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# Effect of glucocorticoids on renal dopamine production

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**Abstract**

This study assess the effects of glucocorticoids on dopamine excretion and evaluates the participation of renal dopamine in the effects of glucocorticoids on renal function and $Na^+$ excretion. Dexamethasone (i.m.; 0.5 mg/kg) was administered to male Wistar rats on day 2 or on days 2 and 5. Daily urinary excretions of $Na^+$, dihydroxyphenylalanine (DOPA), dopamine and dihydroxyphenylacetic acid were determined from day 1 to day 7. Renal function was evaluated 8 h after dexamethasone administration in a separate group. The first dose of dexamethasone increased about 100% diuresis and natriuresis, increased urinary DOPA and renal plasma flow, and did not affect urinary dopamine or the other parameters evaluated. These effects were not affected by previous administration of haloperidol. The second dexamethasone dose increased about 200% diuresis and natriuresis, increased urinary dopamine, DOPA, dihydroxyphenylacetic acid, $U_{osm} \times V$ and both glomerular filtration rate and renal plasma flow. Carbidopa administered before the second dexamethasone dose blunted both the diuretic and the natriuretic response whereas haloperidol abolished or blunted all the effects of the second dexamethasone dose. These results show that modifications in renal dopamine production produced by corticoids may contribute to the effects of these hormones on $Na^+$ balance and diuresis and suggest that regardless the factor that promotes an increase in renal perfusion and glomerular filtration rate during long term administration of glucocorticoids, a dopaminergic mechanism is actively involved in the maintenance of these hemodynamic changes. 

*Keywords:* Glucocorticoid; Dopamine; Natriuresis; Renal function; DOPA (dihydroxyphenylalanine)

## 1. Introduction

Glucocorticoids are known to have pronounced physiological effects in the kidney. These hormones increase glomerular filtration rate (Baylis et al., 1990), regulate renal gluconeogenesis and ammoniagenesis (Rodriguez et al., 1981; Welbourne, 1990) and increase tubule secretion of potassium and hydrogen ions, as well as renal tubule $Na^+$ reabsorption (Rossier and Lawrence, 1990). The effects of glucocorticoids on fluid and electrolyte balance are largely exerted through permissive effects on tubular function and actions that maintain glomerular filtration rate. In vivo studies suggest that $Na^+/K^+$ATPase, an enzyme playing a pivotal role in several tubular transport processes, is regulated in part by glucocorticoids. Natural or synthetic glucocorticoids produce substantial $Na^+/K^+$-ATPase increments in cortical homogenates from adrenal-intact animals, and are at least as effective as mineralocorticoids in restoring enzyme activity after adrenalectomy (Katz, 1990). In addition stimulation of the activity of the enzyme by chronic administration of glucocorticoids appears to coincide with changes in tubular $Na^+$ reabsorption (Katz and Epstein, 1967). Glucocorticoids also stimulate the activity of $Na^+/H^+$ exchanger in renal brush border membrane vesicles (Freiberg et al., 1982) and in isolated proximal tubular cells physiological concentrations of dexamethasone increase the activity of the antiporter within 1 h of administration (Arruda et al., 1993). Acute and chronic administration of glucocorticoids have different effects on $Na^+$ balance and renal hemodynamics. Acute administration of cortisol variably produces either natriuresis or $Na^+$ retention, an effect more clearly demonstrable after the first 12 h of administration, while chronic administration of the corticoid induces $Na^+$ retention (Montrella-Waybill et al., 1991). Chronic administration of corticoids increases glomerular filtration rate and renal

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plasma flow (Maddox and Brenner, 1996) whereas both these effects are not always found after acute administration (Clore et al., 1988).

