REDUCTION OF POST-SURGICAL PERICARDIAL ADHESIONS USING A PIG MODEL

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ABSTRACT

The aim of this study was to reduce pericardial adhesions after open-heart surgery thus enabling re-sternotomies to be much safer and less time consuming for the surgical team. A pig model was developed to test the effects of non-steroidal anti-inflammatory drugs (NSAIDs) and a barrier method in reducing post-surgical pericardial adhesions. Four groups (11 per group) of pigs 8-12 weeks of age were used. Group one was the control group, Group two received indomethacin, Group three received rofecoxib (also a NSAID) and a polyethyleneglycol (Co-Seal) was applied to the pericardium as a barrier in Group four.

After performing a median sternotomy, an adhesion induction model was applied to maximize inflammation in the pericardium. This included abrasion of the heart surface, leaving blood in the pericardium and drying of tissues. The chest was then closed. In Group four, Co-Seal was sprayed on the heart before closure. Post-operatively, Groups two and three received indomethacin and rofecoxib respectively for five days. Plasma markers of inflammation were assessed on days 2, 5 and 10 post-operative. In each group, eight animals were re-opened after 12 weeks and three after 25 weeks to assess adhesions according to adhesion assessment scales. Tissue samples were collected for histopathological examination looking mainly at epicardial and adhesive tissue thickness.

It was observed in this study that adhesions were changed from dense to thin and more easily separable, requiring more blunt rather than sharp dissection. This was seen mainly in Group two, followed by Group four. In Group three, the changes were less in terms of amount of adhesions and tenacity change as compared to the changes in Groups two and four. Comparison was with Group one, which had the densest adhesions.

Adhesive tissue and epicardial thickness was measured. Epicardium was thinnest in Group two. Post-operative inflammatory markers, specifically PGE2 and TXB2 were inhibited mainly in Group two. Less inhibition of these markers was seen in Group three and nearly no inhibition was seen in Groups one and four. The more general

markers used (WCC, ESR and CRP) did not fully show the expected changes in the four groups. The adhesion induction model formulated in this study was successful and may be used in similar future projects.

In conclusion, this model, applied clinically, will reduce adhesions in the pericardium and retrosternal areas after surgery, rendering re-openings safer and less time consuming. Indomethacin has proven to be the best choice to achieve this following a relatively easy and short protocol of administration. The idea of giving patients indomethacin for five days only to achieve significant reduction in adhesion formation after surgery would be attractive to many surgical groups around the world as the short period of administration would minimize any side effects associated with this drug.

Significant reduction in adhesions was also seen following the application of Co-Seal. The attraction here would be the ease of use and the non-pharmacological effects of this barrier method. Rofecoxib was not as effective as indomethacin and Co-seal in adhesion reduction. Future studies in this pig model should examine the extent of adhesion formation following the combined use of indomethacin and Co-Seal.

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ABBREVIATIONS

AA	Arachidonic acid
AMP	Adenosine monophosphate
ANOVA	Analysis of variance
APS	Adhesion percentage scale
APTT	Activated partial thromboplastin time
ASD	Atrial septal defect
ATP	Adenosine triphosphate
ATTS	Adhesive tissue tenacity scale
CAG	Coronary artery grafting
Camp	3', 5'-adenosine monophosphate
COX	Cyclooxygenase
COX-1	Cyclooxygenase-1
COX-2	Cyclooxygenase-2
CRP	C-reactive protein
DAG	Diacylglycerol
ECG	Electrocardiogram
EDTA	Ethylene diamine tetra acetic acid
ELAM-1	Endothelial-leukocyte adhesion molecule-1
ESR	Erythrocyte sedimentation rate
HETEs	Hydroxyeicosatetranoic acids
HPETEs	Hydroperoxyeicosatetranoic acid compounds
HPLC	High pressure liquid chromatography
IC	Inhibitory concentration
ICAM-1	Intercellular adhesion molecule-1
IL-1	Interleukin 1
IL-8	Interleukin 8
INR	International normalization ratio
IP3	Inositol-1,4,5-triphosphate
LFA	Lymphocyte function-associated antigen

LTA4	Leukotriene A4
LTD4	Leukotriene D4
LTE4	Leukotriene E4
MANOVA	Multivariate analysis of variance
MRNA	Messenger ribonucleic acid
N/D	Not detectable
NSAIDs	Non-steroidal anti-inflammatory drugs
NSW	New South Wales
NZ	New Zealand
PEG	Polyethyleneglycol
PGD2	Prostaglandin D2
PGE1	Prostaglandin E1
PGE2	Prostaglandin E2
PGF1	Prostaglandin F1
PGF2	Prostaglandin F2
PGI2	Prostaglandin I2
PIP2	Phosphatidylinositol-4, 5-biphosphate
PMN	Polymorphonuclear
PT	Prothrombin time
QLD	Queensland
SEM	Standard error of mean
SRS-As	Slow-reacting substances of anaphylaxis
TNF	Tumor necrosis factor
TPA	Tissue plasminogen activator
TxA2	Thromboxane A2
TxB2	Thromboxane B2
VIC	Victoria
VSD	Ventricular septal defect
WA	Western Australia
WBC	White blood cells
WCC	White Cell Count
5-LO	5-lipoxygenase