Experimental Study of the Effect of Low Dose Aspirin and Betamethasone on the Patency Rate of Microvascular Polytetrafluoroethylene Grafts (PTFE)

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*Thank you very much my **Great God**, I relate to you any success in my life.*

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List of Abbreviations

Abbreviation	*Word*
PTFE	Polytetrafluoroethylene
PUs	Polyurethanes
IH	Intimal hyperplasia
VSMC	Vascular smooth muscle cell
MMPs	Metalloproteinase
PDGF	Platelet derived growth factor
EDRF	Endothelial derived relaxing factor
NO	Nitrous Oxide
ET	Endothelin
ECE	Endothelin-converting enzyme
ECs	Endothelial cells
LDF	Laser doppler flometry
BPU	Blood perfusion unit
PE	phenylephrine
ITB	Isolated tissue bath
L-NAME	Nitro-L-arginine methyl ester

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List of Erratum

Page number	False word	Correction
I	Flometry	Flowmetry
7	1948	1978
7	Makes	Make
19	Radiated	Irradiated
27	The	That
40	Heparin	Heparan
52	No endothelin inhibitors	
128	Depostion	Deposition
128	Sever	Severe

References:

Lime CH., Mardini S., Lim YT., Yeh IT., Wei FC, Chen HC. (2004): Sixty-Five clinical cases of free tissue transfer using long AV fistulas or vein grafts. J. trauma: 56 (5), 1107.

The advances of microvascular surgery over the years have resulted in an increased need for small diameter vessel replacements. Reversed autologous vein grafts are presently the most suitable material for use as arterial substitutes in microsurgical procedures. However dissecting, harvesting and preparing a vein graft add time to any microsurgical procedure, also the choice of veins may be limited by a number of factors like trauma or obliterative vascular disease. Additionally one or more veins must be sacrificed, a donor site scar is left and usually one must compromise in terms of matching sizes and diameters between vein graft and recipient vessel ***(Lanzetta, 1998)***.

Bridging microvascular defects with synthetic grafts would have the great advantage of providing a choice of the most optimal size and shape with decreased operative time. Large-diameter synthetic grafts with their various lengths and numerous configurations have gradually found their place in vascular surgery and are currently very widely used in a great variety of clinical situations. However small diameter synthetic grafts have not left the laboratory as they are disappointing in their high rate of thrombosis and still considered unreliable ***(Lanzetta, 1998)***.

Nowadays, there are many types of synthetic grafts on the horizon, such as PTFE, Dacron and Polyurethanes (PUs) grafts.

The ideal vascular graft should be characterized by its mechanical attributes and post-implantation healing responses. Mechanical strength is a paramount issue; grafts placed in the arterial circulation should be capable of withstanding long-term haemodynamic stress without material failure which might be catastrophic. Availability, suturability and simplicity of handling are desirable for minimizing operating time and risk. The graft should be resistant to both thrombosis and infection and optimally would be completely incorporated by the body to yield a new vessel resembling a native artery in structure and function ***(Conte, 1998)***.

The most widely used synthetic graft is PTFE because of a relatively low inherent thrombogencity and satisfactory tissue healing. PTFE also exhibits physical properties such as biocompatibility, inertness, negative charge and hydrophobia which all help to reduce the occurrence of thrombosis with promising patency rate ***(Cooley, 1998)***.

However with such ideal characteristic, authors have reported highly varying patency rate ranging from complete failure to as high as 90 % patency rate after 2 weeks by ***Parsa and Spira (1979), Caudrs (1984), Daniel (1985), Zdanowski et***

al. (1992), Van der lei and Robinson (1993), Lemson et al. (2000).

The factors responsible for synthetic grafts failure were thoroughly investigated and optimized, as regard the graft materials by using PTFE grafts (with radial support, large pores and fibril length of at least 60 μm) and as regard the technical error (by meticulous techniques and the intra-operative observation of the anastomosis for 1 hour to insure early patency). Therefore the remaining factor incriminated in synthetic grafts failure is **intimal hyperplasia (IH)** that develops at the anastomosis sites with subsequent slowing of the circulation, platelet aggregation and thrombus formation ***(Demiri et al., 1999)***.

Intimal hyperplasia is a process by which the cell population increases within the innermost layer of the vessel wall, such as occurs physiologically during closure of the ductus arteriosus and during involution of the uterus. It also occurs pathologically in pulmonary hypertension, atherosclerosis, transplanted organs, and after angioplasty. The underlying cause of intimal hyperplasia is migration and proliferation of vascular

smooth muscle cells (VSMCs) from media to intima (phenotypic modulation) ***(Newby and Zaltsman, 2000)***.

The key stimuli for IH are injury, inflammation and increased mean wall stress. They activate heparanases and a cascade of proteases that together loosen the connections of the extracellular matrix with the VSMCs surface which provides the trigger for phenotypic modulation. Also peptide growth factors agents such as thrombin, endothelin-1 and angiotensin-II and inflammatory cytokines act co-operatively to trigger proliferation and migration of VSMCs ***(Newby and Zaltsman, 2000)***.

Complex interactions with platelets and subsequent release of platelets derived factors and interaction with the adjacent endothelial cells lead to collagen and fibrin deposition and the development of IH. A successful drug that could limit this hyperplastic response may help to improve patency rate of synthetic grafts ***(Petrik et al., 1998)***.

Therefore the extent of the intimal hyperplasia formation may be theoretically decreased by the use of pharmacological drugs that might inhibit (1) the platelets activity (Antiplatelet) like ***Low Dose Aspirin***, (2) the fibrin deposition

(Glucocorticoids) like ***Betamethasone***, (3) The action of endothelin (Endothelin Receptor Antagonist) like ***BQ123***, (4) the endothelin formation ***(***Endothelin Converting Enzyme Inhibitor) like ***Phosphoramidon***, with subsequent improvement of the patency rate.