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Der Pharmacia Lettre, 2021, 13 (6): 65-66
(http: //scholarsresearchlibrary. com/archive. html)

ISSN 0975-5071
USA CODEN: DPLEB4

Continuous Ultrafiltration as an Immunomodulatory Therapy during Cardiac Surgery and Cardiopulmonary Bypass

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COMMENTARY

Cardiac surgery and cardiopulmonary bypass can be associated with systemic inflammation, post-operative vasoplegic shock and organ dysfunction. The use of intra-operative ultrafiltration has been hypothesized to be an immunomodulatory therapy to dampen these toxic effects and enhance recovery for infants and children undergoing heart surgery. There are a variety of intra-operative ultrafiltration protocols and it is unclear which yields the highest clinical benefit.

The use of cardiopulmonary bypass (CPB) was first used in 1953 by Dr. John Gibbon to facilitate the repair of an atrial septal defect in an 18-year-old woman [1]. This revolutionized the field of cardiac care as surgeons could now arrest the heart to complete complex repairs of both congenital and acquired forms of heart disease. Despite its necessity, cardiac, pulmonary, renal, and coagulation dysfunction were observed following cardiac surgery and CPB. In 1983, Dr. James Kirklin identified that the foreign surface of the CPB circuit activates the complement system and innate immune response, thereby, explaining post-operative organ dysfunction and inflammation [2,3]. Infants and children are especially vulnerable to these adverse effects of CPB due to their small body size and circulating blood volume relative to the CPB circuit. The use of intraoperative ultrafiltration has been used since the 1980s to ameliorate the deleterious hemodilution and systemic inflammation associated with pediatric cardiac surgery and CPB [4].

There are many types of ultrafiltration protocols that can be categorized into two main groups. Non-continuous forms such as conventional ultrafiltration, modified ultrafiltration, and simple modified ultrafiltration are used for a short period of time at the end of the CPB, while continuous forms such as zero-balance ultrafiltration or subzero-balance ultrafiltration are used during the entire CPB time [4]. Non-continuous forms have shown a significant reduction in bleeding and transfusion complications [4]. Continuous forms are hypothesized to extract inflammatory cytokines throughout the entire CPB time, thereby acting as an immunomodulatory therapy, to enhance post-operative cardiopulmonary function and overall recovery for infants and children undergoing heart surgery [4].

There has been little investigation on precisely which components of the innate immune system are extracted by ultrafiltration, which is

germane to the hypothesized mechanism of action of the therapy. Furthermore, randomized studies in both pediatric and adult cardiac surgery patients hint that high rates of effluent removal could be a key factor in determining efficacy of the therapy [4]. Our ongoing research seeks to describe the dynamic activation of complement, cytokine, chemokine and neutrophil adhesion pathways, as well as which factors are extracted by ultrafiltration. We hypothesize that extracting activated inflammatory factors such as complement C3a, C5a and pro-inflammatory interleukin cytokines *via* continuous ultrafiltration will dampen the systemic inflammatory response and yield enhanced recovery for children undergoing heart surgery.

CONCLUSION

Ultrafiltration is used widely in pediatric cardiac surgery and CPB; however, there are a variety of protocols and differences of expert opinion. Ongoing investigations seek to establish the optimal ultrafiltration protocol as an immunomodulatory therapy to enhance recovery after children's heart surgery. Furthermore, these investigations can form a strong foundation for knowledge translation to the adult cardiac surgery population where CPB-associated inflammation is also observed that do not routinely receive any form of ultrafiltration.

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