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Maternal supplementation of omega-3 fatty acids and micronutrients reduces cardiometabolic variables in pregnancy induced hypertension rats☆

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ABSTRACT

Aims: Reports indicate that during pregnancy hypertension is known to have long term adverse effects both in the mother and offspring. However, the effect of maternal micronutrient supplementation on this association of in utero exposure and risk of non-communicable diseases in the later life remains unclear. The present study examines the effect of maternal micronutrient and omega-3 fatty acid supplementation either individual or in combination on cardiometabolic risk factors both in the mother and offspring using an animal model of hypertension.

Main methods: Pregnant Wistar rats were randomly assigned to the following groups; control, PIH (Pregnancy induced hypertention) Induced, PIH + vitamin B_{12}, PIH + folic acid, PIH + omega-3 fatty acids and PIH + combined smicronutrient supplementation (vitamin B_{12} + folic acid + omega-3 fatty acids). The dams and their offspring were shifted to a control diet after delivery and the offspring continued on these diets till 3 mo of age. Hypertension during pregnancy was induced using L-Nitroarginine methylester (50 mg/kg body weight/day).

Key findings: Omega-3 fatty acid supplementation during pregnancy demonstrated lower levels ($p < 0.05$) of plasma cholesterol while a combined supplementation of folic acid, vitamin B_{12} and omega 3 fatty acids demonstrated lower ($p < 0.05$) triglyceride levels as compared to PIH induced dams. PIH induction increased ($p < 0.01$) the triglyceride levels in the offspring at 3 mo of age and maternal supplementation of either individual or combined micronutrients demonstrated lower ($p < 0.01$) triglyceride levels.

Significance: Our findings have implications for planning intervention studies in women with pregnancy induced hypertension.

1. Introduction

Nutritional insults during the intrauterine period are reported to lead to programming of metabolic disorders in the offspring in adult life [1]. Reports indicate that mothers with preeclampsia [2–5] and their offspring are at an increased risk for adverse cardiovascular outcomes in later life [6–8]. However, the mechanisms are relatively unexplored [9]. In addition, the use of nutritional interventions during pregnancy has demonstrated conflicting results. Few studies on multivitamin [10] and folic acid supplementation [11–12] in women with preeclampsia have reported beneficial effects in reducing the risk for preeclampsia while others report no such benefits [13–16]. Report suggests that there is an inverse association between erythrocyte omega-3 fatty acids and risk of preeclampsia [17]. The rate of complications during pregnancy such as preeclampsia is on the rise [18] indicating a need to examine this issue.

A recent review highlights the vital role of long chain polyunsaturated fatty acids in normal fetal development [19]. However, the association between maternal omega-3 fatty acid intake and later cardiovascular health in the progeny remains unclear [20]. A recent review suggests that the sufficient maternal intake of vitamins and minerals may be critical in the prevention of cardio-metabolic risk in the offspring [21]. Similarly, during early development a disturbed one-carbon metabolism is suggested to increase risk for metabolic diseases in later life [22–24]. Previous studies by us and others have extensively reported that these micronutrients (vitamin B_{12} and folic acid) and omega-3 fatty acids especially DHA (docosahexaenoic acid) are interlinked in the one carbon cycle [25–28]. We have recently reported increased systolic and diastolic blood pressure, increased oxidative

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stress, inflammatory markers, and lower placental DHA, interleukin-10 and vascular endothelial growth factor levels in dams with pregnancy induced hypertension (PIH) at d20 of gestation [29–30].

In the current study, we examine the effect of maternal micronutrient (folic acid, vitamin B_{12}) and omega-3 fatty acids supplementation given either in individual or in combination on the cardiometabolic variables both in mothers and the offspring at 3 mo of age in a pregnancy induced rat model.

2. Materials and methods

The present protocol has followed the CPCSEA guidelines (Committee for the purpose of control and supervision of experimental animals) Govt. of India. The study was initiated after seeking approval from the institutional animal ethical committee (IAEC/CPCSEA/2311) of Bharati Vidyapeeth.

We have reported the use of NG-nitro-L-arginine methylester (L-NAME) in inducing hypertension during pregnancy in a rat model [29–30]. In the present study, inhibitor of nitric oxide synthase i.e. L-NAME was administered from d14 of gestation in the dose of 50 mg/kg body weight/day by gavage to induce preeclampsia-like syndrome in rats and has been reported earlier by us and others [29–36].

2.1. Animals, breeding and induction of L-NAME

Pregnant Wistar albino rats (n = 8 per group) were randomly assigned to 6 groups; control and 5 treatment groups: Pregnancy Induced Hypertension (PIH); PIH Induced + Vitamin B_{12} supplemented group (PIH + B_{12}); PIH+ Folate supplemented group (PIH + F); PIH + Omega-3fatty acid supplemented group (PIH + O) and PIH + Vitamin B_{12} + Folate + Omega-3 fatty acid supplemented group (PIH + B_{12} + F + O) and have been shown in study design (Fig. 1). The protocol in the present study has been reported by us recently [29–30].

