

Novel Coronavirus Infection with Liver Failure: Discussion of DPMAS Artificial Liver Treatment Strategy

1. Introduction

Novel coronavirus infections can rapidly develop into respiratory distress syndrome, septic shock, metabolic acidosis, and coagulopathy. As the number of infections increases, so does the number of critically ill patients. Patients with respiratory failure, septic shock, and other organ failures require ICU monitoring and treatment. Critical treatment is mainly to prevent complications, treat underlying diseases, prevent secondary infections, and immediately provide organ function support. Academician Li Lanjuan combated H7N9 bird flu in the past, proposed, the "four-anti-two-balance" treatment concept, using artificial liver technology to achieve good results, namely: antiviral therapy, anti-hypoxemia and multiple organ failure, anti-shock therapy, anti-infection therapy ; Maintain water-electrolyte-acid-base balance and regulate human micro-ecological balance. If the bilirubin is significantly increased during the progress of the disease, the use of DPMAS artificial liver technology can be considered. (Excerpt: " Diagnosis and Treatment Protocol for Pneumonitis with Novel Coronavirus Infection (The 3rd Trial Version)

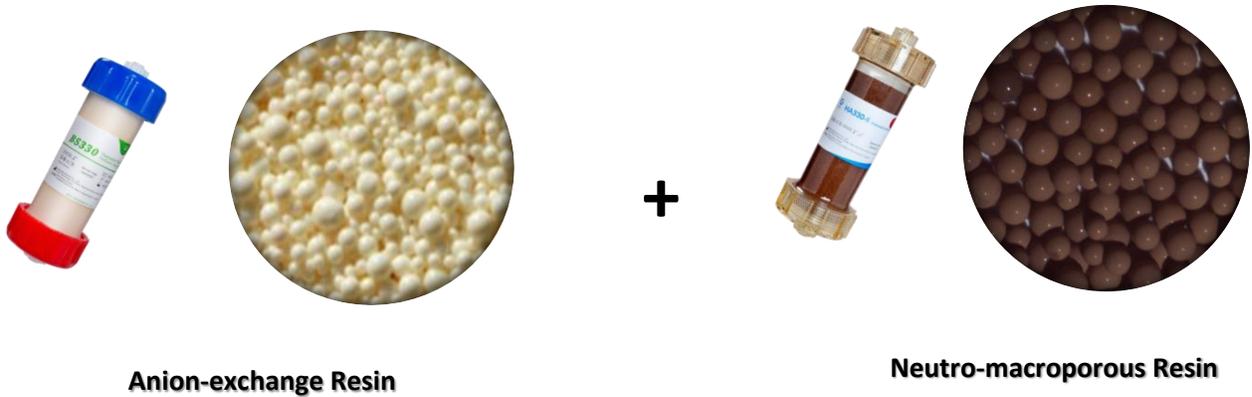
2. Clinical application of artificial liver supporting system recommended by artificial liver guidelines:

- 1) It is recommended in the early, middle and late stages of liver failure but the pros and cons of treatment need to be weighed;
- 2) It is recommended as a bridge for liver transplantation;
- 3) Hyperbilirubinemia caused by various reasons and with no obvious respond to medical treatment;
- 4) Liver failure complicated with hepatic encephalopathy (HE)

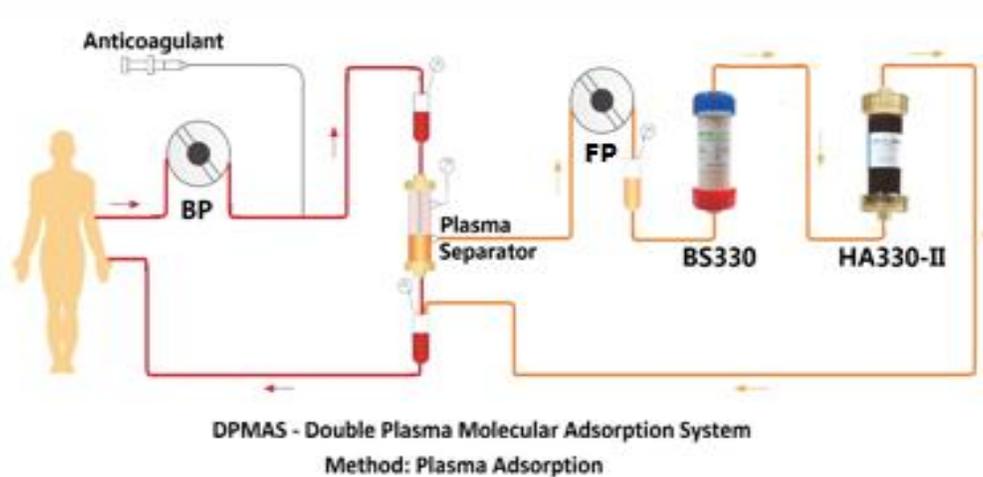
3. The principle of DPMAS technology

DPMAS (Double Plasma Molecular Adsorption System)

