

Effects of L-NAME, DEXA, and L-NAME+DEXA on systemic blood pressure of hypertensive pregnant and non-pregnant Wistar Albino rats

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ABSTRACT

Objective: NO-inhibition has no effect on blood pressure (BP) of some spontaneous hypertensive animals, but when combined with dexamethasone (DEXA), it increases BP. The study compared effects of L-NAME and/or DEXA on systemic BP of spontaneously hypertensive pregnant and non-pregnant Wistar albino rats. **Method:** In two simultaneous experiments 62 female rats were used. All animals were mated for 7 days. Sperm positive (n1 = 33) and negative (n2 = 29) animals were each divided randomly into 4 groups. BPs were recorded in both experiments on the 15th day from tails indirectly, and then animals were given Physiologic Saline (Controls), L-NAME (150mg/kg/day), DEXA (100µg/kgBW/day) or L-NAME+DEXA (150mg and 100-µg per kg BW/day) for consequent 5 days. At 19th day, BPs were measured again, before applications. Then, animals put into individual metabolic cages for 24-h urine collection. Thereafter, blood was collected under ether anesthesia, animals were euthanized and necropsied. Weights of animals (BW), left kidneys, adrenal glands, and fetuses; food consumptions; 24-h urine volume; urinary proteins, blood glucose, and fetus numbers were determined. Data were analyzed by ANOVA and ANOVA for repeated measures. **Results:** In pregnant animals, L-NAME had higher BWs than DEXA and L-NAME+DEXA (P = 0.021 and P = 0.012, respectively). In non-pregnant animals, DEXA reduced BWs significantly compared with controls (P=0.042). Interventions influenced only the diastolic blood pressure of pregnant animals (P = 0.043). The difference between DEXA and L-NAME+DEXA was significant (P = 0.044). The effects of interventions on other variables varied according to whether animals are pregnant or not. **Conclusion:** L-NAME and/or DEXA did not influence BP in hypertensive rats.

Keywords: Wistar albino rats, L-NAME, dexamethasone

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Introduction

Hypertension, characterized by a systolic blood pressure of ≥ 140 mmHg and diastolic blood pressure of ≥ 90 mmHg, is one of the most important reasons of premature deaths, and the most important risk factor for cardiovascular diseases in men worldwide (Baker et al., 2007). It may be primary, developing because of environmental or genetic factors, or secondary, with multiple etiologies including vascular, renal, nervous,

endocrine and nutritional causes. Consequently, there are many risk factors implicating in the genesis of hypertension (Zhang et al. 2013). In general, they include genetic and environmental factors. More than 90-95% of cases are essential hypertension with yet unknown cause(s), but there are strong shreds of evidence for a possible familial background of the condition. Therefore, several studies targeting genes aimed to explain the genetic roots of various types of hypertension (Bernatova, 2014). However, none of

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the determined genetic abnormalities yet found to be responsible alone for a significant proportion of hypertension occurring in the general population.

Many other well-known pathophysiological risk factors of the hypertension include: overactivity of the sympathetic nervous system; immune reactivity and inflammation; overproduction of sodium-retaining hormones and vasoconstrictors; long-term dietary high sodium intake as well as low potassium and calcium intakes; disordered (high or inappropriate) renin secretion with consequent high production of angiotensin II and aldosterone; deficiencies in vasodilators including impairments of the nitric oxide (NO) system, prostacyclins and natriuretic peptide; increased secretion and/or activity of vascular growth factors; derangements in expressions of the kinin-kallikrein system involving in renal salt handling and vascular tone; alterations in cardiac adrenergic receptors and inotropic properties of the heart and systematic vascular tone; altered ion transport at the cellular level; abnormalities or lesions of vasculature due to various reasons including insulin resistance, diabetes and obesity; chronic kidney and lung diseases and activation of circulating proteins interfering with angiogenesis (Török, 2008; Bernatova, 2014).

There are also many pregnancy-related multifactorial disorders with different etiologies and characterized under others by hypertension with or without concomitant proteinuria (WHO, 2005). Preeclampsia and its severe form, eclampsia, are the most important conditions among these.

As for all other conditions and diseases of the men, research animals prove as a valuable tool also to understand the physiopathological mechanisms of hypertension. Because of the dramatic consequences of their implications on mother and their infants and so on the general population, numerous animal models described gaining insight into possible physiopathological mechanisms and treatment options of preeclampsia and eclampsia. The common models use mainly placental oxygen dysregulation, abnormal trophoblast invasion, maternal vascular damage and abnormal maternal-fetal immune interactions (Pennington et al., 2012).

