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ORIGINAL ARTICLE

Twin-to-twin transfusion syndrome and potential applicability to the Barker hypothesis

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Abstract Twin-to-Twin Transfusion Syndrome (TTTS) carries significant risk of morbidity and mortality in affected monozygotic twin sets. As research into TTTS progresses, the effects of the adverse intrauterine environment on the long-term morbidities of TTTS survivors, is becoming more apparent. In TTTS, there is impaired vascular development and significant cardiac change in both foetuses, leading to high risk of long-term cardiac and neurologic morbidities in survivors. This appears to reflect the Barker Hypothesis of the Developmental Origins of Disease.

This review will discuss the Barker Hypothesis and its potential applicability to TTTS. It will outline foetal development in TTTS and subsequent consequences for the neonate. Current TTTS research will be discussed in addition to relevant neonatal care provision.

It will become evident that in order to improve long-term outcomes for TTTS survivors, a significant body of research focussing upon the correlation between foetal development in TTTS and associated adult disease states is required.

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Introduction

Twin-to-Twin Transfusion Syndrome (TTTS) is a rare but life threatening condition affecting a proportion of monozygotic pregnancies. Monozygotic pregnancies arise from the division of a single zygote after fertilisation, with the resulting foetuses sharing similar genetic material (Silva et al., 2011) — commonly referred to as identical twins. It has a significant risk of functional and structural cardiac changes to the affected foetuses, increased risk of adverse neurological outcomes, carries a high chance of premature delivery, and if untreated, carries an exceptionally high risk of foetal demise. As such, understanding and developing appropriate interventions to treat TTTS is a significant priority. As more research is emerging, it is becoming evident that the effects of the intrauterine environment on TTTS survivors development is having a significant impact upon long-term morbidities, particularly in relation to impaired vascular development in-utero and long-term cardiac and neurologic morbidities. This appears to relate to the Barker hypothesis of the developmental origins of adult disease, which postulates that adverse influences during perinatal development can impact upon the risk of adult disease states. The following review will discuss the origins of the Barker hypothesis and its potential applicability to Twin-to-Twin Transfusion Syndrome, with reference to current evidence and the possible mechanisms that may be involved. It will outline foetal development of TTTS and the short and long term consequences for neonates. The role of the neonatal nurse in care provision will also be identified. It will be evident that although links between TTTS and the Barker hypothesis are emerging, an increasing body of research is required to understand and further develop best practice to improve outcomes both in the acute care setting and across the lifespan.

Methodology

Medical Subject Heading (MeSH) terms were utilised for the purposes of obtaining relevant literature on the topic. The databases of choice for this review were CINAHL, Medline, PubMed, and Informit. Literature searches were conducted in three parts, using Boolean search types. The first search conducted utilised the MeSH terms of "Barker", "Hypothesis", "Twin-To-Twin" "Transfusion" "Syndrome" and yielded no relevant literature. The topic then was separated into two search focuses, with the resulting literature analysed together to review potential applicability of the Barker Hypothesis to Twin-To-Twin Transfusion Syndrome. The search for "Barker" "Hypothesis" yielded 290 results. The search for "Twin-To-Twin" "Transfusion" "Syndrome" yielded 3563 results, which were further filtered to results from the last five years, generating 1330 results. The resultant literature utilised in this review were hand selected based upon relevance to the topic, highlighting potential for links to be made between Twin-To-Twin Transfusion Syndrome and The Barker Hypothesis.

The Barker hypothesis

In the late 1980's, David Barker identified relationships between low birth weight neonates who survived infancy and an increased risk of disease in adulthood. This led him to further research and hypothesize that adverse influences during intrauterine life and early development could lead to permanent physiologic and metabolic changes, which increase the risk of disease later in life (De Boo and Harding, 2006). The hypothesis was called "developmental origins of adult disease" and is often referred to as the "Barker Hypothesis" (De Boo and Harding, 2006). A number of conditions have been linked to the hypothesis such as hypertension, ischaemic heart disease and diabetes (Poulter, 2001), as well as stroke, coronary heart disease and obesity (Kimm, 2004). However, the hypothesis has been met with scepticism at times due to a lack of compounding evidence of the mechanisms involved in the relationship, the links identified being largely observational, and the impact of other factors such as prematurity or multiple gestations influencing the results.

Although not yet proven, a number of mechanisms have been proposed which support the Barker Hypothesis. According to De Boo and Harding (2006), the most likely mechanism involved is the process of foetal programming whereby insults or specific stimuli during critical or sensitive periods of development, result in long-term, irreversible, adverse consequences affecting subsequent development. These could be related to altered foetal nutrition, exposure to excess glucocorticoids, the thrifty phenotype hypothesis and predictive adaptive responses, the foetal insulin hypothesis, genetic and epigenetic links, intergenerational effects, and periconceptional events (De Boo and Harding, 2006). For example, Daniels (2007) suggests that for hypertension, it appears that the combination of a

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