Kinetic oscillation stimulation of the nose: a novel treatment for myocardial ischemia-reperfusion injury

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Background and Aims

❖ Rrestoration of coronary blood flow by means of either primary percutaneous intervention or thrombolysis is standard treatment for patients with acute ST-elevation myocardial infarction. However, reperfusion of the jeopardized myocardium results in a cascade of harmful events, referred to as myocardial ischemia-reperfusion (IR) injury. Therefore, targeting to reduce IR-injury is a highly desarble goal.

❖ Kinetic oscillation stimulation (KOS) is a technique developed to stimulate the nervous system in the nasal cavity. The efficacy of KOS has been demonstrated in patient with non-allergic rhinitis and migraine by a mechanism suggested to involve activation of parasympathetic nerves. Parasympathetic activation of the heart by vagal nerve (VN) stimulation protects from myocardial ischemia-reperfusion (IR) injury. The present study was aimed to determine whether KOS protects from myocardial IR injury and whether such effect involves VN activation.

Materials and Methods

❖ Anaesthetised (sodium pentobarbital) and thoracotomized Spargue Dawley rats (body weight 280-400 g) subjected to 30 min left coronary artery (LCA) followed 2 hrs reperfusion

❖ To evaluate myocardial infarct size (IS) Evans blue (2%) was injected after 2 hrs reperfusion to mark ischemic myocardium (area at risk , AAR). Left ventricles (LV) were cut into 5-7 slices and put in 1% triphenyltetrazolium chloride for 15 min at 37°C to distinguish the viable myocardium from the necrotic. The incidence of ventrical fibrillation (VF) during myocardial ischemia was recorded.

Experimental and the kinetic oscillation stimulation protocol

Rats were randomoized and subjected to 30 min LCA occlsuion followed by 2 hrs reperfusion. Following insertion of a stimulation probe into the nasal cavity that delivered KOS at a frequency of 68-75 Hz the rats were allocated to **(1) control IR** (n=6, CIR); (**2) KOS-pre** (n=8, KOS starting 5 min before ischemia and continued throughout reperfusion**); (3) KOS-per** (n=8, starting 15 min before onset of reperfusion); **(4) bilateral vagotomy (BV, 30 min before ischemia)+KOS-pre** (n=6) and **(5) BV** (n=5). **Kinetic oscillation stimulation:** The treatment equipment in this study consists of an external energy unit and a tube connected distally to a probe. The probe delivers low frequency vibration energy (air pressure variations) topically to the nasal mucosa in the cavity when it is in position in the cavity (Figure 1). The probe consists of a thin flexible unit with small openings in its distal part. To have a suited probe dimension to treat the nose cavity of small animals, rats, the probe is dimensioned so that the length of it is 20-30 mm and the width up to 0.7 mm. Then the probe can be inserted, through the opening (nares) into the nose cavity of the rat without trauma. Sham treatment is delivered when the probe is disconnected from the energy unit.

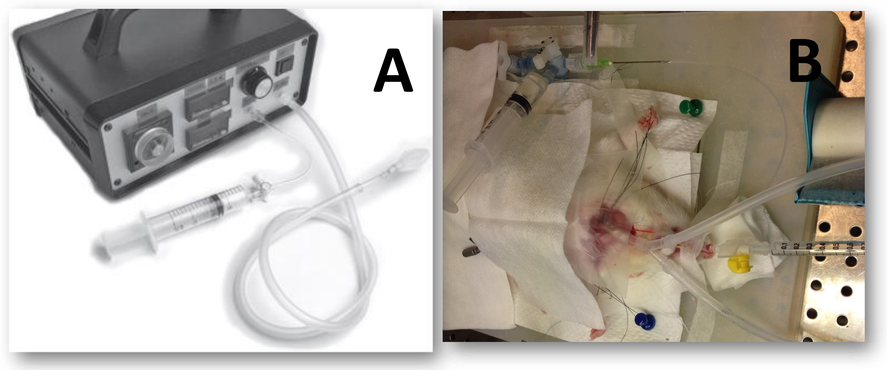

Figure 1.
Human treatment apparatus (A) and the modified appartus for rodent (B)