A blood purification system, combination of BS330 and HA330-II adsorption cartridge



- 1) Specifically adsorb bilirubin and bile acid.
- 2) Remove other middle molecular toxins induced by liver disorder, such as inflammatory mediators, ammonia, phenol, mercaptan, etc.



DPMAS compatible with different machines



DPMAS on Jafron (DX-10) machine



DPMAS on Fresenius Machine



DPMAS on B. Braun Machine

4. Three recommended guidelines for DPMAS

- 1) Guidelines for Non-biological Artificial Liver support system in treatment of liver failure, Edition :2016^[1]

• Standards and Guidelines •

Guidelines for Non-bioartificial Liver Support System in Treatment of Liver Failure (2016 Edition)

Liver Failure and Artificial Liver Group, Society of Infectious Diseases, Chinese Medical Association

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Double Plasma Molecular Adsorbing System, DPMAS: on the basis of plasma bilirubin adsorption treatment, a broad spectrum adsorbent is additionally used for the adsorption of middle molecule and macromolecule toxins. Thus DPMAS can not only adsorb bilirubin, but also remove inflammatory mediators and there is no loss of plasma, and make up the shortcoming of specific bilirubin adsorption.

- 2) Guideline for diagnosis and treatment of liver failure (2018), Edition: 2018^[2]

3) Guidelines for the Diagnosis and Treatment of Cirrhosis and Hepatic Encephalopathy, Edition: 2018^[3]

的芳香族氨基酸进入大脑^[85-86]。

4、其他微量营养素 HE 所致和精神症状可能与缺乏微量元素、水溶性维生素，特别是硫胺素有关，低锌可导致氨水平升高。对失代偿期肝硬化或有营养不良风险的应给予复合维生素或锌补充剂治疗^[87]。

(四) 人工肝治疗

肝衰竭合并 HE 时，在内科治疗基础上，可针对 HE 采用一些可改善 HE 的人工肝模式，能在一定程度上清除部分炎症因子、内毒素、血氨、胆红素等。常用于改善 HE 的人工肝模式有血液灌流、血液滤过、血浆滤过透析、分子吸附再循环系统 (MARS)、双重血浆分子吸附系统 (DPMAS) 或血浆置换联合血液灌流等^[88-89]。

(五) 肝移植

4. Artificial liver therapy

When liver failure is complicated with hepatic encephalopathy (HE), in addition to the conventional treatment, the use of artificial liver models to improve HE is also considered, it eliminates definite inflammatory factors, endotoxins, blood ammonia, bilirubin, etc. Artificial liver models commonly used to improve HE include hemoperfusion, Hemofiltration, plasma filtration dialysis, MARS, Double Plasma Molecular Adsorption System (DPMAS), or plasma exchange combined with hemoperfusion, etc.

5. The advantages of DPMAS technology

- 1) Comprehensive, large-scale, continuous removal of middle molecules, protein-bound toxins, and specific removal of bilirubin and bile acids;
- 2) Isotonic removal with little impact on the internal environment;
- 3) Do not rely on plasma substitution, to avoid the risk of infection and allergies.

6. Clinical application

1) Research article published on Journal of American Society for Apheresis (ASFA) by Dr. Yao Jia, academician of gastroenterology department of Shanxi Dayi Hospital, and Zhongping Duan, academician of difficult & complicated liver diseases and artificial liver center, Beijing Youan Hospital and others jointly reported "Therapeutic effect of DPMAS and sequential half-dose plasma exchange in patients with HBV-related acute-on-chronic liver failure", the research study shows that: 24h and 72h after PE or DPMAS+PE treatment, the total bilirubin and direct bilirubin reduction rates in the DPMAS + PE group were more significant than in the PE group; The 28-day

survival rate of patients with intermediate and advanced stage of HBV-related acute-on-chronic liver failure was significantly higher in the DPMAS+PE group than in the PE group^[4].

