CARDIOLOGY AND STEM CELL RESEARCH

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STEM CELL RESEARCH

In 2011 Earlier this year the British Heart Foundation (BHF) wrote to Cardiologists throughout the UK advertising the "Mending Broken Hearts" research programme appealing for financial support. Shortly afterwards, a similar advertisement and appeal appeared in one of the main Catholic newspapers. As the advertisement mentioned "stem cells" I decided to seek further information regarding the BHF and the "Mending Broken Hearts" appeal. I particularly wanted to find out what type of stem cell research the BHF supports and whether it included unethical human embryonic stem cell research.

Consulting the BHF website the answer was clear. The mission statement includes the following:

"We fund research that uses stem cells from human or animal embryos, and adult tissues, because we believe that both approaches are important. Many of the advances in stem cell research have only been possible through the knowledge and insight gained using embryonic stem cells. We recognise that this is an area some people have concerns about…"

The claim that "advances in stem cell research have only been possible through the knowledge and insight gained using embryonic stem cells" is disputed by many leaders in that area of research. It is also important to note that, to date, no clinically important advances have been made using human embryonic stem cells in any area of medicine but that many important advances have been made using adult stem cells and human umbilical cord blood stem cells.

In cardiology, several clinical trials involving human adult stem cells have been reported. The main areas of cardiovascular medicine where adult stem cell research is on going and showing considerable promise are: heart failure, acute myocardial infarction and chronic intractable angina.

The STAR-heart study,[1] presented and published in 2010, explored the acute and long-term effects of intracoronary stem cell transplantation in 191 patients with chronic heart failure. It is important to emphasise that this study and other stem cell studies have limitations and further work is needed to explore the potential benefits that adult stem cells may offer.

In this study, the treatment group consisted of 191 patients, all of whom had chronic heart failure of ischaemic origin with previous myocardial infarction. The average left ventricular ejection fraction (a marker of left ventricular systolic function) in this group was 29.4%. A normal ejection fraction is usually >55% and figures less than 30% tend to represent severe heart failure or systolic impairment. All 191 subjects were receiving conventional therapy for heart failure. Each of these patients was, in addition, treated with an intracoronary infusion of autologous bone marrow mononuclear cells, a form of adult stem cell treatment.

One of the limitations of this study is that it wasn't a randomised controlled trial. The control group consisted of 200 patients, all of whom also had chronic heart failure of ischaemic origin and the average ejection fraction was slightly better than that of the treatment group at 36.1%. All were receiving standard heart failure therapy. These subjects had been offered the opportunity to receive

the same stem cell treatment as those in the treatment group but had declined the offer and in that way were considered part of the control group. Both groups were followed over a five-year period.

Despite the study limitations, the results presented are interesting. In the control group, the average ejection fraction dropped slightly to 32.3% (from initial value of 36.1%) while that of the treatment group improved to 36.8% (from 29.4%). There was a significant improvement in reported heart failure symptoms among those in the treatment group with the New York Heart Association (NYHA) score improving from an initial value of 3.22 to 2.25 with a simultaneous deterioration in the control group from 3.06 to 3.5 over the study period. NYHA scores of 3 and 4 represent more severe functional limitations and symptoms related to heart failure, while scores of 1 and 2 represent better symptom control. Most impressive was the major difference observed in the mortality rates between the two groups. There were 32 deaths among the 200 control subjects, representing a mortality rate of 3.68% per annum, while only 7 deaths occurred among the 191 treatment subjects, a mortality rate of 0.75% per annum. In addition, no significant adverse effects were noted in the treatment group, suggesting that this form of stem cell treatment is safe and well tolerated, at least over a 5-year period.