Results

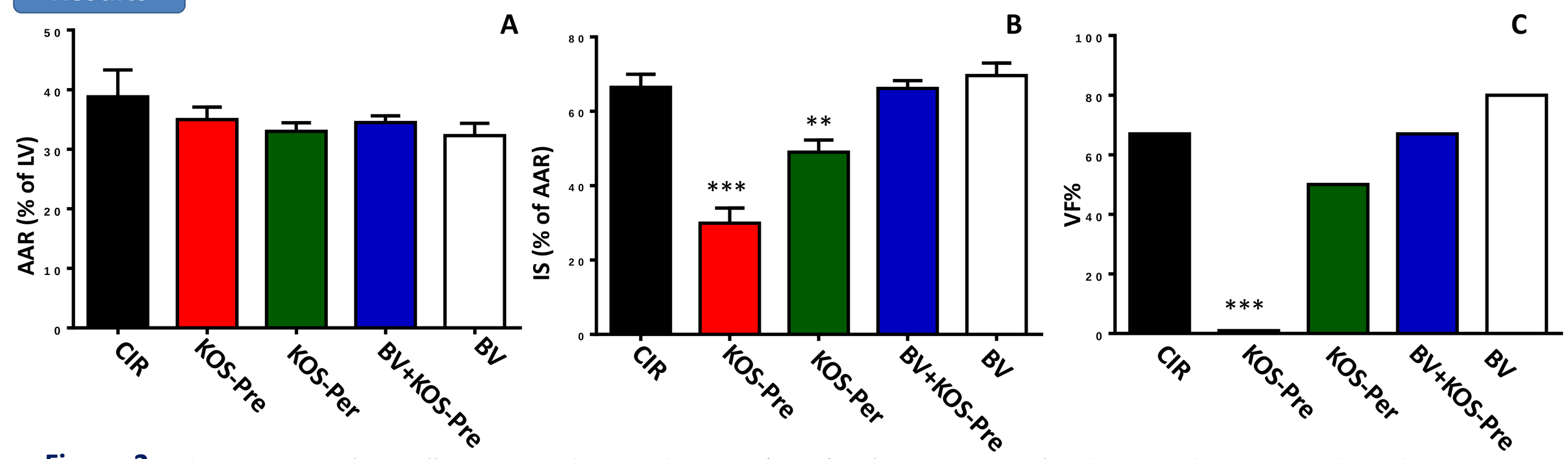

Figure 2. . There was no significant difference in AAR between the groups (Fig 2A). Infarct size was significantly reduced by KOS was applied either prior to or during myocardial ischemia in comparison to CIR (Fig 2B). However, bilaterial vagotomy completly abolished the infarct size limiting effect of KOS (Fig 2B). Moreover, KOS was applied prior to myocardial ischemia prevenst ischemia induced ventricular fibrillarion (Fig 2C), this effect was abolsihed by vagotomy. ***P*<0.001 and ****P*<0.0001 vs. CIR.

