

**[2003] [P1714] A dual thromboxane inhibitor and thromboxane receptor antagonist prevents pig myocardial infarction induced by coronary thrombosis**

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**Objectives:** to characterise the effects of BM-573 (N-terbutyl-N'-[2-(4'-methylphenylamino)-5-nitro-benzenesulfonyl] urea), a novel dual thromboxane A2 receptor antagonist and thromboxane synthase inhibitor, on myocardial infarction induced by topical ferric chloride (FeCl<sub>3</sub>) application to the left anterior descending (LAD) coronary artery in pigs.

**Methods:** Experiments were performed on 12 healthy pure pietran anaesthetised pigs of either sex weighing from 20 to 30 kg. After a 30 min stabilisation period, a tissue strip saturated with ferric chloride solution (50% w/v) was rolled around the LAD coronary artery for 45 min. The animals were randomised in two groups: a control group (n=6) intravenously infused with vehicle (propylene glycol-NaCl 0.9%, 50:50), and a BM-573-treated group (n=6) infused with BM-573 (10 mg.kg<sup>-1</sup>.h<sup>-1</sup>). The infusion started 30 min before ferric chloride application and was continuously infused till 6 hours after strip application. The strip was removed 45 min after its application.

**Results:** All control animals (n=6) developed an occlusive thrombus in the LAD coronary artery. The mean infarct size, revealed by triphenyl tetrazolium chloride (TTC) and the area at risk evidenced by Evans blue corresponded to 35.3 ± 2.2% and 36.9 ± 2.1% of the left ventricular (LV) mass, respectively. Among the BM-573 treated group, four pigs did not develop coronary artery thrombus and their myocardium appeared healthy. Histopathological examination of FeCl<sub>3</sub>-injured coronary artery revealed an occlusive and adherent thrombus in control group while pretreatment with BM-573 prevented thrombus formation. In infarcted zones, lack of desmin staining and muscle structure disorganisation were obvious. Depletion of myocardial ATP content was observed in the myocardial necrotic region of the control group, but not in myocardial samples of BM-573-treated pigs which did not develop myocardial infarction. When BM-573 prevented LAD artery occlusion, the area under the curve (AUC) of plasmatic troponin T was reduced by 77% over 6h.

**Conclusions:** These data suggest that BM-573 could be useful for the prevention of myocardial infarction.

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