

Title of Manuscript: A Canadian perception of the nursing practice, research, and theoretical implications associated with Autologous Cell Transplantation

Word Count: 2677

Abstract

Heart failure is a progressive disorder. An estimated 400,000 Canadians are diagnosed annually with heart failure, and a quarter experience severe heart failure that is unresponsive to medical therapy. Autologous cell transplantation (ACT) has been proposed as a new approach for cardiac repair, and holds enormous potential for the regeneration of injured myocardium cells. Currently, ACT is under investigation in Canada. The use of ACT as a treatment alternative for heart failure patients has been established over the past 5 years across Europe and the United States. This paper will present a Canadian perception of the nursing practice, research, and theoretical implications associated with this new and innovative therapy.

Key words for indexing:

Patient education

Heart failure

Self-care

Symptom management

Complications

INTRODUCTION

Cell transplantation is an exciting and promising area for practice, research, and education throughout all areas of health care, particularly in the cardiovascular nursing environment. Autologous Skeletal Myoblast Transplantation, the use of a patient's own cells for transplantation, has been proposed as a new approach for cardiac repair ^{1, 2, 3, 4}. This procedure holds enormous potential for the regeneration of injured heart cells ¹. The purpose of this paper will be to discuss the implications for nursing associated with this innovative therapy.

Heart Failure

Heart failure affects 1 to 2% of the Canadian population ⁵. The incidence of heart failure is increasing annually in Canada ⁶. Currently, there are more than 350,000 Canadians affected with this cardiovascular condition, and approximately 50,000 new cases added each year ^{5, 6, 7}. Of those diagnosed, approximately 90,000 Canadians will require aggressive treatment and frequent hospitalizations, especially in the end-stage of the disease process⁷. The diagnosis for heart failure is foreboding for patients with a 1-year mortality ranging from 11% in less severe patients, to 44% in more severe patients depending on the New York Heart Association (NYHA) class ^{5, 8}. Compared with other major disease states, heart failure is associated with one of the highest number of days spent in hospitals, and the third highest number of patients affected ⁷. It is the most common cause of hospitalization in people over the age of 65 ⁷. Morbidity, including hospital readmissions is substantial; almost one-third of all hospital admissions are readmissions, with one-fifth of patients (over 14,000) being admitted two or more times, placing a severe strain on the Canadian health care system ^{7, 9}.

As the number of individuals affected with heart failure continues to spiral, there have been dramatic increases in its associated health care costs. Health care expenditures for the treatment of this illness have escalated to over one billion Canadian dollars annually for inpatient care alone ^{5,6}. This is approximately 3 % of the Canadian health care budget ^{6,10}.

Treatments options are limited. The availability of reversal therapies such as heart transplantation and left ventricular assist devices are very low ⁵. Pharmacological treatment regimes are the foundation of heart failure management. However, these therapies only serve to slow the progression of heart failure ^{5,6}.

The epidemiology and economics of heart failure have exerted immense demands on families, society and the health care system ⁷. In response, health care providers are implementing alternative approaches to meet the diverse, yet resource intensive, health care needs of this population. A novel approach in the treatment of advanced heart failure is the concept of Autologous Skeletal Myoblast Cell Transplantation (ACT). This procedure involves the use of a patient's own cells for transplantation to augment ventricular function. Autologous skeletal myoblast cell transplantation has been proposed as a new approach for cardiac repair ^{1,2,3,4,11}. The outcomes of this therapeutic intervention may have a significant impact on the lives of patients with heart failure as it can serve to decrease the severity of symptoms, while enhancing the individuals' overall quality of life ².

Specifically, ACT involves the successful engraftment of the patient's own cells into their heart muscle. Stem cells are known as "pluripotent" cells, meaning they can produce many kinds of cells when transplanted, hence it is imperative that the cells be

pre-differentiated before being transplanted. An approach to pre-differentiation involves the harvesting of the cells in serum-containing media that is derived from fetuses. The most common source of fetal serum comes from cows, e.g. fetal bovine serum (FBS)^{1, 2, 3, 4}.

Autologous cell transplantation is a complex treatment that is made up of two procedures: a biopsy and a surgery. These procedures are usually conducted in specialized medical centers. The biopsy encompasses the harvesting of the patient's own cells. This procedure involves obtaining a ten gram specimen of skeletal muscle from the patient's thigh, which is then transported in a preservation medium to the Cell Therapy Laboratory^{1, 2, 3, 4, 11}. The cells are then separated and expanded in the laboratory until approximately 1.2 billion cells are available in order to replace the number of cells which were lost during myocardial infarction^{12, 13}. Harvesting of the cells in the laboratory takes between two to three weeks to occur. The cells are then shipped to the cardiac surgery department for implantation into the patient.

