International Journal of Pharmacy
Journal Homepage: http://www.pharmascholars.com

Review Article **CODEN: IJPNL6**

REVIEW ON USE OF PLASMAPHERESIS IN FOGOSELVAGEM

[*1]Kiron S.S, [2]**Arun Shirwaikar**, [3]**Yogala C.K,** [4]**Saritha M**

[1]Dept. of Pharmacy Practice, Academy of Pharmaceutical Sciences, Pariyaram Medical College, Kannur, Kerala
[2]College of Pharmacy, Gulf Medical University, Ajman, UAE
[3]Academy of Pharmaceutical Sciences, Pariyaram Medical College, Kannur, Kerala
[4]Dept.of Pharmacy Practice, Crescent B. Pharm College, Payangadi, Kannur, Kerala

***Corresponding author e-mail:** sskiron@yahoo.com

ABSTRACT

Fogoselvagem (pemphigus foliaceus) is an endemic form of pemphigus foliaceus and was formerly known as Brazilian pemphigus foliaceus because it was originally observed in specific river valleys of rural Brazil. Plasmapheresis is a therapeutic option in patients with recalcitrant disease. It may decrease autoantibody titers in some patients and favourably influence the clinical outcome, especially in patients with otherwise therapy-resistant pemphigus foliaceus.

Key Words: Fogoselvagem, Plasmapheresis, Antibodies

INTRODUCTION

Fogoselvagem (FS), or endemic pemphigus foliaceus (PF), is an autoimmune, organ-specific blistering disease, in which autoantibodies specific for desmoglein 1 may lead to acantholysis (ie, cell-cell detachment). Desmoglein 1 is a glycoprotein that belongs to the cadherin superfamily (ie, calcium adhesion molecules present in the desmosomal core). Other target antigens are also postulated to be relevant in the pathogenesis of pemphigus foliaceus.. Pemphigus foliaceus is characterized by clinical involvement of healthy-appearing skin that may blister when rubbed. [1] Fogoselvagem is an endemic form of pemphigus foliaceus and was formerly known as Brazilian pemphigus foliaceus because it was originally observed in specific river valleys of rural Brazil. It is also reported in Columbia; El Salvador; Paraguay; Peru; and, most recently, in Tunisia.[2]

The epidemiology, age distribution, and human leukocyte antigen (HLA) associations distinguish fogoselvagem from nonendemic pemphigus foliaceus. Fogoselvagem is Portuguese for wild fire. The description wild fire refers to photosensitivity and the common symptom of severe stinging or burning that occurs with ultraviolet (UV) exposure. In fact, in patients with pemphigus foliaceus, exposure to UV-B may induce acantholysis in uninvolved skin. Epidermal exposure to UV light may enhance autoantibody epidermal binding and preferential neutrophil adhesion, which can contribute to acantholysis in endemic pemphigus foliaceus. Six types of pemphigus foliaceus exist. Bites of black flies, in particular SIMULIUM NIGRIMANUM, may initiate this disorder, possibly due to salivary proteins that contain pharmacologically active compounds.[3] In the 1960s, the presence of anti–immunoglobulin G (IgG) circulating autoantibodies and in situ autoantibodies was described in patients with fogoselvagem. These autoantibodies were detected by means of indirect and direct immunofluorescence (IF), and intracellular staining was demonstrated within the epidermis. The autoantigen related to EPF is desmoglein 1, a 160-kd glycoprotein of the desmosomal core, targeted by in situ and circulating IgG autoantibodies, mainly of the IgG4 subclass. [4] The IgG fraction from fogo selvagem was shown to be pathogenic by means of

