EDITORIAL

This edition of the New Zealand Medical Student Journal continues to showcase original student research from around the country and overseas. The interest and submissions directed toward the journal are evidence that we are fulfilling an important publication niche. Primarily, we see our role as an education tool for students seeking experience in writing and submitting research. Our submission and review process prepares students for future publications in other peer reviewed journals. We extend our sincere thanks to academic advisors and reviewers for their input to the submission process, and to Minister of Health, Right Honourable Annette King for the generous funding of two editions of the journal.

We also publish feature articles that are interesting, informative and thought provoking. In this issue we look at the new Green Prescription Scheme, explore the option of taking a year out of the undergraduate medical programme to conduct research, provide details on how to write academic articles, and find out about an elective in the Kingdom of Cambodia. Letters to the editor in response to any article are welcome.

We are also proud to announce the Inaugural New Zealand Medical Students' Journal Writing Competition. This new award recognises excellence in academic writing by New Zealand medical students. We look forward to presenting so of the high quality submissions in our next edition.

With best wishes for the new year and your continued studies,

NZMSJ Executive

REVIEW ARTICLE

Use of autologous skeletal myoblasts in cellular cardiomyoplasty

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INTRODUCTION

Discoveries of molecular aspects of cellular function are changing concepts of health and disease.[1] However despite recent advances in the treatment of myocardial infarction and heart failure, the heart's capacity for repair and regeneration is limited.[2] Restoring blood flow, improving perfusion, reducing clinical symptoms and augmenting ventricular function are currents goals of treatment after myocardial infarction. Other than replacing the whole heart (cardiac transplantation) no standard clinical procedure is available to restore or regenerate the damaged myocardium following a heart attack.[11]

The pharmacological therapy of heart failure includes many drugs, such as angiotensin-converting inhibitors, angiotensin II-receptors antagonist, diuretics , -adrenergic blockers and inotropic therapy. The emphasis of these therapies is on migrating the consequences of myocardial damage; they do not reverse the structural cause of heart failure, which is the permanent loss of myocardial tissue.[10] The ideal therapy would be to replace damaged tissue with healthy tissue.[2, 3, 5, 15] This is the goal of cellular cardiomyoplasty.

Cellular cardiomyoplasty consists of in situ cell implantation intended to induce the growth of new muscle fibers and the development of angiogenesis in the damaged myocardium.[3] The objective of cellular cardiomyoplasty is to limit the consequences of decreased contractile function and compliance of damaged ventricles following myocardial infarction.[3]

Current possibilities in myogenic and angiogenic cell therapy for myocardial regeneration are the transplantation of autologous cell lines into myocardium. These cells include autologous myoblasts from skeletal muscle (satellite cells), bone marrow-derived mesenchymal stem cells, smooth muscle cells, vascular endothelial cells, and embryonic stem cells. [3, 4, 6, 12]

Autologous Skeletal Myoblasts

Satellite cells, first identified in skeletal muscle in 1961, have been confirmed as myogenic precursor cell responsible for growth, repair, and adaptation to physiologic demands of skeletal muscle.[11] The identification of muscle satellite cells has led to major advances in our understanding of muscle regeneration.[14]

Although satellite cells have been considered as monopotential stem cells, recent in vivo and in vitro studies early indicate that satellite cells from adult mammalian skeletal muscle are multipotential stem cells.[11,14] The use of cultured autologous skeletal myoblasts, does not raise immunological, ethical, tumorogenesis, or donor availability issues. Cellular cardiomyoplasty using autologous myogenic cells offers a number of advantages: they avoid the need for immunosuppressive treatment[2] because they are allogenic organs; they are not transformed cells, and tumorigenesis is unlikely; they form gap junctions with cardiac moycytes and arrhytmia has not been a complication; they are not fetal tissue and will not engender ethical issues; they are readily available from all patients and donor availability is not a limitation.[11]