Vascular endothelium produces various vasoactive factors including most potent vasoconstrictors angiotensin II (Ang II) and its mediator endothelin 1 (ET-1) (Cediel et al., 2002). On the other site, endothelium-derived NO is also the known most potent endogenous vasodilator and a local regulator of the vascular system. Increased production of NO during late gestation decreases systemic vascular resistance under normal conditions (Nathan et al. 1995). Thus, any decrease or failure of the NO

contributes to the development of hypertension (Rafikov et al., 2011). Therefore, animal models of preeclampsia *via* nitric oxide synthase (NOS) inhibition are often preferred as an alternative approach which aims to target mechanisms at the level of the endothelium instead trying to reproduce entire disease (Podjarny et al., 2004). The effects of the L-NAME on the uterine vasculature, however, may differ depending on whether animals are pregnant or not (Osol et al., 2009). Púzserová et al. (2007) have also been reported a significant relationship between BP and L-NAME-sensitive component of relaxation of the femoral artery.

Increased production of endogenous glucocorticoids and their parenteral applications or applications of their synthetic analogs (e.g., dexamethasone) results also in hypertension. A recent study demonstrated that the hypertensive effect of glucocorticoids is a consequence of their direct effects on blood vessels (Goodwin et al., 2011). There is also evidence of multiple interactions between NO-system and corticosteroids (Yallampalli et al., 1994; Changbin and Baylis, 2000). Dexamethasone is able to modify α -adrenoreceptor-mediated effects of L-NAME on vascular smooth muscles (Adeagbo and Triggler, 1993). However, there is no comparative information about the interactions between L-NAME and corticosteroids regarding systemic blood pressure in pregnant and non-pregnant rats.

This study aimed to determine the effects of NOS-inhibition (L-NAME), dexamethasone (DEXA) and the combination of L-NAME and DEXA on blood pressure of both pregnant and non-pregnant Wistar albino rats with a high blood pressure of dietary origin.

Materials and methods

Study conditions: Institutional Animal Ethics Committee has approved the study (#2012/105). The study has been carried out in a semi-climatized experimental room with a microenvironment of $23\pm 1^\circ$ C temperature, 50-70% relative humidity and 12:12 h light:dark cycle, which was similar to their rearing conditions. A total of 62 female Wistar rats (33 pregnant and 29 non-pregnant) were used in two different experiments, which were carried out simultaneously to avoid possible effects of time. Animals were allowed an adaptation period for ten days. Then, all animals were mated on the following 9 days in the harem system. Pregnancy was detected by daily vaginal sperm controls where the sperm [+] day recorded as the beginning of pregnancy (day 0) for given animal. During the mating period 33 animals were sperm [+], and 29 sperm [-].

The animals received pelleted diet for rats and mice and daily fresh top water throughout the study (including adaptation and mating periods) *ad libitum*.

L-NAME was given to animals by oral gavage and DEXA by intraperitoneal injections.

Experiment I: In this experiment, 33 pregnant rats were used. Animals were divided randomly into four groups. The animals in Group I served as controls. Animals in other groups were given L-NAME (150 mg/kg/d) (Group II), DEXA (100 µg/kg/d) (Group III) or L-NAME + DEXA(150 mg/kg/d + 100 µg/kg/d) (Group IV) for 5 days starting at the 15th day of their pregnancy. Animals in the control group were given equal volumes of physiological saline on the same days.

Experiment II: In this experiment 29 non-pregnant animals were divided randomly into four groups as in Experiment I. The animals in Group I served as controls. Animals in other groups were given same amounts of physiological saline, L-NAME (Group II), DEXA (Group III) or L-NAME + DEXA (Group IV) for 5 days; exactly, on the same last 5 days of the experiment, as in Experiment I.

Data collection: The body weights of animals were recorded at the beginning (day 0) and 15th and 19th days of the experiments. Blood pressures were recorded *via* non-invasive method from tails of animals on days 15 and 19 of the experiment before substance applications. On day 19, animals were put into individual metabolic cages for 24 h after blood pressure measurements, and 24 h-urine samples were collected on day 20 of the experiment. Thereafter, 4-5 ml blood samples were collected by hearth punctures under ether anesthesia, and then the animals were euthanized. Body weights, and weights of the suprarenal glands and left kidneys and fetuses' numbers (in Experiment I) were recorded from necropsied animals.