The second procedure requires surgery to inject the harvested cells into the patient's infarcted region^{12, 13}. If the cells maintain viability in the myocardium, an improvement in heart function will occur and the severity of the HF will be reduced^{12, 13}. However, should the new cells not be viable, then an exacerbation of the patient's current state of health may occur or death may ensue^{3, 4, 11, 12, 13}. The length of time for the entire procedure can range between 3-6 months depending on the multiplication process. The surgical procedure requires opening the sternum to gain access to the heart. This is an invasive procedure as the heart is stopped for the injection of the cells. Prior to the second procedure, the patient may receive medication to reduce the side-effects caused

by the serum-containing medium. These side-effects include: nausea, fever, chills, and hives ^{3,4}.

The patients' in-hospital experience is characterized by having to ambulate at least 3 times a day, to increase circulation and prevent the formation of blood clots ⁹. In addition, HF patients are required to perform deep breathing and coughing exercises to further enhance circulation and avoid pulmonary complications, and are encouraged to avoid drinking large volumes of fluid to prevent the onset of complications such as pulmonary edema and congestive heart failure ⁹. Moreover, patients are encouraged to carry out many of the self-care behaviours performed during hospitalization, such as ambulation, deep breathing and coughing, and fluid restrictions upon discharge ⁹.

Post-procedure, patients are at increased risk for complications related to infections and bleeding. To prevent the occurrence of complications, patients are required to take numerous medications ^{3,4,11,12,13}. As well, the need for periodic transfusions of red blood cells and platelets is quite high due to the increased risk of bleeding. The patient is required to stay in hospital until normal blood values return. The length of hospitalization may last up to 10 weeks ^{3,4,11,12,13}. Usually, one year is required for recovery post-ACT as this is the time interval required for blood cells and immune systems to recover, as well as for the transplanted cells to begin to reproduce. Immediately following the ACT procedure, the patient is required to undergo many of the same kinds of tests that they experienced prior to the transplant to monitor changes in condition. As well, supplementary nutrition may be required to compensate for nausea and diarrhea.

Currently, cell transplantation is under investigation in Canada. However, the use of ACT as a treatment alternative for heart failure patients has been established over the past 5 years across Europe and the United States^{13, 15, 16, 17}. Data obtained from European and American clinical settings that have incorporated ACT as a treatment option for heart failure patients provide support for the use of this intervention as a means of prolonging the life span of the heart failure patient, while significantly reducing the prevalence and exacerbation of symptoms^{13, 15, 16, 17}. This new and innovative therapy has significant implications for nursing. Implications for nursing practice, research, and theory will be discussed in the remainder of this paper.

NURSING IMPLICATIONS

Practice Implications

The length of time for ACT ranges between 3-6 months^{1, 2}. Patients are required to endure two procedures. The preparation and care before, during, and after each procedure is important in order to prevent complications, exacerbations of illness, and ensure successful harvesting of cells. Self-care activities before, during, and after each procedure include: routine monitoring of fluid and nutrition intake; ongoing assessment and modification of activity performance, such as bathing, dressing, and moving about; the management of new and at times, complex drug therapies; early recognition and response to signs and symptoms of pulmonary, wound, and abdominal complications such as pain, dyspnea, fatigue, and edema; and management of stress and emotional fatigue⁶. Nurses are required to have a strong knowledge base of pre, peri, and post procedures to be able to effectively educate their patients. The knowledge required by nurses includes a thorough understanding of the different types of cells being transplanted, source of the

cell product—autologous versus allogeneic, the different procedures related to how the cells are transplanted, the complications associated with the ACT procedure, and self-care behaviours required pre-peri, and post-procedure. Nurses may consider working closely with colleagues from various parts of the world who have established a staff training program or workshop to ensure that nursing staff have a baseline understanding of ACT. Individualization of the workshop/training session can occur once increase familiarity with the procedure has been acquired.

Similarly, the design of patient education initiatives could mimic similar patient education initiatives that have been used at different sites across the globe, however individualization of the patient education initiatives to reflect the learning needs specific to the heart failure patients from specific geographical locations (e.g. Canada, US, Europe) could be considered. Individualization of learning needs can occur through the use of research initiatives in which the learning needs of the patient at each stage of the ACT procedure can be assessed; a teaching intervention can be designed to reflect these needs; followed by the evaluation of the intervention.

