**CONVALESCENT PLASMA THERAPY**

**The Practice School Report is submitted to**

**BCDA COLLEGE OF PHARMACY & TECHNOLOGY**

***Under the supervision of Ms. Priyanka Chakraborty***

***By***

**Student Name : Sayan Bera**

**B. Pharm. 7th Semester**

**University Roll No:- 20101918002**

**Registration No:- 182010220005**

**BCDA COLLEGE OF PHARMACY & TECHNOLOGY**

**Affiliated to Maulana Abul Kalam Azad University of Technology (Formerly known as West Bengal University of Technology), Kolkata**

**78, Jessore Road (south), Hridaypur, Barasat, Kolkata – 700127**

**INDIA**

**2021**

**CERTIFICATE**

This is to certify that Mr. Sayan Bera has successfully completed his / her 150 hrs Practice School (PT-781) work entitled **“CONVALESCENT PLASMA THERAPHY**

**”** and submitted the report for partial the fulfillment of syllabus requirements of 7th semester of **BACHELOR of PHARMACY**, under MAKAUT, at **BCDA COLLEGE OF PHARMACY & TECHNOLOGY** under my supervision.

………………………………………..

Name of the supervisor

Designation

**Forwarded By**

**………………………………….**

**Prof. (Dr.) N. N. Bala**

**Principal**

BCDA COLLEGE OF PHARMACY & TECHNOLOGY

Affiliated to Maulana Abul Kalam Azad University of Technology (Formerly known as West Bengal University of Technology), Kolkata

78, JessoreRoad (south), Hridaypur, Barasat, Kolkata – 700127

INDIA

***ACKNOWLEDGEMENT***

I take this opportunity to express my profound gratitude to my guide **Ms. Priyanka Chakraborty.** Assistant professor, **BCDA College Of Pharmacy & Technology**. For her exemplary guidance, monitoring and constant encouragement throughout the course of this project. The blessing, help and guidance given by her time to time shall carry me a long way in the journey of life o which I am about to embark.

I am obliged to my Principle **Professor(Dr.) N.N BALA** for the valuable information provided by him. I am greatful for hid cooperation during the period of my project.

Lastly, I am thankful to the almighty, my Parents, Brothers, Sisters and Friends for their constant encouragement without which this project wouldn’t be possible.

------------------------------------

(SAYAN BERA)

***INDEX***

|  |  |  |
| --- | --- | --- |
| SL NO. | TOPICS | PAGE NO. |
| 1. | *INTRODUCTION* | **5** |
| 2. | *WHAT IS PLASMA THERAPY* | **6-7** |
| 3. | *METHODOLOGY* | **8** |
| 4. | *USES* | **9** |
| 5. | *CONTRAINDICATION* | **10** |
| 6. | *CASE STUDIES* | **11-12** |
| 7. | *ADVANTAGES* | **13** |
| 8. | *DISADVANTAGES* | **14** |
| 9. | *CONCLUSION* | **15** |
| 10. | *REFERENCES* |  |

***INTRODUCTION:***

While there is no proven treatment available for Ebola virus disease (EVD), whole blood collected from patients in the convalescent phase of infection has been used as an empirical treatment with promising results in a small group of EVD cases. During the current ongoing EVD outbreak, whole blood and plasma collected from EVD recovered patients has been prioritized for investigation, as one of the treatment modalities. The concept that this treatment could be efficacious is biologically plausible, as convalescent plasma has been used successfully for the treatment of a variety of infectious agents.