Laboratory analysis: Protein concentrations were determined *ad modum* Esbach in urine samples, and

glucose concentrations were determined *via* glucometer in blood samples, both by using strips.

Blood pressures measurements: Systolic and diastolic blood pressures were recorded from animals by non-invasive, indirect method (NIBP 200-A, Commat®, Ankara, Turkey). For this reason, animals were transported in pre-warmed recording room 2 hours before the measurements. Then, shortly before measurements they held for 15-20 minutes in a heated measurement box with inner temperature of 33-34 °C. Measurements were carried out when animals were relaxed and regular waves occurred. Three subsequent measurements were made from each animal.

Data were recorded, stored and evaluated by Biopac Version 3.7.2 Program (BIOPAC Systems, Inc. Aero Camino, USA).

Statistical analyses: SPSS for Windows® Version 21 was used to store and analyze the data gathered. Data were analyzed *via* ANOVA and ANOVA for repeated measures in factor time. Tukey test was used as *post hoc*. P≤ 0.05 was accepted as significant.

Results

Body weights: The body weights changes of the female Wistar rats are summarized in Table 1. There was no significant difference in mean body weights of both pregnant and non-pregnant animals at the beginning of the experiments (P>0.05).

During the 3-weeks experimental period, body weights of pregnant rats showed remarkable changes. The effects of interventions on the body weights of pregnant rats were significant (P=0.006). Paired comparisons for groups revealed significant differences for the groups given L-NAME, DEXA, and L-NAME + DEXA. Namely, the average body weight of the group given L-NAME was higher than those given DEXA and L-NAME + DEXA (P=0.025 and P=0.014 respectively). Analysis of variance for repeated

Table 1. Body weights of animals [g]

Groups	Pregnant rats			Non-pregnant rats		
	$\bar{X} \pm Sx$			$\bar{X} \pm Sx$		
	Day 0	Day 15	Day 20	Day 0	Day 15	Day 20
Control	214 ± 19	294 ± 22	317 ± 30	217 ± 08	268 ± 42	273 ± 44*
L-NAME	227 ± 21	313 ± 20*	315 ± 27	215 ± 50	255 ± 36	236 ± 29
DEXA	201 ± 07	274 ± 12 ^Ω	286 ± 16	202 ± 22	223 ± 23	209 ± 18 ^Ω
L-NAME + DEXA	213 ± 22	282 ± 34 ^Ω	269 ± 32	215 ± 13	258 ± 36	216 ± 28

In the same colon* - Ω: P<0.05

Table 2: Blood Pressures of Rats [mmHg]

Groups	Pregnant rats		Non-pregnant rats	
	15 th day	19 th day	15 th day	19 th day
	Systolic blood pressures			
Control	165.38 ± 18.84	151.57 ± 10.26	148.29 ± 16.70	135.57 ± 20.07
L-NAME	144.67 ± 11.09	142.50 ± 18.15	146.29 ± 10.08	153.43 ± 12.31
DEXA	150.0 ± 19.28	143.78 ± 15.92	133.14 ± 07.03	150.86 ± 10.89
L-NAME + DEXA	154.56 ± 20.43	161.22 ± 18.38	122.25 ± 19.64	151.14 ± 22.70
	Diastolic blood pressures			
Control	134.50 ± 18.45	123.29 ± 05.47	122.57 ± 14.55	115.57 ± 15.97
L-NAME	118.33 ± 13.80	117.38 ± 14.61	117.71 ± 08.12	132.29 ± 13.09
DEXA	118.0 ± 18.29	115.44 ± 11.18	109.0 ± 09.13	119.29 ± 10.08
L-NAME + DEXA	125.67 ± 14.77	132.22 ± 16.09	104.38 ± 14.46	135.43 ± 22.84

measures in factor time revealed that the effect of time was significant, and there was a significant interaction between the time and interventions (P=0.000). Paired comparisons for time revealed significant differences between the 1st and 2nd and 1st and 3rd measurement points (P=0.000). However, the differences between the 2nd and 3rd measurements were not confirmed statistically (P=0.058, %95 CI: - 12.157 - .150).

However, the effects of the interventions on the body weights of non-pregnant animals could not be confirmed statistically (P=0.066, F=2,729). Also, paired comparisons for groups did not confirm the difference in mean body weights of controls and DEXA (P=0.054, %95 CI: -.494 - 83,065). In contrast, the effect of time on the body weights of non-pregnant animals and the interaction between time and interventions proved to be significant (P=0.000). Paired comparisons for time revealed significant differences between the 1st and

2nd, 1st and 3rd and 2nd and 3rd measurements (P=0.000, P=0.007 and P=0.0000 respectively).