passive transfer in BALB/c mice. These animals develop the clinical, histologic, and immunologic features of the human disease within 24 hours after the intraperitoneal injection of human IgG. The predominant IgG subclass in fogo selvagem is IgG4. Fogoselvagem is mediated by pathogenic antibodies to the enoyl-CoA delta isomerase 2 (ECI-2) domains of desmoglein-1. [5] A preclinical phase has been described with antibodies to only EC5. One hypothesis is that a component of insect vector saliva triggers an antibody response to EC-5. In susceptible individuals, a response to the EC1-2 domains may subsequently develop by epitope spreading with development of fogoselvagem. Inflammatory cytokines and apoptosis are also involved. [6] Its etiology is unknown, but blister formation appears to be mainly IgG4 mediated. The anti-Dsg1 response in fogoselvagem is probably initiated by sensitization to an environmental allergen, with cross-reactive IgE, IgM, and pathogenic IgG4 anti-Dsg1 responses as their serological markers.[7] The intense cutaneous burning sensation with this disease was evaluated in testing for neural autoreactivity in patients affected by a new variant seen in Colombia. Autoreactivity to neural structures, mechanoreceptors, nerves, perineural cell layers of the arachnoid envelope around the optic nerve, brain structures, and to neuromuscular spindles was detected, with antibodies also colocalized with desmoplakins 1 and 2. These findings may explain the "burning sensation."[8]

ROLE OF PLASMAPHERESIS:

Plasmapheresis is a therapeutic option in patients with recalcitrant disease. It may decrease autoantibody titers in some patients and favorably influence the clinical outcome, especially in patients with otherwise therapy-resistant pemphigus foliaceus. It is often used in conjunction with cytostatic agents, such as cyclophosphamide or azathioprine, to reduce a predictable rebound increase in autoantibody synthesis. Potential complications, including the need for maintaining venous access, a bleeding tendency, electrolyte shifts, pulmonary edema, fever, chills, hypotension, and septicemia, should be considered. Amagai.et.al reported that a single cycle of intravenous immunoglobulin at 400 mg/kg/d for 5 days is effective and safe for patients with pemphigus that is relatively resistant to systemic steroid therapy.[9] Toth and Jonkman also reported on successful therapy with intravenous immunoglobulin (low dose).[10]

Procedures of Plasmapheresis

Donating plasma is similar in many ways to whole blood donation, though the end product is used for different purposes. Most plasmapheresis is for fractionation into other products; other blood donations are transfused with relatively minor modifications. Plasma that is collected solely for further manufacturing is called Source Plasma. Plasma donors undergo a screening process to ensure both the donor's safety and the safety of the collected product. Factors monitored include blood pressure, pulse, temperature, total protein, protein electrophoresis, health history screening similar to that for whole blood, as well as an annual physical exam with a licensed physician or an approved physician substitute under the supervision of the physician. Donors are screened at each donation for viral diseases that can be transmitted by blood, sometimes by multiple methods. For example, donors are tested for HIV by ELISA, which shows if they have been exposed to the disease, as well as by nucleic acid methods (PCR or similar) to rule out recent infections that the ELISA test might miss. Industry standards require at least two sets of negative test results before the collected plasma is used for injectable products. The plasma is also treated in processing multiple times to inactivate any virus that was undetected during the screening process.

In a few countries, plasma (like blood) is donated by unpaid volunteers. In others, including the United States, most donors are paid for their time as the time commitment for regular donors is over 200 hours per year. Standards for donating plasma are set by national regulatory agencies such as the U.S. Food and Drug Administration (FDA), the European Union, and by a professional organization, the Plasma Protein Therapeutics Association (or PPTA),[11] which audits and accredits collection facilities. A National Donor Deferral Registry (NDDR) is also maintained by the PPTA for use in keeping donors with prior positive test results from donating at any facility. Almost all plasmapheresis in the US is performed by automated methods such as the Plasma Collection System (PCS2) made by Haemonetics or the Autopheresis-C (Auto-C) made by Fenwal, Inc., a former division of Baxter International. In some cases, automated plasmapheresis is used to collect plasma products like Fresh frozen plasma for direct transfusion purposes, often at the same time as plateletpheresis.