As well, the need for patients to be educated throughout all stages of the procedure is imperative to prevent the occurrence of new symptoms and complications and for the management of existing conditions to effectively occur¹⁸. Specifically, nurses are encouraged to consider providing information related to the ACT surgical procedures, and how this intervention will assist with decreased severity of symptoms, while enhancing the patient's overall quality of life. As well, teaching related to the immediate post-operative management, including drainage tubes, ventilator support, endotracheal tube, cardiac monitoring, pain management, and the need for the continued use of drug

therapy is necessary. Finally, teaching related to the need for patients to partake in post-discharge self-care behaviours such as: use of incentive spirometers, deep breathing and coughing exercises, nutrition, activity performance, and symptom management is encouraged as this can enhance the patient's recovery process, while decreasing their overall level of anxiety, and rate of morbidity and mortality ^{13, 15}.

Furthermore, the delivery of patient focused psychosocial counseling interventions can be considered as anecdotal data suggests that patients feel overwhelmed throughout various stages of the surgical procedure. Specifically, the multiplication and harvesting stages in which a length of time is required for the cells to divide (during multiplication) and to attach to the heart and turn into heart cells (during harvesting) ^{12, 13}. Psychosocial counseling interventions may encompass motivating, encouraging, and supporting the client in treatment related decision-making endeavors. Post-operatively, psychosocial counseling in the form of debriefing related to the success or failure of the ACT procedure will be required. In addition, since the use of autologous cells within the cardiac population is a relatively new procedure, the long-term outcome of this technique is not known, hence the need for ongoing psychosocial counseling, weeks after the procedure has been performed, is necessary to meet the specific needs of the client within the post-discharge environment.

Finally, a familiarity with the management, observation, and monitoring of arrhythmic events may be necessary for nurses caring for these patients, as ACT patients are at an increased risk for experiencing cardiac arrhythmias ^{12, 13}. Preliminary findings report approximately, 40% of autologous cell transplantation patients experienced ventricular arrhythmias ^{12, 13}. Arrhythmias or dysrhythmias are abnormal heart rhythms

and can cause the heart to pump less effectively. To manage ventricular arrhythmias, a prophylactic implantation of an automatic internal cardioversion-defibrillator (AICD) combined with the use of amiodarone (an anti-arrhythmic drug) tend to be used most often post-cell transplantation^{12, 13}. Hence, nurses may require additional knowledge of AICD care and practice procedures. For patients and families, this acuity of the presenting need for an AICD may be frightening with uncertainty surround the potential for a fatal outcome. Nurses are in the best position in identifying the knowledge deficit gaps and serving as a source of information to help decrease anxiety for patients and their families.

Research Implications

With respect to nursing research, the area of ACT within the heart failure population has yet to be explored. Possible areas for nursing research include descriptive, non-experimental studies to address a gap in the heart failure literature, related to ACT. The heart failure patients' learning needs during the different phases of the procedure to assess the adequacy of continuity of care throughout the cell transplantation process is another potential area for investigation

As well, experimental and quasi-experimental designs can be used to evaluate the effectiveness and efficacy of different nursing interventions aimed at improving or ensuring enhanced quality of care is being delivered to these individuals. In addition, qualitative designs can be employed to gain further insights into the needs of patients with respect to continuity of nursing care throughout cell transplantation procedures.

Currently, a descriptive non-experimental pilot study is about to begin with the aim of describing the quality of life of heart failure patients as they undergo cell

transplant surgery. Specifically, the study seeks to answer the following research questions: 1.) what is the quality of life of heart failure patients as they undergo cell transplant surgery? and 2.) What is the quality of life of heart failure patients 1 month post cell transplant surgery? This pilot study will address a gap in the heart failure literature, related to the quality of life of heart failure patients who undergo cell transplantation. The information obtained from this pilot study will be used to design appropriate interventions aimed at addressing specific quality of life issues related to cell transplantation. As well, the results will be used to shape the design of policy and nursing practice guidelines for caring for heart failure patients who have undergone or are currently going through this new and innovative treatment.

Theoretical Implications

Anxiety, pain, self-care, and symptom and complication management have not been explored from the perspective of cell transplantation. Continued exploration of these concepts as they relate to ACT is required. As well, expansion and testing of existing theories that address quality of life, patient education, and self-care is recommended to address ACT.