Systolic and diastolic blood pressures: Mean blood pressure values are presented in Table 2.

In pregnant rats, there was no significant difference in mean systolic blood pressure values, when recorded at day 15 before interventions. Statistical analysis did also not confirm the effects of interventions on systolic blood pressures recorded at day 19 (P=0.083, F= 2.456). The effect of time and interactions between time and interventions were also not significant (P>0.05).

There were significant differences in mean systolic blood pressure values of the non-pregnant Wistar albino rats at day 15 of the experiment, also before interventions. *Post hoc*s revealed lower mean systolic blood pressure of the L-NAME + DEXA group when compared with control and DEXA groups (P=0.010 and P=0.018 respectively). However, no significant

Table 3. Other Variables

Variables	Control	Pregnant rats		
		L-NAME	DEXA	L-NAME+DEXA
Glucose (mEq/L)	134.83 ± 38.45	93.13 ± 37.78	86.88 ± 12.63	111.50 ± 46.64
Abs. Left Kid. Wt (g)	0.96 ± 0.12	0.89 ± 0.13	0.80 ± 0.04	0.87 ± 0.13
Rel. Left Kid. Wt. (%)	0.0030 ± 0.00027	0.0028 ± 0.00047	0.0028 ± 0.00021	0.0033 ± 0.00047
Adrenal Glands Wt. (g)	0.08 ± 0.02	0.10 ± 0.02	0.09 ± 0.01	0.07 ± 0.01
Urine Vol. (mL/24h)	2.59 ± 3.48	5.25 ± 7.31	4.83 ± 5.86	3.56 ± 1.74
Urinary Protein (g/dL)	0.80 ± 0.84	1.00 ± 0.00	0.33 ± 0.71	1.75 ± 0.89
Numbers of Fetuses	7.57 ± 3.60	10.00 ± 3.07	13.22 ± 1.86	10.22 ± 2.95
Total Wt of Fetuses (g)	43.96 ± 19.54	50.75 ± 14.66	58.14 ± 15.04	41.96 ± 15.34

Kid; Kidney, Abs: absolute, Rel: relative, Vol: volume, Wt: weight

difference was found for systolic blood pressure at day 19. There was a significant effect of the time on systolic blood pressure of animals ($P=0.011$), and a significant interaction has occurred between time and interventions in this respect ($P=0.005$).

No significant difference was in mean diastolic blood pressure values of pregnant Wistar albino rats when measured before intervention at day 15. *Post hoc*s did also not confirm the difference between mean diastolic blood pressures of control and L-NAME groups ($P=0.098$, %95 CI: -2.716166 – 44.132833). However, the diastolic blood pressure values at 19th day of the experiment revealed significant differences between groups, indicating important effects of the interventions ($P=0.043$). *Post hoc*s revealed that the difference between DEXA and L-NAME + DEXA groups is significant ($P=0.044$). Time had no important effect, and no significant interaction could be detected between time and interventions in this respect.

Mean diastolic blood pressure values of non-pregnant Wistar albino rats showed significant differences before interventions at day 15 of the experiment. *Post hoc*s confirmed the difference between mean diastolic blood pressure values of the control and L-NAME + DEXA groups ($P=0.035$). In contrast, the differences between the mean diastolic blood pressure values at day 19 was not confirmed statistically ($P=0.083$, $F=2,506$). However, ANOVA for repeated measures in factor time confirmed the effect of time ($P=0.001$) and its interactions with interventions ($P=0.005$).

Blood glucose concentrations: The mean blood glucose concentrations of animals are seen in Table 3. Statistical analyses did not confirm the effects of interventions on blood glucose concentrations of the pregnant Wistar albino rats ($P=0.088$, $F=2.424$). Similarly, multiple comparisons did not confirm the difference between control and DEXA groups ($P=0.090$, %95 CI: -5.403682 – 101.320349).

In contrast, the interventions had significant effects on blood glucose concentrations of non-pregnant Wistar albino rats ($P=0.008$). Mean blood glucose concentrations of control and L-NAME groups was higher than that of the DEXA group ($P=0.017$ and $P=0.025$, respectively).