Hemodynamic parameters

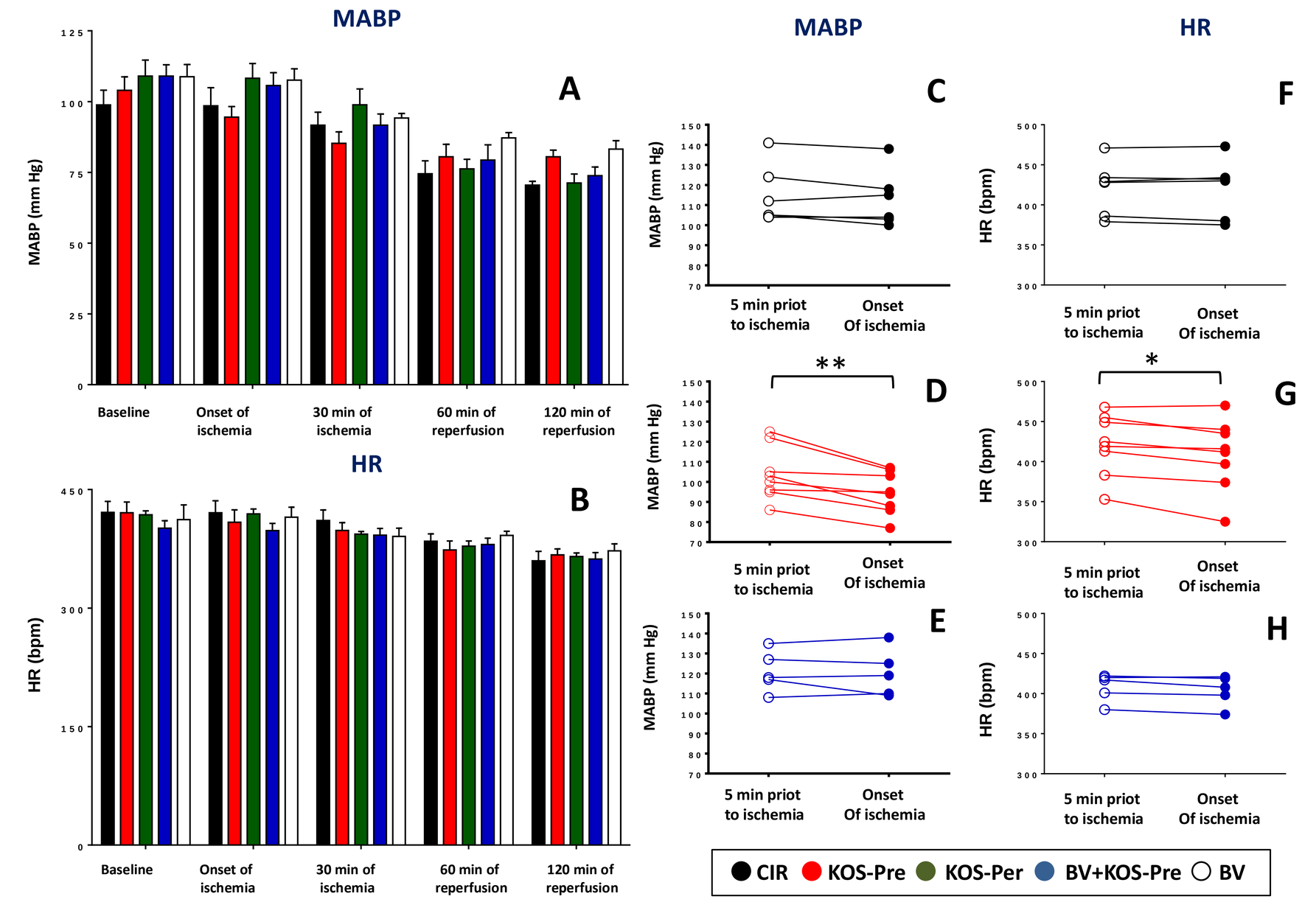

Figure 3. There were no difference in arterial blood pressure (MABP) and heart rate (HR) between the group at basline levels (Fig 3A and B). In addition, it was a similar trend in reduction of MABP during IR in all group (Fig 3A). However, KOS reduced both MABP and HR within 5 min (Fig 3E). This effect of KOS was abolished by bilaterial vagotomy.. **P*<0.05 and **P*<0.01 vs. 5 min prior to ischemia of KOS-Pre group.

Conclusions

Our results provide the first evidence that kinetic oscillation stimulation protects the heart against IR-injury via a mechanism involving vagal nerve activity. KOS might reprent a novel, non-invasive and clinically feasable treatment to reduce myocardial IR-injury.