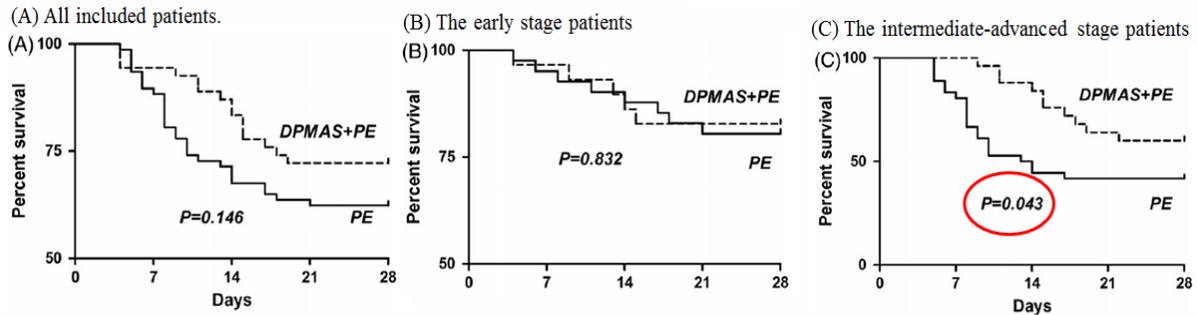


FIGURE 3 Comparison of liver transplantation free hospital survival at 28-days after treatment between PE group and DPMAS+PE group.

2) Clinical study of DPMAS + PE in the Second Affiliated Hospital of Chongqing Medical University shows: DPMAS combined with PE for early liver failure has better recovery rate and survival rate than PE alone, suggesting that low-volume replacement of PE combined with DPMAS can significantly reduce the amount of plasma and significantly improve the treatment efficacy of liver failure. It is an ideal artificial liver method for treating early stage liver failure.

3) Academician Li Lanjuan reported the impact of artificial liver on H7N9 bird flu:

- Li Lanjuan, an academician of the Chinese Academy of Engineering, director of state key laboratory of diagnosis and treatment of infectious diseases, reported that many critically ill patients treated in the first Hospital of Zhejiang university were with organ failure, the artificial liver and extracorporeal membrane oxygenation have played a very important role in the management procedures.
- The artificial liver support system implemented by Academician Li Lanjuan can significantly improve the treatment effect of severe viral hepatitis, and is beneficial in rescue treatment for patients with various types of liver failure. The artificial liver support system has been used to treat H7N9 bird flu, and has achieved remarkable results.
- Inflammatory factors in the serum of bird flu patients are significantly increased. Application of artificial liver support system treatment can reduce or eliminate inflammatory factors, reduce or eliminate liver toxins, supplement nutrients, improve liver



and kidney function, improve electrolyte disorders, and maintain a stable internal environment.

7. Treatment course and treatment modes

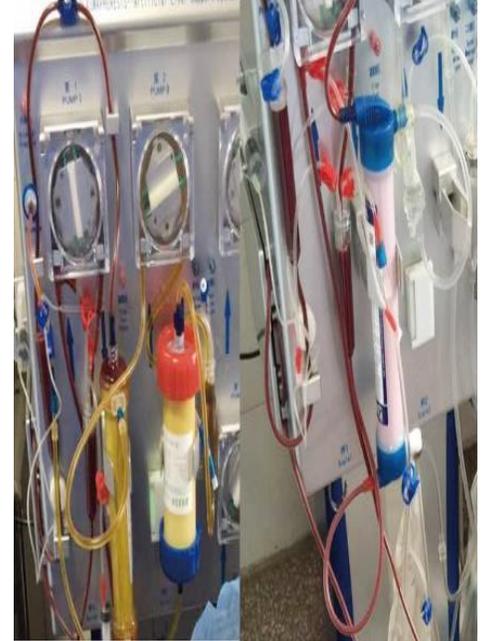
1) **Course of treatment:** 2-5 times a week, 3-5 times/session

2) **Treatment modes:**

1) DPMAS

2) DPMAS + PE

3) DPMAS + CVVH



Reference :

[1] Epidemiology branch of Chinese medical association, liver failure and artificial liver group. Guidelines for the treatment of liver failure by non-biological artificial liver (2016) [J]. Chinese journal of clinical infectious diseases, 2016,9(2):97-103.

[2] Guideline for diagnosis and treatment of liver failure (2018), J Clin Hepatol, Vol. 35 No. 1, Jan 2019

[3] Guidelines on the management of hepatic encephalopathy in cirrhosis, Infect Dis Info, Vol. 31, No. 5, October 30, 2018.

[4] Yao J, Li S, Zhou L, et al. Therapeutic effect of double plasma molecular adsorption system and sequential half-dose plasma exchange in patients with HBV-related acute-on-chronic liver failure[J]. Journal of Clinical Apheresis, 2019.