This interim guidance to national health authorities and blood transfusion services outlines the steps required to collect convalescent whole blood (CWB) or plasma (CP) from EVD recovered patients for transfusion to patients with early EVD, as an empirical treatment modality. It covers:

• The identification of patients recovered from EVD as potential blood donors;

• Informed consent and selection of donors;

• Donor’s blood grouping and screening for transfusion transmissible infections (TTI);

• Blood collection and donor care;

• Labelling, storage and data collection in blood transfusion services (BTS);

• Informed consent of EVD patients;

• Patient’s blood grouping and compatibility testing;

• Storage and transportation of CWB/CP to the sites where transfusions is to be given;

• Selection of EVD patients for this intervention;

• The clinical transfusion process;

• Data collection at the transfusion site; and

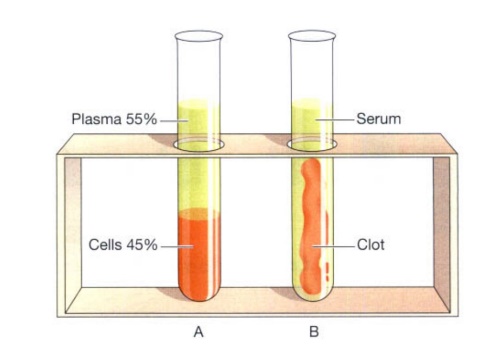
• Assessment of the effectiveness of this empirical treatment.

The convalescent WB or plasma should be collected, prepared, stored and transfused in facilities capable of implementing the guidance provided in this document. If the transfusions are planned to be given in a field situation, the WHO Checklist for essential items for blood transfusion in emergency settings can provide a useful source of additional information. This interim guidance will be updated as further evidence and experience accumulates.

[1]

***WHAT IS PLASMA THERAPY:***

Blood is composed of a straw-coloured transparent fluid. Plasma, in which different types of cells are suspended. Plasma constitutes about 55% and cells about 45% of blood volume.



***Plasma***

The constituents of plasma are water (90 to 92%) and dissolved substances, including:

• plasma proteins: albumins, globulins (including antibodies), fibrinogen, clotting factors

• inorganic salts (mineral salts): sodium chloride, sodium bicarbonate, potassium, magnesium, phosphate, iron, calcium, copper, iodine, cobalt

• nutrients, principally from digested foods, e.g. mono saccharides (mainly glucose), amino acids, fatty

acids, glycerol and vitamins

• organic waste materials, e.g. urea, uric acid, creatinine

• hormones

• enzymes, e.g. certain clotting factors

• gases, e.g. oxygen, carbon dioxide, nitrogen.

Plasma proteins:

Plasma proteins, which make up about .ting the osmotic pressure of blood (normally 25 mmHg or 3.3 kPa\*), which keeps plasma fluid within the circulation. If plasma protein levels fall, because of either reduced production or loss from the blood vessels, osmotic pressure is also reduced, and fluid move into the tissues (oedema) and body cavities.

***Cellular content of blood***

There are three types of blood cells :

• erythrocytes or red cells

• thrombocytes or platelets

• leukocytes or white cells.

All blood cells originate from pluripotent stem cells and go through several developmental stages before entering the blood. Different types of blood cells follow separate lines of development. The process of blood cell formation is called haemopoiesis and takes place within red bone marrow. For the first few years of life, red marrow occupies the entire bone capacity and, over the next 20 years, is gradually replaced by fatty yellow marrow that has no erythropoietic function. In adults, erythropoiesis is confined to flat bones, irregular bones and the ends (epiphyses) of long bones, the main sites being the sternum, ribs, pelvis and skull.

Convalescent plasma (CP) therapy is not a new therapy and banks on the age-old concept of passive immunity.

***Basis of the Therapy:***

The convalescent plasma therapy seeks to make use of the antibodies developed in the recovered patient against the coronavirus. The whole blood or plasma from such people is taken, and the plasma is then injected in critically ill patients so that the antibodies are transferred and boost their fight against the virus.

***Time Period for Infusion:***

A study in The Lancet Infectious Diseases stated that a Covid patient usually develops primary immunity against the virus in 10-14 days. Therefore, if the plasma is injected at an early stage, it can possibly help fight the virus and prevent severe illness.