Dopamine is formed by the mammalian kidney in non-neuronal structures (Lee, 1993). It has been recently shown that circulating DOPA is filtered by the kidney and that a major proportion of the dopamine in rat and human urine derives from decarboxylation in proximal tubular cells of DOPA reabsorbed from ultrafiltrated plasma (Grossman et al., 1992; Lee, 1993; Wolfovitz et al., 1993). Although it is accepted that about 85% of the dopamine in the urine is derived from circulating DOPA, the existence of sources other than DOPA in the plasma has been postulated to account for the unaccounted fraction (Grossman et al., 1992). Other potential sources for urinary dopamine such as dopamine in the plasma filtered through the kidney and dopamine released from renal nerves have been shown to be, if at all, only minor contributors (Lee, 1993). There is strong evidence suggesting that renal dopamine may play an important role in regulation of $Na^+$ excretion (Hegde and Lockhandwala, 1990). The inhibition of the decarboxylation of DOPA attenuates natriuretic responses (Sowers et al., 1984), decreases urinary excretion of dopamine (Ball and Lee, 1977), and blunts dopamine excretory responses to volume challenge (Sowers et al., 1984). The effects of dopamine on $Na^+$ regulation have been related to the inhibition of the activities of $Na^+/K^+$ATPase (Aperia et al., 1987) and the $Na^+/H^+$ exchanger (Felder et al., 1990) in the proximal convoluted tubules of the kidney and other segments of the nephron (Bertorello and Katz, 1993). Both in vivo and in vitro studies have suggested that the synthesis of dopamine in proximal tubular cells is influenced by extracellular concentrations of $Na^+$ (Lee, 1993). Thus, factors affecting renal tubule $Na^+$ reabsorption (i.e., glucocorticoids) may conceivably affect renal dopamine production. In fact, changes on urinary excretion of dopamine have been reported in a patient on chronic corticosteroid therapy (Schoors et al., 1990).

This study assess the effects of glucocorticoids on dopamine excretion and evaluates whether changes in renal dopamine production may mediate some of the effects of glucocorticoids on renal function and $Na^+$ excretion. For this purpose we determined urinary excretions of $Na^+$ and renal function as well as urinary excretions of DOPA, dopamine, the dopamine metabolite dihydroxyphenylacetic acid (DOPAC), in rats treated with dexamethasone, a synthetic glucocorticoid, with or without the concomitant administration of haloperidol, a dopaminergic blocking agent.

## 2. Materials and methods

Three month-old male Wistar rats were used in these studies. All animals were inbred in our laboratory, kept at 22°C on a 12:12-h dark–light cycle and given free access to normal rat diet (protein content 25%) and tap water.

### 2.1. Experimental design

On the morning of day 1 animals were placed in metabolic cages, a 24-h urine was collected and animals were randomly assigned to one of the following groups:

#### 2.1.1. Dexamethasone 1

Dexamethasone acetate (0.5 mg/kg; Pacak et al., 1992) ($n = 10$) or vehicle (sham; $n = 9$) were injected i.m. on day 2, renal function was evaluated as described below in four animals of each group 8 h after dexamethasone administration. Serial 24-h urines were collected from the rest of the animals up to day 7.

#### 2.1.2. Dexamethasone 2

Dexamethasone (0.5 mg/kg) ($n = 9$) or vehicle (sham; $n = 9$) were injected i.m. on day 2. A second dose of dexamethasone (0.5 mg/kg) or vehicle was also administered on day 5. Renal function was evaluated in four animals of each group 8 h after administration of the second dexamethasone dose. Urines were collected up to day 7 in all remaining rats.

#### 2.1.3. Dexamethasone 1 + haloperidol

Haloperidol (25 μg/kg, i.p.; Sato et al., 1987) was administered one hour before administration of 0.5 mg/kg dexamethasone ($n = 9$) and 3 more times every 4 h. Renal function was evaluated in four animals after administration of the 3rd haloperidol dose. 24-h urine was collected starting after the first haloperidol injection in the remaining animals. Animals were sacrificed after the study.

#### 2.1.4. Dexamethasone2 + haloperidol

Animals received one dose of dexamethasone on day 2. On day 5 haloperidol (25 μg/kg; i.p.) was administered 1 h before administration of the second dose of dexamethasone ($n = 9$) and 3 more times every 4 h. Renal function was evaluated in four animals after administration of the 3rd. haloperidol dose and a 24 h urine collection was obtained from the remaining animals. Animals were sacrificed after the study.