Kidney weights: Only the left kidney's weights were evaluated (Table 3). Statistical analyses indicated significant effects of the interventions on kidney weights of pregnant Wistar albino rats ($P=0.05$, $F=2.929$). *Post hoc*s revealed higher mean kidney weight of controls than that of DEXA given group ($P=0.032$).

In contrast, no significant effect of interventions

on kidney weights of non-pregnant rats could be detected.

Weights of Adrenal Glands: The mean adrenal gland weights of animals are summarized in Table 3.

Statistical analyses showed that the weights of adrenal glands of the pregnant Wistar albino rats were influenced by interventions ($P=0.000$). *Post hoc*s showed that the mean weight of the adrenal glands of L-NAME given group was higher than those of control and L-NAME + DEXA given groups ($P=0.038$ and $P=0.000$, respectively). Similarly, the mean weight of the adrenal glands of the DEXA group was higher than that of animals given L-NAME + DEXA ($P=0.002$). However, interventions had no significant effect on mean adrenal gland weights of the non-pregnant animals.

Urine volumes and urinary protein concentrations:

Average urine volumes and protein concentrations in the urine of pregnant and non-pregnant Wistar albino rats are shown in Table 3.

Statistical analyses of the data showed that interventions had no significant effect on 24-h urine volumes of pregnant Wistar albino rats, but their urinary protein excretions were influenced ($P=0.010$). *Post hoc*s revealed significantly lower urinary protein concentrations of DEXA than that of L-NAME + DEXA group ($P=0.005$).

In non-pregnant rats, neither 24-h urine volumes nor urinary protein excretions were affected by interventions ($P>0.05$).

Numbers and weights of the fetuses: The mean numbers of fetuses of pregnant Wistar rats and their total weights are seen in Table 3. ANOVA revealed significant effects of interventions ($P=0.005$). The difference between control and DEXA groups was confirmed in *post hoc*s ($P=0.003$). However, total fetal weights did not differ among groups.

Discussion

In studies using L-NAME interventions, the body weight changes of animals were rarely assessed. Available two studies indicate possible effects of L-NAME on body weights. Osol et al. (2009) reported that L-NAME given in drinking water (0.5g/L) for 10 days had no effect on body weights of non-pregnant rats, but body weights of pregnant animals receiving L-NAME were in mean 5% lower than those of pregnant controls. Ribeiro et al. (1992) observed also a slowed growth of the rats with chronic L-NAME application. In contrast, short or long-term DEXA causes a decrease in body weight of animals (Beatty et al., 1971; Tonolo et al., 1988; Michel and Cabanac, 1999; Franco-Colin et al., 2006). Tonolo et al. (1988)

reported 10 g weight loss per week when rats were given 10 µg DEXA per day for 4 weeks. Motta et al. (2015) reported that DEXA decreased the body weights of non-pregnant animals significantly, and it abolished the weight gain of pregnant animals. Also, dexamethasone administered by continuous infusions (16 µg/kg/h/sc) to pregnant rats from day 16 of gestation resulted in a 30 g cumulative weight gain from day 15 to 21 of gestation while the cumulative weight gains of controls was 80 g in this time-period (Mostello et al. 1981).

The findings of this study reveal that the effects of L-NAME, DEXA, and L-NAME + DEXA combination depend on the physiological conditions (being pregnant or not pregnant) of female Wistar rats. Compared to controls, L-NAME and DEXA resulted in a slower weight gain while L-NAME + DEXA caused a slight decrease in body weights of pregnant animals within five days. However, all of these interventions caused decreases in mean body weights of non-pregnant rats (Table 1). Thus, these findings indicate that DEXA with or without L-NAME has a significant negative effect on body weights of the rats, in general.

Findings of previous studies suggested also that the applications of L-NAME and DEXA result in significant increases in systolic and diastolic blood pressures of pregnant and non-pregnant female rats (Kemse et al., 2014; Tain et al., 2014; Safaeian et al., 2015). Initially, the mechanism of hypertension by the L-NAME application has been explained *via* NOS inhibition. Findings from recent studies, however, suggested the involvement of a very complex regulation network including several factors in the development of hypertension by L-NAME. These include among others the renal angiotensin-converting enzyme (Giani et al., 2014), thromboxane (Francois et al., 2008), peroxisome proliferator-activated receptor gamma (PPAR-γ) (Kriska et al., 2014) and glucocorticoids (Wallerath et al., 1999).