**[2]**

***METHODOLOGY:***

A Convalescent plasma therapy uses antibodies (a type of protein i.e. produced by plasma) from patients who have completely recovered from COVID-19 infection. Here is how this procedure will fight coronavirus in your body. Blood is taken from a previously infected but completely recovered patient, the plasma component of that blood is separated and that contains the antibodies against SARS-CoV-2 virus. This plasma is injected into an infected person’s body that will fight the virus and neutralize it from spreading. Once the patient has recovered, he/she will be asked to donate their blood so that their antibodies will be used to treat other infected patients. The blood sample will be checked for any existing harmful diseases such as Hepatitis B & C including HIV. The recovered blood will be taken into study and a researcher will extract plasma from the blood that can be injected into an infected person.

***How to Prepare for the Treatment?***

Firstly, a doctor will recommend a convalescent plasma treatment that is suitable for your blood type. Here’s how you need to prepare before treatment and what you must do after treatment.

***Before Treatment:***

Your healthcare professional will assess your health before you undergo the treatment. This procedure involves a health care member who will insert an intravenous/ IV tube into a vein on your arms.

***During Treatment:***

The recovered plasma from a recovered infected person will be attached to the IV tube and supplied to you in drips. It takes 2hours for the procedure to be completed.

***After Treatment:***

You will be monitored by your healthcare specialist and you will have to make frequent visits to the hospital for further assessment by the doctor. Depending on your overall health, your healthcare specialist will decide if you require further hospitalization or not.

**[3]**

***USES:***

***Previous Application:***

1. The United States used plasma of recovered patients to treat patients of

Spanish flu (1918-1920).

1. Hong Kong used it to treat SARS (Severe Acute Respiratory Syndrome)

patients in 2005.

1. In 2009, the Swine flu (H1N1) patients were treated with plasma.
2. It has also been used to treat critically ill patients during Ebola as well.

* The report of a study, Proceedings of National Academies of Sciences (U.S.),

highlighted that CP therapy shows a potential therapeutic effect and low risk in the

treatment of severe Covid-19 patients.

* According to the study, one dose (200 ml) of convalescent plasma with a high

concentration of neutralizing antibodies is well-tolerated by patients and it can

rapidly reduce the viral load in patients and improve clinical symptoms

significantly.

***Infusion into Covid-19 Patients:***

* The plasma can be infused into two kinds of Covid-19 patients, those with a

severe illness or individuals at a higher risk of getting the virus.

* However, while plasma transfers immunity from one person to another, it is not

known if it can save lives in Covid-19 infection.

* The treatment could be effective for patients in the age group 40-60, but may

be less effective for people aged beyond 60 years.

**[4]**

***CONTRAINDICATIONS:***

***Risks of Plasma Therapy:***

Though this kind of treatment has proved to be effective over COVID patients, it needs to be done under proper medical supervision keeping in mind underlying risks. Here are some potential risks you need to be aware of.

* Since this process involves blood transfusion, there could be a risk of transmitting a prevalent virus from a recovered person. Thus, a doctor must assess the recovered person’s health before opting to conduct blood transfusion.
* Every human body reacts in different ways to a treatment or medication. This treatment cannot be useful for some patients as it can result in the contraction of an infection.
* You could be at risk of contracting the infection once again.

1. **HOUSTON:** The clinical administration of the blood component plasma from recovered Covid-19 patients to those severely affected by the disease could be a safe option without adverse side effects, according to a study which may lead to better treatment protocols against novel coronavirus infection.

On March 28, researchers from the Houston Methodist Hospital in the US, began clinical trials to transfuse plasma from recovered Covid-19 patients into critically ill patients, they noted in a statement.

1. In the study, published in The American Journal of Pathology, the scientists described the clinical outcomes of the convalescent plasma transfusion trial, showing 19 out of 25 patients improving with the treatment, and 11 discharged from the hospital.
2. "With no proven treatments or cures for Covid-19 patients, now was the time in our history to move ahead rapidly," Musser added. The scientists noted that the century-old therapeutic approach dates back to at least as early as 1918 to fight the Spanish Flu.
3. More recently, the researchers added that convalescent plasma therapy was used with some success during the 2003 SARS pandemic, the 2009 influenza H1N1 pandemic, and the 2015 Ebola outbreak in Africa.