The REPAIR-AMI study,[2] also published in 2010, assessed the clinical outcome 2 years after intracoronary administration of bone marrow-derived progenitor cells in acute myocardial infarction. This was also a small study but, unlike the STAR-heart trial, it was a randomised, double-blind, controlled study. A total of 204 patients were studied. All had suffered acute myocardial infarction and all had received successful revascularisation with percutaneous intervention. All patients subsequently received standard secondary prevention therapy and any additional conventional therapy considered necessary. They were then randomised to receive intracoronary infusion of autologous bone marrow-derived stem cells or intracoronary infusion of a saline solution. The additional active treatment or placebo solution was administered between 3 and 7 days after the initial successful revascularisation intervention. Subjects were followed up over 2 years and the results can be summarised as follows:

•Death, myocardial infarction and the need for further revascularisation was reduced in the active treatment group relative to the placebo group ($p=0.025$)

•Death, recurrence of myocardial infarction and re-hospitalisation for heart failure was reduced in treatment group ($p=0.015$)

•There was no increase in the rate of re-stenosis or in the progression of atherosclerosis in the treatment group

•There was no increased risk of ventricular arrhythmias or neoplasm in the treatment group

•Regional left ventricular contractility of infarcted segments was higher in the treatment group as assessed by MRI ($p<0.001$)

It should be emphasised again that these studies are small and there are other inherent limitations that must be taken into account. In addition, there have been other reported studies,[3,4] of similar size and design, where there has been no statistically significant benefit observed in patients receiving adult stem cell therapies compared to current standard treatments. This indicates that more research in this area is needed and that it is too soon to become excited about significant breakthroughs in the management of heart failure, myocardial infarction or other cardiovascular diseases using stem cell therapies.

Indeed, there is already evidence on the internet of questionable activities among private companies advocating stem cell therapy for patients with heart failure, possibly raising patients' expectations to an unrealistic degree and possibly offering false hopes to some, presumably at considerable financial expense. Such advertising is premature, probably misleading and potentially dangerous.

Nevertheless, adult stem cell research is already providing promising results in the management of a variety of cardiovascular disorders and it is reasonable to be optimistic that real therapeutic advances will be made in the near future with further research.

A NUMBER OF KEY QUESTIONS REGARDING CONTINUING STEM CELL RESEARCH SHOULD BE ASKED:

1. Do we really need to persist with human embryo stem cell research, especially as such research raises very grave moral and ethical concerns?

2. Is research involving human embryos wasteful of resources and likely to remain futile, even apart from the ethical questions raised?

3. Why not devote more time, energy and resources to bone marrow, adipose tissue, umbilical cord blood – derived stem cell research as these areas of research are much more likely to yield positive results and beneficial therapies?

Professor Andreas Zieher of Frankfurt, Germany, speaking at a Heart Failure Symposium on "Cell Therapy and Cardiovascular Regeneration" at the American College of Cardiology Annual Scientific Meeting in April 2011 stated that he was "very pessimistic about the role of human embryo stem cells…" in cardiovascular disease and that "human embryo stem cells are unlikely to be helpful"[5] in continuing research to develop therapeutic strategies in heart failure. Professor Zieher is a recognised world leader in stem cell research and was one of the main investigators in the REPAIR-AMI study.

A more basic question relating to how human beings treat other human persons also needs to be asked. Is it permissible to make use of the weak and the vulnerable in the interests of the wealthy and the strong or even in the interests of others who are also weak and vulnerable?

It is a core belief of our Faith that life begins at the moment of conception and that human embryos, regardless of how they have come into existence, are human persons worthy of the same respect and possessing the same human dignity and value as any other person created by God.

Of course, not all people accept this truth. Many will dispute the fact that human life begins at conception and there is a wide variety of opinions as to when life actually begins. Others might believe that life begins at conception or shortly afterwards but that the embryo is not yet a person and does not acquire the status of personhood until some later stage.