Dietary Groups: Control; PIH Induced; PIH + B_{12}: PIH Induced + vitamin B_{12} supplementation; PIH + F: PIH Induced + folate supplementation; PIH + O: PIH Induced + omega 3 fatty acid supplementation; PIH + B_{12} + F + O: PIH Induced + vitamin B_{12} + folate + omega 3 fatty acid supplementation.

All dams from different groups were allowed to deliver naturally on d22 of gestation after which both dams and their offspring were shifted to a control diet and the offspring were continued on the same diets till 3 mo of age. Dam blood was collected at d20 of gestation for biochemical estimations. The offspring were then dissected at 3 mo of age to collect the blood for biochemical estimations. The collected blood samples centrifuged immediately to separate into the plasma and erythrocyte fractions which were then collected in cryovials and stored immediately at −80 °C for further biochemical estimations.

2.2. Diet preparation

All the treatment diets used vitamin-free casein. The AIN-93 guidelines for purified diets for laboratory rodents [37] were followed while preparing the diets and have been reported by us previously [29–30].

2.3. Observations recorded

The weekly body weights of the offspring were recorded till 3 mo of age to obtain the growth curves.

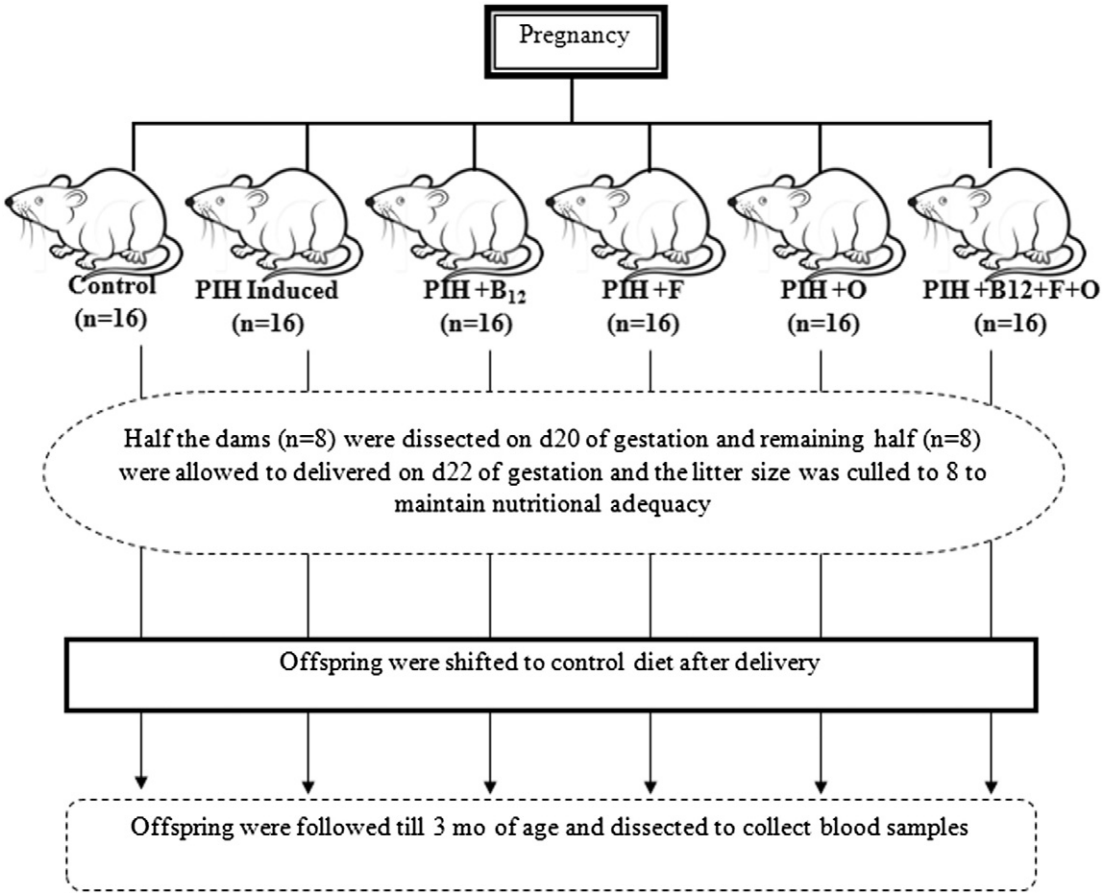

Fig. 1. Study design.