They said early on in the Covid-19 pandemic, there were a handful of critically ill patients in China who showed improvement from plasma therapy, following which their team at Houston Methodist hospital targeted the Covid-19 virus with the procedure.

**[5]**

***CASE STUDIES:***

**TABLE-1 COVID-19- Recent trials and locations with key findings**.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Table-1 COVID-19 | No. of patients in trials/location | Dose of CP | Titres | Key Findings |
| COVID-19 | 5, Shenzhen, China | 400ml in two  consecutive doses of  200 ml each | •ELISA anti-SARS CoV-2  antibody titre less than  1:1000  •Neutralising antibody  titres > 40 | Clinical status improved, SOFA score decreased,  ARDS resolved, viral antibodies not detectable,  increase in PAO2/FIO2 (range 172-276 before  and 284-366 after), all were on other medications  including steroids and antiviral, no significant  adverse effects reported. |
| COVID-19 | 10, Wuhan, China | 200ml | • Neutralising anti-SARS  CoV-2 antibody titres >  1:640 | Clinical status improved, increased oxyhemoglobin saturation, absorption of lung lesions in radiographic examination noted, no significant adverse effects, other therapy included steroids, antimicrobials and antiviral. |
| COVID-19 | 2, Korea | 500 ml in total; infused 250ml twice in 24 hrs | Not stated |  |
| COVID-19 | 245 | Not stated | Not stated | 91 patients benefitted, plasma therapy said to be safe and effective. |
| COVID-19 | 4 | Different amount of plasma were infused in each patients (900ml, 200ml, 2400ml, 300ml) | Not started | See table no. 2 |

**Table 2 COVID-19- Case files.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Case | Drugs | Past Medical History | Secondary Infection | Amount of Plasma Diffused | Key findings: |
| 1) Age 69/  Female | Arbidol (200mg/TDS),  Lopinavir/Ritonavir  (400mg/BD), Interferon  alpha inhalation (50ug/  BD); Additional drugs:  Human albumin, Zadixin,  Immunoglobulins (Dose not  stated) | Hypertension (HT) | Co-infection with bacteria and aspergillus (For this, patient was treated with Caspofungin and Voriconazole) | 900ml in three  consecutive doses | •Radiographic examination revealed  absorption of consolidation.  •RT-PCR test results negative. |
| 2) Age 55/ Male | Arbidol (200mg/TDS), Lopinavir/Ritonavir(500mg/ BD), Interferon alpha 2b (5milion units/BD) | Chronic Obstructive Pulmonary Disease (COPD) | ---- | 200ml | •Chest images showed absorption of  interstitial pneumonia.  •RT-PCR test results negative. |
| 3) Age 73/ Male | Arbidol (200mg/TDS), Lopinavir/Ritonavir (400mg/BD), Interferon alpha 2b (5milion units/BD), Oseltamivir (75mg/BD), Ribavirin (500mg/BD) | Hypertension (HT) with Chronic Renal Failure (CRF) | Septic Shock, Coinfection with bacteria and aspergillus (For this, patient was treated with Caspofungin and Voriconazole) | 2400ml in 8 consecutive doses | •Reduced viral load.  •Radiographic examination showed  absorbed infiltrative lesions.  •RT-PCR test results negative. |
| 4) Age 31/ Female | Lopinavir/Ritonavir (400mg/BD), Ribavirin (500mg/BD) | Pregnancy | Multiple Organ Failure Syndrome, Septic Shock | 300ml | •RT-PCR test results negative |

**[6]**

***ADVANTAGES :***

In comparison to the conventional textile wet processing, plasma treatment of textiles has many advantages such as:

* 1. Endless chemical modifications are possible by choosing appropriate gasses or chemicals.
  2. In most cases it can be a dry process, reducing water consumption and energy to dry the treated materials.
  3. Reduction in the amount of water usage results in reducing the amount of waste water and the waste water treatment cost.
  4. It has an economical advantage over the conventional wet processing due to its low chemical consumption and reduction in chemical and water costs.
  5. Although for the above reasons all plasma processing is more environmentally friendly in comparison to the textile wet processing, the closed plasma treatment systems are an even more environmentally friendly process because the plasma byproducts can be trapped rather than being released into the environment.

