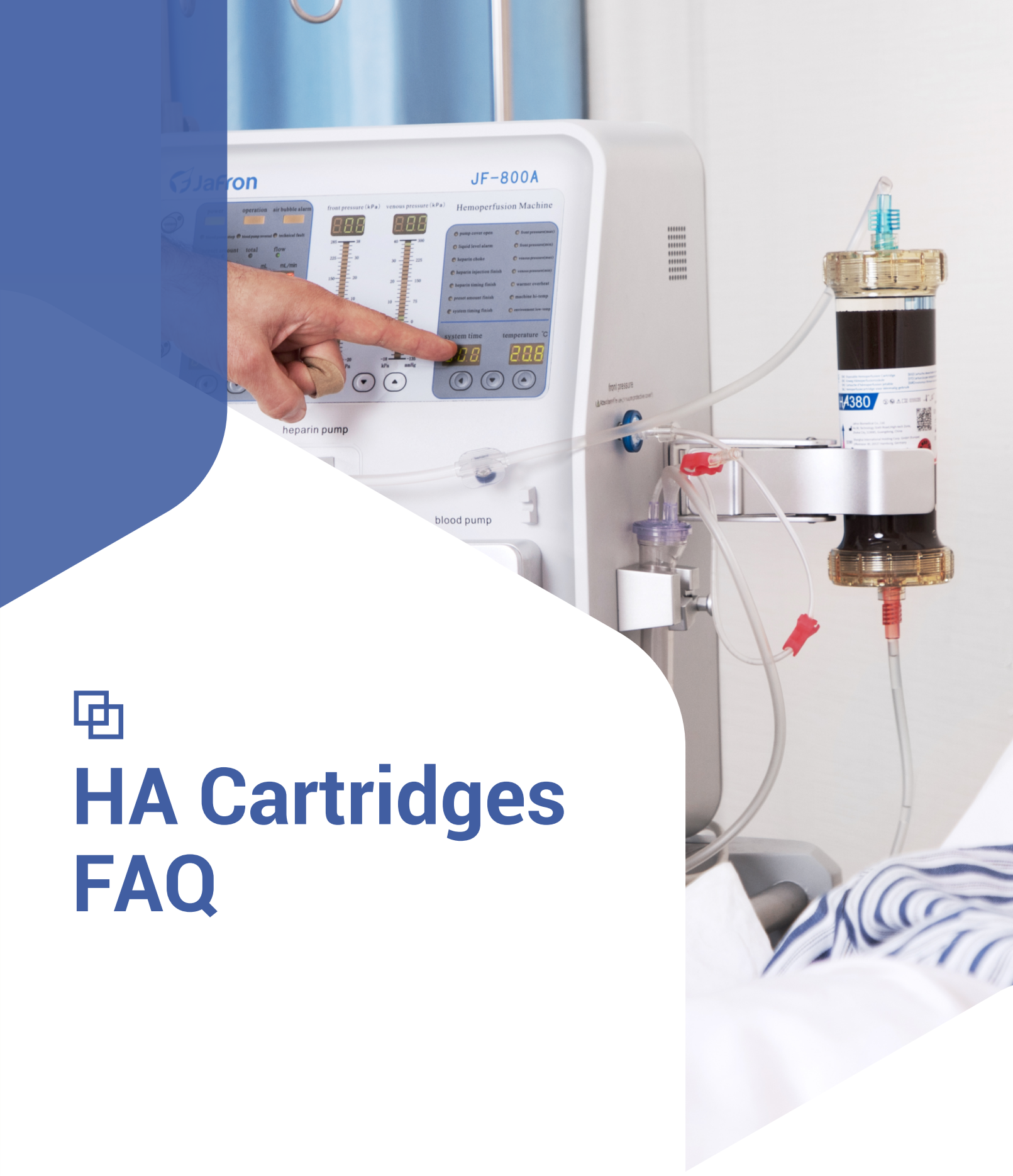

HA Cartridges FAQ

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JaFron

Stock Abbreviation: JFSW
Stock Code: 300529

Basic FAQ Related to Jafron Hemoperfusion

1. How do the structure of Jafron HA resins look like?

- The adsorbent materials of HA cartridges are neutro-macroporous resin made of double cross-linked styrene-divinylbenzene copolymers.
- The adsorption principles of the resins include the molecular sieve, van der waals, and the hydrophobic characteristics of the resins.
- Jafron's porosity control technology adjusts the resin pore size distribution and adsorption range.
- Collodion coats the resins to mitigate the possible adverse effect of direct contact with blood.

