

**A METHOD REVIEW OF PHARMACOLOGICALLY INDUCED HYPERTENSION IN
PREGNANT RATS MODEL:
N₀-NITRO-L-ARGININE METHYL ESTER HYDROCHLORIDE (L-NAME)**

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ABSTRACT

Background: Hypertensive disorders of pregnancy contribute a high percentage in maternal and fetal mortality and morbidity. They affect about 8% of pregnancies worldwide. There are various animal models used in the study of pregnancy-associated hypertensive disorders including induction of animals by surgical, environmental, pharmacological, immunological, or genetic manipulation. L-NAME is a drug that has been used to induce hypertension by inhibition of Nitric oxide synthase (NOS). **Purpose:** The objective of this study is to establish hypertension in a pregnant rat model by using L-NAME. **Methodology:** Thirty-two female Sprague-Dawley rats were randomly assigned to four groups (n=8 in each): Control- non-pregnant (C), control-pregnant (P), Non-pregnant-L-NAME (CL) and pregnant-L-NAME (PL). On Day 13 of gestation, the treated groups were given 60mg/kg/day of L-NAME via oral gavage until the day of delivery. A series of blood pressure were measured via pre-warmed tail-cuff method. The number and weight of the litters and total maternal weight gain were recorded. **Result:** Introduction of L-NAME to PL group resulted in an increase of the mean SBP and MAP however, it does not follow the definition of hypertension in pregnancy. Introduction of L-NAME to CL group resulted in an increase of the mean SBP and MAP which is higher compared to PL group. The mean of maternal weight gain, number of litters and litters' weight were not significant. There were several complications that we observed in the treated groups including one rat had died and some of them experienced temporary neurological deficits such as unilateral upper limb paralysis and bloody eye discharge. **Conclusion:** This method caused maternal morbidity and mortality, but it was relatively safe for the fetus. The pregnancy itself has hypotensive mechanism to protect the fetus. This method used oral gavage as the route of administration could not established hypertension in pregnancy rat model might be due to short-acting of L-NAME. The alternative way is to change the method of administration of L-NAME by giving chronic inhibition of NOS through subcutaneous injection or mixing the drug with drinking water.

Keywords: L-NAME, hypertension, pregnant, animal model

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