ORGAN PROTECTION AND IMPROVEMENT OF SURVIVAL AFTER HEMORRHAGIC SHOCK BY TREATMENT WITH INHALED NITRIC OXIDE(NO) IN A RAT MODEL

Author: Mimuro S.¹, Kobayashi K.¹, Iwata H.², Makino H.¹, Shiraishi Y.², Nakajima Y.¹

Institutes: ¹Hamamatsu University School of Medicine, Dept of Anaesthesiology & Intensive Care, Hamamatsu, Japan,
²Fujieda Municipal General Hospital, Dept of Anaesthesiology, Fujieda, Japan

Introduction:

- Organ dysfunction following hemorrhagic shock and the vital prognosis have not improved sufficiently over time.
- Control of NO production by intravenous administration of NO donors and NOS inhibitors has been attempted, but these are not suitable for clinical application.
- Inhaled NO is an agent with sufficient clinical safety and experience, but it has not been reported for use in the treatment of hemorrhagic shock.
- Thus, we investigated whether inhaled NO administration leads to differences in survival and central venous NO₂ levels in a rat hemorrhagic shock model.

Methods:

- Thirty male SD rats were used.
- Tracheotomy was applied under general anesthesia, microdialysis probes were placed in the arterial line and central vein, and NO₂ was measured in the dialysis probes using an oxidized nitrogen analysis system (ENO-20, Eicom Japan, Kyoto).
- The systolic arterial pressure was maintained at 40 mmHg by withdrawing and returning blood for one hour (hemorrhagic shock).
- The animals were resuscitated with saline in a volume equivalent to the residual blood.
- After resuscitation, rats were exposed to 20 ppm NO by inhalation for 30 minutes.
- The rats were randomly divided into the following 3 groups:
 - (1) Sham (hemorrhagic shock–, inhaled NO–)
 - (2) hemorrhagic shock+NO+
 - (3) hemorrhagic shock+NO–
- Hemodynamic changes and NO₂ levels were measured over time, and the survival rate was calculated.

Results:

- The survival rate was higher in the group with hemorrhagic shock followed by inhaled NO compared with the group without inhaled NO ($p=0.033$) (Fig. 1).
- NO₂ levels were significantly lower in the Shock+NO– group (vs. Shock+NO+ group 3Hr, vs. Shock–NO– group 7Hr), and significantly higher in the Shock+NO+ group (vs. the Shock+NO– and Shock–NO– groups 3Hr) (Fig. 2).
- Hemodynamic change was not observed significantly during NO inhalation

Discussion

- NO₂ production was decreased during the early phase of hemorrhagic shock (–7hr), suggesting that the shock decreased survival, and that inhaled NO protected the organs and improved survival.
- It was not possible to study the late phase of shock (12hr–) in this model due to excessive stress.

- Khazaei reported that the survival rate was not changed by intravenous administration of NO donors in rat model.
- It was reported that the inhaled NO and the intravenous administration was different in utilization ratio.
- Inhaled NO improves microvascular perfusion.

Conclusions:

- The survival rate increased in hemorrhagic shock rats that were treated with inhaled NO compared with rats that were not.
- It was suggested that administration of inhaled NO is effective for the early phase of hemorrhagic shock.

Survival Rate

(n mol/L) Plasma NO₂ concentration