2. What are the indications for HA cartridges?

According to clinical practices and studies, disposable hemoperfusion cartridge is indicated to remove the following substances[1-11]:

- Inflammatory mediators and cytokines such as IL-1, IL-6, IL-8, IL-10, TNF-α.
- Overdosed drugs and poisons such as organophosphorus, paraquat, carbamazepine.
- Accumulated β2-MG, PTH, leptin and protein-bound toxins in end stage renal disease hemodialysis-related complication.
- Excessive triglyceride and cholesterol in hyperlipidaemia severe acute pancreatitis.
- Other substances: bilirubin, myoglobin.

3. Could you illustrate the safety and biocompatibility of Jafron cartridges?

The biocompatibility of the cartridges has been evaluated both in vitro and in vivo. In vitro, CT imaging showed an excellent distribution of the flow inside the HA cartridges without channeling phenomena[10]. The cytotoxicity test demonstrated that HA cartridges carried out an optimal level of biocompatibility, and their use was not associated with adverse reactions[11]. Clinically, the publications did not show significant adverse reactions related to Jafron hemoperfusion[1,2,8,12,13].

4. What is the platelet loss rate during hemoperfusion with Jafron?

According to the previous studies, Jafron hemoperfusion did not show a severe reduction in platelet levels[14-15]; the loss of the platelets is low, usually is less than 10%, and usually recovered within 24 hours.

5. Do hemoglobin and albumin adsorbed by the cartridges?

The previous studies did not show significant decrease of hemoglobin and albumin after the hemoperfusion treatment[16,17].

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JaFron
Stock Abbreviation: JFSW
Stock Code: 300529

HA130 Related FAQ

1. What are the main clinical applications of HA130 hemoperfusion?

MHD patients have the following clinical manifestations, they recommended to the HP treatment[1]:

- Severe uremic pruritus
- Severe uremic-related sleep disorders
- Protein energy consumption
- Microinflammatory status
- Severe secondary hyperparathyroidism
- Severe hyper β2-MG
- Refractory hypertension
- Restless Leg Syndrome (RLS)
- Uremic peripheral neuropathy

2. What is the treatment scheme for Ha130?

The treatment scheme of HA130 could be as follow[2,3]:

- Intensive program: 4 times/month
- Maintenance program: 1-2 times/month
- Treatment duration: 4 hours combined with HD or HDF
- The treatment scheme could be adjusted according to the patient’ s condition.

3. In some cases, why is the PTH still higher or did not reduce after the HA130 treatment?

HP treatment is expected to improve the symptoms and reduce the middle uremic toxins and protein-bound uremic toxins; try to analyze the factors which may affect the results:

- Patient's diet: A high phosphate diet and phosphate levels may increase PTH secretion[4].
- Serum low vitamin D and calcium may increase the phosphate levels and increase PTH secretion[4].

- Secondary hyperparathyroidism: Associated with high levels of PTH[5].
- Note: Compare the HA130 group to the non-HA130 group to better outline the effect of HA130.

4. Is there any impact of HA130 on quality of life?

Combining HA130 and HD could improve body pain, general health, vitality, emotional role, mental health, and total QoL score[2].

5. Is there an impact of HA130 on survival?

The Systematic Review and Meta-Analysis on the survival outcomes for the patients with End-Stage Renal Disease showed that the 1-year overall survival (OS) rate, the 2-year OS rate, and the 5-year OS rate of patients with ESRD treated with HP + HD were better than those treated with HD[6].

6. Is there a cost-effectiveness study on hemoperfusion treatment?

The cost-effectiveness study with 1,407 patients recruited to the HD/HP trial from 30 clinical centers with two years' follow-up period demonstrated that[7]:

- In the base case analysis, compared with HD alone, HD + HP results in 2.87 LYs saved, 1.32 QALY gains and an additional cost of RMB 33,340 per patient. The probabilistic ICER of HD + HP is USD 25,251 per QALY, which is lower than the USD 30,778 willingness-to-pay threshold. Therefore, HD + HP is considered to be cost-effective.
- HP+HD reduces the incidence of severe CVD events and subsequent CVD deaths.

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JaFron
Stock Abbreviation: JFSW
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HA230 Related FAQ

1. What are the adsorption principles and the clinical applications of the HA230 hemoperfusion cartridge?

It mainly removes poisons and overdose drugs with a molecular weight of 500Da~10KDa or hydrophobic or high protein-binding properties[1].

The clinical applications could be divided into poisons and drug overdose as listed below[2-12] :

- Parquat poisoning, Acute severe organophosphate poisoning (ASOP), 2,4-Dinitrophenol, Snake venom, Mushroom poisoning, Abrin, Paroxetine, Thallium, Aconitine, etc.
- Methotrexate (MTX), Ticagrelor, Carbamazepine, Paroxetine, Amitriptyline, Digoxin, Acetaminophen, Imipramine, Amlodipine (CCBs), etc.