Satellite cells have been shown to proliferate and differentiate into new myotubes in culture. Myoblasts also have the capacity to form new muscle fibers or fuse to existing fibers when introduced directly into the skeletal muscle of a synergic host.[9] The communication between the grafted skeletal myocytes and native myocardial cell is probably the key for the acquisition of myocardial phenotypes from the skeletal cells .[10] Myoblasts have been shown to differentiate into skeletal myoblasts when injected in the center of the scar. In contrast, when injected into in the scar periphery (close to the healthy tissue) they differentiate into immature myocardial cells.[10]

Cell Culture

In European Hospital Georges Pompidou, Dr. Chachques has developed a technique harvesting a sample of the thigh vastus lateralis, through a 5 cm incision under local anesthesia. The skeletal muscle from biopsy is subjected to enzymatic digestion to release satellite cells. The cells are then washed and the enzymatic reaction is stopped by adding one ml of the patient's serum. A benefit of human autologous serum cell culture is that it can be performed without risk of prion, viral or zoonoses contamination.[3] Cells are collected by sedimentation and the supernatant is discarded. Cell cultures are incubated for three weeks at 37 °C in a humidified atmosphere containing 5% CO_2.[6] Commonly, after three weeks, more than 200 X 10^6 cells are routinely obtained.[6] Recommended density of implanted cells is between 50 to 70 million cells per ml. Cellular implantation can be performed by an epicardial or an endovascular delivery approach[6].

Clinical Trials Using Myoblasts

Menasché's group in Paris began using skeletal myoblasts in cell cardiomioplasty in humans, in 2000.[4] Autologous cultivated skeletal myoblasts have been implanted in postinfartion myocardial scars during coronary artery bypass graft surgery.[3, 6, 8, 12]

As of 2003 over 100 patients had been treated worldwide[3], with different techniques and variety of cell types.[3, 4] Cellular cardiomyoplasty using autologous skeletal myoblasts was performed by the group of Chachques in 18 patients by 2003.[3]

Inclusion criteria for adult patients are: a low ejection fraction, akinesis and non-viable post-infarction scar.[3] In 2002 in Argentina, Trainini *et al.* reported a case of a patient with a diagnosis of ischemic-necrotic myocardiopathy who was treated with an implant of autologous skeletal myoblasts. This implant was the first one of this kind performed in Latin America[5] and results were favorable.

Cellular cardiomyoplasty promises a variety of beneficial effects such as: reduction of size and fibrosis of infarct scars, limitation of postischemic ventricular remodeling, improved of left ventricular wall thickening, and an increase of regional myocardial contractility (these are preliminary results in humans)[6]. Implanted cells orient themselves against cardiac stress preventing thinning and dilatation of the injured region.

CONCLUSIONS

Trainini *et al.* confirms that no definitive treatment exists and that such therapy is an urgent research priority.[8] Cell therapy has emerged as a strategy for the treatment of many human diseases.[11] Myogenic cell grafting within the myocardium to improve contractile function has emerged as a promising technique for ischemic left ventricular systolic dysfunction.[2, 15] This novel therapy may be a dream, but if successful, it could be a definitive treatment for heart failure.[9] Our group (México-Research Group at Universidad Autónoma de Ciudad Juárez) is currently working on animal model of myocardial infarction. Our goal is to regenerate a myocardial scar with satellite cells. While thus far, success has been elusive, we continue strive for a day when we can provide a definitive therapy for heart failure.

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ARTICLE

Should routine antenatal screening for HIV be introduced into New Zealand?

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The issue of antenatal HIV screening becoming routine, rather than based on risk assessment, which is currently the case, has become an important discussion point in New Zealand. This article aims to present arguments for and against the adoption of this new screening policy.