6. Pore-free, uniform thin films with superior properties that can’t be achieved with conventional chemistry can be deposited on almost any substrate.

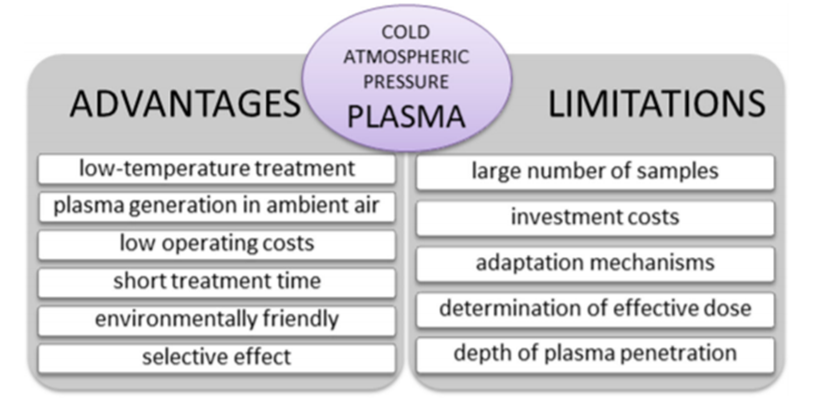
**[7]**

***DISADVANTAGES :***

1. System dependency is one of the most important disadvantages of the plasma treatment. This means that the same flow rate, gas pressure and power input may not produce the same level

of the needed reacting species.

1. Although initial investments such as purchasing expensive plasma equipment and high vacuum pumps are considered to be limiting factors and could be considered as a disadvantage, these costs can be recovered by savings that were mentioned above.
2. Scaling up and converting pilot batch process into a continuous process could also present some technical challenges.
3. Optimal process parameters must be established for each process and equipment. However, it is not too difficult to overcome these challenges.
4. Treating thin surface layers without changing the bulk could also be a disadvantage for some end-use and an advantage for when the objective is to keep the bulk untreated and only thin surface treatment is needed.
5. Textile materials are made from yarns or directly from fibers. In either case the fibers are covering each other, especially when they are in high twist yarns. This creates a shadow effect and the shadowed areas are generally protected from plasma treatment.
6. It is harder to predict the exact structural characteristics of the plasma treated area for a more complex molecule. This is due to the fact that plasma causes the complex molecular structure to fragment into a multitude of coexisting active species which could react or deposit on the surface.



**[7]**

***CONCLUSION:***

CAPP technologies in biological sciences have undergone a very dynamic progress in last decade, especially in medicine, food industry, and agriculture. Many benefits of plasma treatment have been frequently accompanied by limitations, such as scaling-up for continuous production, which have to be addressed in future development of novel CAPP technologies. High variability in plasma configurations can be considered both beneficial and limiting. Benefits are related to high number of different plasma sources. However, this can complicate research of plasma-biological target interactions. The plasma interaction with biological objects can also have adverse effects that have to be considered.

**[8]**

***REFERENCES:***

[1] World Health Organization 2014.

[2] Anatomy and Physiology in Health and illness – Ross & Wilson (9th Edition).

[3] The Times of India (22nd September 2020).

[4] Indian Council Medical Research report From Kerala News.

[5] The economic Times News published on June 03, 2020.

[6] Research Article -- imedpub Journal published on June 22nd , 2020.

[7] 21st International Symposium on Plasma Chemistry (ISPC 21).

[8] Arjunan KP, Sharma VK, Ptasinska S (2015) Effects of atmospheric

pressure plasmas on isolated and cellular DNA - a review. Int J

Mol Sci 16:2971–3016.