2. What is the recommended treatment scheme for HA230?

- The treatment should be initiated as early as possible (4-6 h from exposure to poison or drug, the therapy after 12 hours of the exposure is less effective).
- The recommended scheme is 3-5 cartridges for each patient, with a suggested duration of 3-4 hours for each cartridge and no more than 12 hours.
- Hemoperfusion should be carried out more frequently at the beginning (1-3 cartridges/day).
- The treatment frequency and duration could be adjusted according to the type of poison/drug and the patient' s condition.

3. What are the expected benefits of using HA230 hemoperfusion?

According to the previous publications, hemoperfusion HA230 therapy could benefit on[2,11,12]:

- Accelerate the elimination of poison and overdose drugs.
- Stabilize the hemodynamic status.

- Alleviate complications such as consciousness disorder, respiratory depression, coma, etc.
- Shorten hospitalization.
- Improve the survival.

4. What are the treatment modes for HA230 hemoperfusion cartridge?

HA230 could stand alone as single hemoperfusion or combined with HD or CRRT.

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JaFron
Stock Abbreviation: JFSW
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HA380 Related FAQ

1. What are the main clinical applications of Ha380?

- Sepsis/Septic shock[1,2]
- COVID-19[3,4]
- Severe acute pancreatitis/ hyperlipidemia induced pancreatitis[5]
- Trauma/Burn[6]
- Cardiopulmonary bypass surgery[7]

2. When to initiate the HA380 hemoadsorption treatment?

The timing of the application of hemoperfusion for critical illness is still under investigation. The inclusion criteria from previous publications and expert experiences may differ in different countries; however, inflammatory mediators of critically ill patients may release in the early stage of the disease. The early use could have more benefits and control the disease's development.

At the 2021 International Critical Illness Conference (ISICEM), Professor Claudio Ronco and others stated that:

- Start early to remove the pro-inflammatory cytokines in the first 24 hours of admission to the ICU and before the organ dysfunction.
- Start immediately for severe burn patients and long period cardiac bypass CPB patients.
- For other types of patients, especially during the coronavirus, do not wait for the indication of CRRT to perform hemoperfusion.
- A recent publication demonstrated that the early start of hemoperfusion could be more effective and significantly reduce the mortality rate among COVID-19 patients with critical diseases[3].

3. What is the recommended treatment scheme for HA380?

1~2 cartridges/day for three consecutive days, the suggested duration of each cartridge is 6 hours, no more than 12 hours. The physician could adjust the treatment scheme according to the patient’ s condition.

4. What are the expected benefits of using the HA380 hemoperfusion cartridge?

HA380 hemoperfusion may benefit the patients by[2-8]:

- Reduce inflammatory cytokines and other target substances such as IL-6, IL-8, IL-1 and TNF-α.
- Reduce the triglyceride and cholesterol levels of severe acute pancreatitis.
- Improve hemodynamics and reduce the vasopressor requirement.
- Improve organ function, oxygenation index, SOFA score, APACHE II score.
- Reduce mechanical ventilation, shorten ICU stay, and improve the survival.

5. Could HA380 be used for traumatic patients?

Hemoperfusion could reduce myoglobin, creatinine kinase and stabilize the hemodynamics in indicated patients[9].

6. Could HA380 be used for severe acute pancreatitis (SAP)?

Hemoperfusion could reduce the cytokines and lipids (Triglyceride & cholesterol). It could reduce the severity of the disease and stabilize the hemodynamics[10].

7. Could HA380 adsorb the Ticagrelor?

The lab results showed that hemoperfusion could remove the Ticagrelor, and the removal rate could reach 80% in 6h[11].

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Stock Abbreviation: JFSW
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DPMAS Related FAQ

1. Why do we need bilirubin adsorption?

High bilirubin levels could lead to mitochondrial dysfunction and capillary leak syndrome; cholemic nephrosis is also associated with elevated bilirubin in ACLF. Bile acid could lead to hepatotoxicity and nephrotoxicity. Systemic inflammation and bile acids are critical drivers for liver failure in ACLF. High ammonia is supposed to be associated with brain swelling. DPMAS is not only to adsorb the bilirubin but also to adsorb bile acid, ammonia, and cytokines; this may benefit on:

- Decrease bilirubin, bile acid, cytokines, and ammonia[1-5].
- Alleviate liver injury[1-6].
- Reduce hepatic encephalopathy grading[6].
- Increase liver transplant waiting time[2,3].