Perinatal transmission of the human immunodeficiency virus can occur during multiple stages, this includes the intrauterine (during pregnancy), intrapartum (during labour) and the postpartum (after delivery through breast-feeding) periods.[1, 2] The risk of transmission from mother to baby varies from 15-45%, with factors such as viral load, viral subtype, maternal immune status, presence of maternal sexually transmitted disease (STD), obstetric technique, labour duration as well as they extent of breastfeeding in infancy accounting to various degrees for this variability.[1, 2] Breast-feeding in particular sees to be an important mode of transmission, increasing the risk by approximately 10-20%.[2] This is why mothers with HIV are advised to use other available and effective alternative to breast-feeding.

In 1994 research in the United States showed that giving AZT to HIV infected women and to their infants after birth could reduce the rate of HIV transmission from mother to child from 25% to 8%, with even further reduction after implementation of other preventive measures, such as caesarean delivery and refraining from breast-feeding.[3] With all the prevention strategies in place the risk of perinatal transmission can be reduced to below 2%.[2, 4] Since the advent of such effective interruption of transmission of HIV from mother to baby, the antenatal identification of HIV-infected women has become of great importance in reducing the number of newborns born HIV-positive of seroconverting after birth.

In many countries overseas, universal counseling as well as offering and HIV test to all pregnant women has been instigated. In 1997 the Ministry of Health in New Zealand developed interim guidelines for risk-based HIV testing of pregnant women.[4] This means that women should be asked a set of questions which screen for various risk behaviors and if any risk factors are present or unclear, they should then be offered counseling and voluntary testing. However, it has become apparent that this policy is not being adhered to very well, and therefore reassessment of the screening strategy needs to be done.[5]

There are several reasons why the implementation of the current risk-based screening method is not adequate. Time constrains, lack of skills at counseling as well as the inaccurate assessment of maternal risk are all cited as factors that play a role.[1] Other reasons that also influence the reluctance of health professionals to ask question about risk status are the generally low rates of HIV in the community and the feeling of fear of offending their patients.[4] There is also a certain degree of embarrassment when addressing such issues, both on the side of the health professional and the woman. Moreover, women may feel targeted or singled out when HIV testing is recommended and this has the potential of having a negative impact on the maternity carer/woman relationship. Thus, a proportion of at-risk women are not being tested. Another issue to consider is that some women may not be aware of, or underestimate, their risk and therefore would be missed as well.

Putting in practice a routine screening policy has several advantages, which would go some way to counter the barriers of the current screening program. One such advantages is that it would increase acceptability of HIV screening, as it would remove the stigma of being targeted, especially in the populations, which are already at increased risk, such as specific ethnicities or socio-economic groups.[1, 6] Since pre-test counseling would have to be widely implemented, this would provided a good setting for health professionals to discuss HIV and other sexually transmitted diseases, as well as exploring any personal issues related to sexual health. Educating women and thereby increasing knowledge on a population scale would go a low way to increase awareness and reduce stigmatization of the subject. Moreover, women who are better informed about the risks and transmissibility of HIV are more likely to address risky behaviors since they would be more aware of their consequences. This would be a form of primary prevention in those at risk of infection.

The primary reason for screening of pregnant women, however, is to reduce the incidence of perinatal HIV infection. In the 5-year period from 1999-2003, 13 children were diagnosed with HIV, of whom 5 were born to mothers whose status was not known when they were pregnant.[7] According to the discussion document on HIV screening in pregnancy publish in October 2003 by the National Health Committee, if all infected pregnant women in New Zealand were detected, an additional 4 -18 would be diagnosed with HIV annually, and if intervention to prevent perinatal HIV transmission were taken up by all of these women, it is estimated that on average 1-4 perinatal HIV infections could be prevented each year. It should be noted that these figures are only estimates. Although the main route of HIV transmission in New Zealand is still through men having sex with men, the number of men and women infected by heterosexual spread has increased in recent years.[7] With more women becoming infected, the problem of perinatal HIV transmission may become more marked in the years to come. However, with routine screening, more of these women would be diagnosed early and thus would be able to make informed choices