Observations of modified effects of L-NAME in stress situations with high levels of endogenous glucocorticosteroids or by applications of synthetic glucocorticoids (Li et al., 1992; Wen et al., 2000) indicated possible interactions between L-NAME and glucocorticoids regarding the development of hypertension. Various studies revealed that these interactions have both synergistic and antagonistic properties (Changbin and Baylis, 2000; Li et al., 1992; Wen et al., 2000). Accordingly, as many other effects, the hypertensive effects of glucocorticoids are also mediated partly *via* suppression of the endothelial nitric oxide synthetase (eNOS) expression (Liu et al.,

2009). Also, pregnancy seemingly alters the sensibility of the organism to L-NAME and DEXA (Nathan et al., 1995; Li et al., 2003; Losonczy et al., 1996; Troiano et al., 2016). Consequently, the effects of these substances on the cardiovascular system of pregnant and non-pregnant animals may differ. The findings of this study, however, did not support the findings of other studies, which clearly demonstrated that both L-NAME and DEXA applications induce hypertension, and, they have additive or synergic effects when used in combination in this respect (Changbin and Baylis, 2000; Wen et al., 2000; Lou et al., 2001).

The findings are also consistent with previous evidence gathered from human studies that L-NAME significantly increases blood pressure in healthy individuals, but not in hypertensive patients (Calver et al., 1992). However, the finding of this study did not support the hypertensive effects of L-NAME and glucocorticoids in this case DEXA in rats, and so far did not support preliminary studies cited above. The reasons may be multiple. First of all, basal blood pressures of animals in both control groups of this study are relatively high and indicate a possible spontaneous hypertension in the colony. The reason of this in the colony is not known exactly, but, basing to our recent experiences, it is assumed to be a dietary origin, because of the blood pressure in the colony is normalized by changing diet. There is evidence that the cardiovascular system of diet-induced hypertensive animals is relatively resistant to NOS inhibition (Roberts et al. 2000).

These findings give also evidence that the effects of L-NAME and/or DEXA are modifiable by physiologic condition, in this case, the pregnancy. A finding, which is in accordance with preliminary studies, cited above. Tong et al. (1997) found significant increases in blood glucose concentrations of normotensive and spontaneously hypertensive Wistar-Kyoto rats given 20 mg/kg BW L-NAME for 4 consecutive days. DEXA also induces a significant increase in blood glucose concentrations of rats (Koricanac et al., 2006; Sood and Ismail-Beigi, 2010). However, Motta et al. (2015) reported a significant decrease in fasting glycaemia of pregnant animals which was absent on non-pregnant animals. Also in this study, DEXA failed to increase blood glucose concentrations, but the findings indicated that DEXA might work differently depending on if animals are pregnant or not.

No information was available about the effects of L-NAME on kidney weights. Jennings and Ferguson (Jennings and Ferguson, 1984) could not observe any effect of DEXA on kidney weights in rats, whereas

Rooman et al. (1999) reported a dose-dependent decrease in mice. In this study, only the average kidney weight of pregnant animals was lower than that of controls.

Also, no information was available about the effects of L-NAME on weights of adrenal glands in rats. Lesniewska et al. (1992) applied 15, 30 or 60 mg DEXA per 100 g BW of rats for 7 days and observed a remarkable decrease in their adrenal gland weights. This effect was reversible and resolved within 7 days after the last application. The findings of this study showed that when compared to the control group, a significant increase in adrenal gland weight was seen only in pregnant rats by giving L-NAME. However, the addition of DEXA had an adverse effect to L-NAME alone.

A common finding of L-NAME-induced hypertension is the proteinuria. Rats given L-NAME in drinking water caused a decrease in glomerular filtration rate and a progressive increase in protein excretion in 24-h urine samples (Qiu et al., 1998). In

this study, the lowest and highest urinary protein excretions were recorded in DEXA and L-NAME + DEXA given pregnant rats, respectively.

Conclusion

This study is designed to evaluate the effects of L-NAME and DEXA, which were used routinely to produce hypertension in animal models, on blood pressure of female Wistar rats from a breeding colony with higher blood pressures seemingly due to dietary factors. The findings of this study indicate that the interventions caused no further increase in blood pressure in previously hypertensive animals and that the animals used are relatively resistant not only to L-NAME induced hypertension but also to DEXA and to a combination thereof. Thus, assessment of possible mechanisms would be important in explaining the ethiopathologies of resistances and predispositions for the NO- and DEXA-mediated hypertensions or hypertensions with multiple ethiopatogenesis.

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