2. What are the treatment modes for liver cartridges?

Jafron hemoadsorption therapy for the liver disease could be performed in different modes:

- HA330-II: Direct blood adsorption as HP, HP+HD or HD+CRRT mode.
- BS3330: Plasma adsorption (PA) mode (Plasma separator + BS330 cartridge).
- DPMAS: Plasma adsorption (PA) mode (Plasma separator+BS330 cartridge+HA330-II cartridge).

3. When do we use HA330-II, BS330 and DPMAS?

HA330-II	BS330	DPMAS
Hyper-inflammation + Hyperbilirubinemia	Hyperbilirubinemia + Hyper-bileacidemia	Hyperbilirubinemia + Hyper-inflammation
Total Bilirubin< 13mg/dl; High PCT, CRP, or IL-6	Total Bilirubin> 222.4 umol/L (13mg/dl).	Total Bilirubin⩾ 13mg/dl; High PCT,CRP, or IL-6

4. Why do we need a plasma separator when using BS330?

The direct contact of blood to BS330 resin may cause severe adverse reactions; the reasons are:

- The BS330 resins are anion exchange resins; direct exposure to the blood may cause coagulation.
- BS330 cartridge has finer resins than HA cartridges; whole blood adsorption may lead to cartridge blockage.
- Filtration fabric at the outlet end of the BS330 column may result in clotting if direct blood adsorption.

5. Why sometimes there are white or translucent jelly-like substances appear on BS330 during the process of plasma adsorption?

- It is a sign of coagulation problem resulting from inadequate anticoagulation. There is no blood cell, so it will not form a clot. The visible white or translucent jelly-like material is activated fibrinogen and precipitation phenomena.
- Mostly, it is caused by insufficient anticoagulation, or the patient is in a hypercoagulable state. Arterial pressure, venous pressure, and TMP should be monitored carefully during the treatment. The adjustment of anticoagulant should be considered.

6. When combining PE+DPMAS, which treatment should start first?

- PTA<30%, recommend conducting PE then DPMAS.
- PTA>30%, could start from either PE or DPMAS.
- PE is recommended to be admitted first for patients with PTA<30%, because it could supply the patients with the coagulation factors and improve the coagulation function.

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JaFron
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HA Cartridges Operation Related FAQ

1. Why should we heparinize the HA cartridges?

- Heparin molecular weight: 15kDa.
- Heparin is expected to be adsorbed if used for systemic anticoagulation.
- Jafron recommends heparinization by injecting heparin into the cartridge 30 minutes before priming to prevent the possible adsorption of heparin and prevent coagulation problem, ensuring more safety procedures.
- Citrate anticoagulation is recommended for patients who do not tolerate heparinization.

2. Should we heparinize the cartridge when using citrate anticoagulation?

If the patient will go through citrate anticoagulation, you could prime the HA cartridge with 3000mL normal saline without heparin.

3. What is the blood flow rate and the duration of HP treatment?

The recommended blood flow rate and treatment duration are as follow:

HP	Blood flow rate: increase gradually from 100~150mL/min to 200~250mL/min.
	Duration: 2~2.5 hours.
HP+HD/HDF	Blood flow rate: usually less than 320mL/min.
	Duration: 4 hours.
HP+CRRT	Blood flow rate: usually 150~250mL/min.
	Duration: can be up to 12 hours.
HP+CPB	Blood flow rate: can be up to 700mL/min.
	Duration: usually less than 2.5 hours.
Blood flow rate: 100 ~700mL/min. Treatment duration: 2~12 hours.	

4. What kind of machines do we need to perform the hemoperfusion treatment with Jafron cartridges?

Hemoperfusion using HA cartridges is compatible with all common hemodialysis and CRRT machines.

5. How do you anticoagulate the patients during the hemoperfusion treatment?

The suggested anticoagulant type and dosage are as follow:

Heparin

Initial recommended dosage: 62.5~125U/kg.

Additional dosage:1250~2500U/hour.

Stop adding heparin 30 minutes before the end of treatment.

Low molecular weight heparin

It might be used for anticoagulation according to treatment requirements.

Citrate

When using regional anticoagulation, the concentration of citrate and calcium ions should be closely monitored during the entire treatment.

***Note:**

Due to the individual differences, above anticoagulant dosage should depend on patient' s condition.

Other anticoagulation agents may be used according to the patient' s condition.

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- Established in 1989, IPO on ChiNext in 2016
- Widely used in more than 80 countries
- Applied in over 8000 influential hospitals
- Annual application over 5 million pcs

*Contraindications, Warnings and Precautions refer to Instructions For Use

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