PP098—NICORANDIL INDUCED ENDOTHELIUM-INDEPENDENT RELAXATION OF ARTERIAL BYPASS GRAFT
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Introduction: Spasm of the human internal mammary artery (HIMA) is a rare but life-threatening complication after coronary artery bypass grafting (CABG). The reversal of this vasoospasm is often challenging, and the most effective therapy is not well defined. The present study was aimed to investigate vasorelaxant effect of nicorandil, K+ channel opener, on the HIMA and to define the role of different K+ channel subtypes in nicorandil action on this blood vessel.

Patients (or Materials) and Methods: Discarded segments of HIMA were collected from patients undergoing CABG and studied in organ baths. HIMA rings were precontracted with phenylephrine (10 μM) followed by cumulatively adding increasing doses of nicorandil. The endothelium was removed mechanically.

Results: Nicorandil (0.001 μM–300 μM) induced a concentration-dependent relaxation of HIMA rings precontracted by phenylephrine. Glibenclamide (10 μM), a highly selective blocker of ATP-sensitive K+ (KATP) channels, partially inhibited relaxation of HIMA induced by nicorandil. Tetraethylammonium (TEA, 1 mM), a nonselective blocker of Ca2+-activated K+ (KCa) channels, as well as iberiotoxin (100 nM), a most selective blocker of large-conductance Ca2+-activated K+ (BKCa) channels, partly antagonized relaxation of HIMA. A nonselective blocker of voltage-gated K+ (Kv) channels, 4-aminopyridine (4-AP, 0.5 mM), as well as margatoxin (10 nM), a potent inhibitor of Kv1.3 channel, did not significantly modify the nicorandil-induced relaxation of HIMA.

Conclusion: The results from our study demonstrate that, in HIMA, nicorandil has a potent vasorelaxant effect which is endothelium-independent. It seems that mechanism of this relaxation includes KATP and 4-AP-sensitive K+ channels located in the smooth muscle of HIMA.

Disclosure of Interest: None declared.

PP100—POTENTIAL OF NATTKINASE AS AN ANTITHROMBOTIC & FIBRINOLYTIC AGENT
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Introduction: Thrombosis is 1 of the major causes of death worldwide. Atherothrombotic diseases such as myocardial or cerebral infarction are serious consequences of the thrombus formed in blood vessels. Nattokinase is new fibrinolytic enzyme with a molecular weight of 27 728 Da that cleaves directly cross-linked fibrin in vitro. In this study, we investigated the effect of nattokinase supplementation on thrombus formation using different animal models.

Patients (or Materials) and Methods: To study the fibrinolytic activity, in vitro clot dissolution assay was done in which clot was formed in helix and then kept in contact with different concentrations of nattokinase and streptokinase (standard drug) and its clot dissolution property was studied. Further it was studied for its antithrombotic activity in venous thrombosis. Rats were pretreated orally for 7 days with Nattokinase (100 and 200 mg/kg). One hour after the last dose, stasis was developed in the inferior vena cava in rats, and its activity was intensified with the help of ferric chloride. It was also studied for its antithrombotic activity in arterial thrombosis using arteriovenous shunt-induced thrombosis in rats. In this rats were pretreated orally for 7 days with Nattokinase (100 and 200 mg/kg) and on last day 1 hour after last dose thrombosis was induced by arterio-venous shunt. In both the above studies, % inhibition of thrombus forma-
tion was calculated. Because hemorrhage is an important side effect of antithrombotic and thrombolytic therapies, the drug was studied for its effect on hemorrhage using rat tail transaction method. Here, effect of 7 days pretreatment of 2 doses of nattokinase (100 and 200 mg/kg) on hemorrhage was studied.

Results: In vitro clot dissolution assay, there was significant and dose-dependent clot dissolution with different concentration of nattokinase. Maximum activity, 94.43 % inhibition, was seen in 3000ug/mL concentration which was comparable with 1000 IU of streptokinase. In venous thrombosis model, it showed significant and dose-dependent inhibition of thrombus formation as indicated by decrease in weight of thrombus. Antithrombotic potential of nattokinase at the highest dose (200 mg/kg) showed 45.431% inhibition with respect to saline control group. In arterio-venous shunt, it showed no significant inhibition of thrombus formation on thrombogenic surface. In the rat tail transaction model, both the doses of nattokinase (100 and 200 mg/kg) has significantly increased the bleeding time with not much effect on blood loss. Also, the platelet MDA was significantly decreased in both groups treated with 100 and 200 mg/kg of nattokinase.

Conclusion: The results of various in vitro and in vivo models studied indicate that nattokinase has a good potential as an antithrombotic and fibrinolytic agent.

Disclosure of Interest: None declared.

PP101—REACTIONITY MODIFICATIONS IN HEART RESISTANCE VESSELS TO ANGIOTENSIN II IN ISOLATED PERFUSED HEART OF HYPERTENSIVE RATS
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Introduction: High blood pressure (HBP) is a disease with high morbidity and mortality worldwide and is considered 1 of the main etiologic factors of multiple cardiac pathologies like cardiac hypertrophy, myocardial infarction, among others. One of the regulatory mechanisms of blood pressure is the renin angiotensin system (RAS), so much so that the first-line drugs in the treatment of hyperten-
sion are directed to some of the components of the RAS. However, these treatments frequently lead to the development of changes in morphology and physiology characterized by vascular complications. It is therefore necessary to consider adjuvant therapies to improve the outlook and quality of life of patients with HBP. A therapy that has been shown clinically to improve the condition of patients with HBP is hyperbaric oxygenation (HBO), which consists in subjecting a subject at a pressure >2 atmospheres absolute with 100% oxygen. This therapy has been shown to improve vascular smooth muscle relaxation, although the mechanism of action has not yet been specified.