CONCLUSION

ACT appears to be a viable treatment option for heart failure patients. Nurses are in a unique position to contribute to the body of knowledge in defining care for heart failure patients who receive ACT. Determining that emotional support for patients during the acute and post-discharge phases is adequate, as well as providing teaching and psychosocial counseling where deficiencies exist will facilitate achievement of positive

outcomes. In addition, nursing research, particularly in the arena of quality of life manifestations, is essential for evaluating patient outcomes.

References

1. Al-Radi OO, Rao V, Li R, Yau T, & Weisel RD. Cardiac Cell Transplantation: Closer to Bedside. *Ann Thorac Surg* 2003; 75:S, 674-677.
2. Hagege AA, Carrion C, Menasche P, et al. Viability and differentiation of autologous skeletal myoblast grafts in ischaemic cardiomyopathy. *Lancet North Am Ed* 2003; 361(9356): 491-492.
3. Hassink RJ, de la Riviere AB, Mummery CL, Doevendans PA. Transplantation of Cells for Cardiac Repair. *J Am Coll Cardiol* 2003; 41(5): 711-717.
4. Nugent HM, Edelman ER, Tissue Engineering Therapy for Cardiovascular Disease. *Circ Res* 2003; 92:1068-1078.
5. Bentkover JD, Stewart EJ, Ignaszewski A, Lepage S, Liu P, Cooper J. New technologies and potential cost savings related to morbidity and mortality reduction in Class III/IV heart failure patients in Canada. *Int J Cardiol* 2003; 88:33-41.
6. Lui P, Arnold M, Belenkie I, et al. Canadian Cardiovascular Society. The 2001 Canadian Cardiovascular Society consensus guideline update for the management and prevention of heart failure. *Can J Cardiol* 2001;17 Suppl E:5E-25E.
7. Tsuyuki RT, Shibata MC, Nilsson C, Hervas-Malo M. Contemporary burden of illness of congestive heart failure in Canada. *Can J Cardiol* 2003; 19:436-438.
8. Montague T, Barnes M, Taylor L et al. Assessing appropriateness of treatment. A case study of transplantation in older patients with congestive heart failure. *Can J Cardiol* 1996; 12(1):47-52.
9. Brophy J. Epidemiology of congestive heart failure: Canadian data from 1970 to 1989. *Can J Cardiol* 1992; 8:495-498.

10. Federal Support for Health Care: The Facts. *Department of Finance Canada*. October 2003. Retrieved Aug 4, 2004. from http://www.fin.gc.ca/facts/fshc5_e.html.
11. Sim EKW, Jiang S, Lei Y, Lim YL, Ooi OC, Haider, KH. Skeletal Myoblast Transplant in Heart Failure. *J Card Surg* 2003; 18(4):319-327
12. Menasche P, Hagege A, Sorsin M, et al. Myoblast Transplantation for Heart Failure. *Lancet North Am Ed* 2002; 357(9252): 279-280.
13. Menasche P, Hagege A, Vilquin JT, et al. Autologous Skeletal Myoblast Transplantation for Severe Post-infarction Left Ventricular Dysfunction. *J Am Coll Cardiol* 2003; 41(7):1078-1083.
14. Weisel RD, Li R, Mickle D, Yau TM. Cell transplantation comes of age. *J Thorac Cardiovasc Surg* 2001; 121(5):835-836.
15. Chachques JC, Gonzales JH, Trainini JC. Cardiomioplast. *Cel. Rev. Argent. Cardiology* 2003; 71:138-145.
16. Dib N, et al. Safety and feasibility of autologous myoblast transplantation in patients with ischemic cardiomyopathy: Interim results from the United States experience. *Circulation* 2002; 106 supplement II: II-463 [Abstract 2291].
17. Haider HK, Tan AC, Aziz S, Chachques JC, Sim EK. Myoblast Transplantation for Cardiac Repair: A Clinical Perspective. *Mol Ther* 2004; 9(1):14-23.
18. Redman N. *The Practice of Patient Education*. St. Louis: Mosby; 2001.

This manuscript has been accepted for publication by ; Fredericks, S., & DaSilva, M. (2007). A Canadian perception of the nursing practice, research, and theoretical implications associated with Autologous cell transplantation. *The Journal of Cardiovascular Nursing*, 22, 5, pp. 375-379. (Focus Article: Used for Continuing education credit).