It is more comfortable and easier to deny the truth if impersonal and metaphorical terminology is used when speaking about life at its earliest stages. If the aim is to gain popular support for research funding and to hide the truth from the general population it is particularly important to use confusing and misleading terminology. Thus, advocates of human embryo stem cell research often use phrases such as "balls of cells" and technical words like "blastocysts" and even more offensive statements such as "it looks like semolina" when referring to real human persons at various stages of embryonic development. Those who employ such terminology are usually aware of the fact, but choose to hide it from their intended target audience, that they too were once exactly at the same

stage of development as the persons that they callously disregard and readily dispose of under the pretence that their "work" will provide benefit to mankind. This point has been very well expressed in the form of a question put forward by Fr. Tadeusz Pacholczyk, the Director of Education at the National Catholic Bioethics Center in Philadelphia, USA. Referring to the embryo at its earliest stages he asks

"Isn't this exactly what a young human being is supposed to look like at this stage of development?"[6] The question is a challenge to those who claim that human embryos do not possess a dignity and value similar to humans at all stages of development.

If the general population knew the full story of human embryo abuse they might be less supportive of unethical practices. As the American scientist and stem cell researcher at the National Institute of Health, Ronald D.G. McKay, stated in 2004 "People need a fairy tale" to get behind the research.[7] It seems many people in this country are being misled and fed fairy tales by agencies such as the British Heart Foundation and others seeking public and political support to help finance research using human embryos. Maybe they should concentrate on ethical adult stem cell research, as it is much more likely to prove fruitful.

Even if human embryo research were to lead to beneficial scientific advances there remains the very strong ethical and moral argument against the destruction of any human person even to benefit others. If a young child with severe heart failure desperately needed a heart transplant, would it be justifiable to take a healthy child of an asylum seeker, or a healthy young orphan, or a healthy young child of a prisoner and anaesthetise him to take his heart and transplant it into the child with severe heart failure? Despite the "good" that would result from such an action most would agree that it would be totally unacceptable and unethical. If we believe that the human embryo is indeed, or even might be, a human person do we not have a duty to treat such persons with the same degree of respect and love as we do for each and every other human person?

REFERENCES:

1. Strauer BE, Yousef M, Schannwell CM. The acute and long-term effects of intracoronary Stem cell Transplantation in 191 patients with chronic heart failure: the STAR-heart study. Eur. J Heart Fail, 2010 Jul;12(7):721-729.

2. Assmus B, Rolf A, Erbs S, Elsässer A, Haberbosch W, et al; REPAIR-AMI Investigators. Clinical outcome 2 years after intracoronary administration of bone marrow-derived progenitor cells in acute myocardial infarction. Circ Heart Fail. 2010 Jan;3(1):89-96.

3. Beitnes JO, Hopp E, Lunde K, Solheim S, Arnesen H, et al. Long-term results after intra-coronary injection of autologous mononuclear bone marrow cells in acute myocardial infarction: the ASTAMI randomised, controlled study. Heart. 2009 Dec;95(24):1983-1989.

4. Tendera M, Wojakowski W, Ruzyłło W, Chojnowska L, Kępka C, et al. Intracoronary infusion of bone marrow-derived selected CD34+CXCR4+ cells and non-selected mononuclear cells in patients with acute STEMI and reduced left ventricular ejection fraction: results of randomised, multicentre Myocardial Regeneration by Intracoronary Infusion of Selected Population of Stem Cells in Acute Myocardial Infarction (REGENT) Trial. Eur. Heart J. 2009 Jun;30(11):1313-1321.

5. Joint Session of the European Society of Cardiology and the American College of Cardiology II: New Frontiers in Therapy for Heart Failure. "Rebuilding the Heart: Cell Therapy and Cardiovascular Regeneration." Presentation by Prof A. Zeiher at American College of Cardiology 60th Annual Scientific Sessions, New Orleans, April 5th 2011.

6. Making Sense of Stem Cells. Interview with Fr. Tadeusz Pacholczyk for Faith & Culture, EWTN Original Transmission December 16th 2007.

7. The Washington Post. Editorial October 15th 2004.

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