The manual method of plasmapheresis is approximately the same as a whole blood donation is collected from the donor. The collected blood is then separated by centrifuge machines in separate rooms, the plasma is pressed out of the collection set into a satellite container, and the red blood cells are

returned to the donor. Since returning red cells causes the body to replace plasma more rapidly, a donor can provide up to a liter of plasma at a time and can donate with only a few days between donations, unlike the 56-day deferral for blood donation. The amount allowed in a donation varies vastly from country to country, but generally does not exceed two donations, each as much as a liter, per seven-day period. The danger with this method was that if the wrong red blood cells were returned to the donor, a serious and potentially fatal transfusion reaction could occur. Requiring donors to recite their names and ID numbers on returned bags of red cells minimized this risk. This procedure has largely become obsolete in favor of the automated method. The automated method uses a very similar process. The difference is that the collection, separation, and return are all performed inside a machine connected to the donor through a needle in the arm, typically the antecubital vein. There is no risk of receiving the wrong red cells. [12] The devices used are very similar to the devices used for therapeutic plasmapheresis and the potential for citrate toxicity is similar. The potential risks are explained to prospective donors at the first donation, and most donors tolerate the procedure well. [13]

Complications of Plasmapheresis

Plasmapheresis is an invasive procedure with potential complications relating to vascular access, the extracorporeal procedure itself, the removal of coagulation factors and other plasma proteins, and the use of large volumes of pooled plasma products. Adverse events of the procedure occur in one third of patients, are usually mild, and rarely lead to discontinuation or hospital admission. [14] They comprise fever, urticaria, pruritus, hypocalcemic symptoms, and hypotension and are more common with fresh frozen plasma volume replacement than with albumin/saline. More severe reactions include anaphylaxis, thrombocytopenia, and hemorrhage and occur in 0.5% to 3.1% of treated patients. [15] The risk of hemorrhage after plasmapheresis is increased in the presence of uremia, coagulopathy, and thrombocytopenia or after a surgical procedure including renal biopsy. Complications of vascular access include hematomas, pneumothorax, thromboses, and catheter infections.

REFERENCE

1. Nikolsky PV. Materiali K. uchenigu o pemphigus foliaceus, http:// emedicine.medscape.com/article/1063347-followup.
2. Bastuji-Garin S, Souissi R, Blum L. J Invest Dermatol.1995; 104(2):302-5.
3. Ribeiro JM, Valenzuela JG, Pham VM, Kleeman L, Barbian KD, Favreau AJ. Am J Trop Med Hyg. 2010; 82(6):1060-75
4. Aoki V, Sousa JX Jr, Diaz LA. Dermatol Clin. 2011; 29(3):413-8.
5. Diaz LA, Arteaga LA, Hilario-Vargas J. J Invest Dermatol. 2004; 123(6):1045-51.
6. Rodrigues DB, Pereira SA, dos Reis MA. Arch Pathol Lab Med. 2009; 133(1):97-100.
7. Qian Y, Prisayanh P, Andraca E. J Invest Dermatol. 2011;131(4): 985–987.
8. Abreu-Velez AM, Howard MS, Yi H, Gao W, Hashimoto T, Grossniklaus HE. J Clin Immunol. 2011; 31(3):356-68.
9. Ogawa MM, Hashimoto T, Konohana A, Castro RM, Nishikawa T. Arch Dermatol Res. 1990; 282(2):84-8.
10. Ogawa MM, Hashimoto T, Nishikawa T, Castro RM. Clin Exp Dermatol. 1989; 14(1):29-31.
11. HO Dichtelmuller,L Biesert,F Fabbrizzi, http://onlinelibrary.wiley.com/doi/10.1111/j.1537-2995.2009.02222.x/abstract
12. Donating plasma: The donation process, www.biolifeplasma.com/become-donor/eligibility.html
13. Octapharma Plasma-Plasma Donation Safety, www.octapharmaplasma.com/plasma_donation/plasma_donation_safety/
14. SheminD,Briggs, GreenanM. J Clin Apher. 2007; 22:270-276.
15. Mokrzychi MH, Kaplan AA: Am J Kidney Dis. 1994; 23:817-827.