for 4 hrs. After the procedure, patient's general condition improved significantly, with notable decrease of inflammation markers (CRP and Procalcitonin decreasing to 130.03 mg/L and 49.60 ng/L respectively). Patient's blood pressure stabilized, and vasopressors requirement decreased twice. Patient's renal function also improved with increased clearance of the BUN and creatinine, and increased diuresis

## DISCUSSION AND CONCLUSION

The technique of using various adsorbers, including the removal of endotoxins and exotoxins is used in different fields of medicine [2]. To the best of our knowledge, this is a first successful implementation of HA-330 adsorber in pediatric patients with sepsis.

A four hours procedure of HA-330 adsorption coupled to CVVHDF significantly reduced the markers of inflammation. The reduction rate of leukocytes in average was 71.78%, for CRP – 71.79%, Procalcitonin and IL-6 level – 89.4% and 79.4% respectively.

At the same time, using the HA-330 adsorber has proven to be a safe and effective in a pediatric patient. In addition, a recent study has shown that HA series adsorbers carry an optimal level of biocompatibility and their use in HP is not associated with adverse reactions or signs of cytotoxicity [3]

Despite the significant effect in our case, we would like to note some limitations. There are currently no other reports that would support our opinion in using HA-330 for septic children. In addition, our study is limited to three cases only. We also suggesting that in some cases it may be necessary to repeat the session of hemoadsorption. At the same time, we may encounter complications common to extracorporeal methods: catheter bleeding and infection, side effects of heparinization, platelet reduction. However, the advantage of this method is that the short procedure time reduces the above risks.

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### References

1. Ashkat, G., et al., A New Series of Sorbent Devices for Multiple Clinical Purposes: Current Evidence and Future Directions. Blood Purif, 2019, 47(1-3): p. 94-100.
2. Clark WR, Ferraris F, LaManna G, et al. Extracorporeal Sorbent Technologies: Basic Concepts and Clinical Application. Contrib Nephrol. 2017;190:43-57.
3. Romanov-Martin D, Ashkat G, Lorentz A, et al. Biocompatibility and Cytotoxic Evaluation of New Sorbent Cartridges for Blood Hemoperfusion. Blood Purif. 2018;46(3):187-195.

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