Dexamethasone2 + carbidopa: Carbidopa (20 mg/kg; Rose et al., 1991), an aromatic-L-decarboxylase (EC 4.1.1.28) inhibitor, was administered i.p. 1 h before the second dexamethasone injection on day 5 and 3 more times every 4 h. 24-h urine was collected starting after the first carbidopa injection.

Four doses (one every 4 h) of haloperidol (25 μg/kg, i.p.) were administered to a group of untreated animals ($n = 5$). 24 h urine collections were obtained from these animals starting just before the first haloperidol dose.

All urine collections were stored at −70°C until assayed for catechols, $Na^+$ and osmolality. Urinary concen-

Table 1
Urinary volume and urinary excretions of dopamine (DA), DOPA, dihydroxyphenylacetic acid (DOPAC), norepinephrine (NE), and $Na^+$ in the first day of the study

| | |
|---|---|
| Volume ml/24 h | 9.80 ± 0.40 |
| DA nmol/24 h | 51.00 ± 1.01 |
| DOPA nmol/24 h | 1.34 ± 0.33 |
| DOPAC nmol/24 h | 179 ± 54 |
| NE nmol/24 h | 15.7 ± 4.5 |
| $Na^+$ meq/24 h | 1.90 ± 0.19 |

Values are means ± S.E.; $n = 30$ animals.

trations of DOPA, dopamine, DOPAC were determined as described below. Urine content of $Na^+$ was determined by flame-photometry. Urine osmolality was determined by the freezing-point method.

### 2.2. Renal function evaluation

Renal function was simultaneously evaluated by the measurement of glomerular filtration rate and renal plasma flow clearances by inulin (Inutest, Laevosan-Gesellschaft, n.b.H. Linz, Austria) and paraaminohippurate, respectively (Smith et al., 1945; Young and Raisz, 1952; Ibarra et al., 1996). Animals were anesthetized with pentobarbital, a tracheostomy tube was placed and the right jugular vein, the left carotid artery, and the urinary bladder were cannulated. Blood samples were taken from the carotid artery. After a priming injection of 0.45 ml of a 10 ml saline solution containing 225 mg of Inutest and 70 mg of paraaminohippurate enough to provide a plasmatic concentration of 0.2 and 0.02 mg/ml respectively, a sustaining infusion through the jugular vein was administered at a rate of 20 μl/min using a Harvard infusion pump. After 45 min equilibrium, three 30 min urine samples were collected, and three blood samples were drawn in the middle of each period.

### 2.3. Assays

#### 2.3.1. Determination of catechols

The catechols in 10 μl urine were determined as reported previously (Eisenhofer et al., 1986). Briefly, catechols in the samples were partially purified by batch alumina extraction, separated by reverse-phase high-pressure liquid chromatography using a 4.6 × 250 mm ODS 5 μm column (Axxiom Chromatography, USA) and quantified amperometrically by the current produced upon exposure of the column effluent to oxidizing and then reducing potentials in series using a triple-electrode system (ESA, Bedford, MA). Recovery through the alumina extraction step averaged 70–80% for dopamine, 45–55% for DOPA and 40% for DOPAC. Catechol concentrations in each sample were corrected for recovery of an internal standard, dihydroxybenzylamine. Levels of DOPA, DOPAC were further corrected for differences in recovery of the internal standard and of these catechols in a mixture of external standards. The limit of detection was about 15 pg/volume assayed for each catechol.

### 2.4. Data analysis

Data are means ± S.E. One-way ANOVA for repeated measures followed by Newman–Keuls test was used to assess the significance of differences among serial determinations in sham and dexamethasone treated animals. One way ANOVA and independent means *t*-test were used to assess the effect of haloperidol treatment. Correlation coefficients were calculated by linear regression analysis. $P < 0.05$ defined statistical significance.

## 3. Results

Urinary volume and urinary excretions of dopamine, DOPA, DOPAC, norepinephrine and $Na^+$ on the first day of urine collection (day 1) are shown in Table 1. Urinary dopamine correlated positively and significantly with $Na^+$

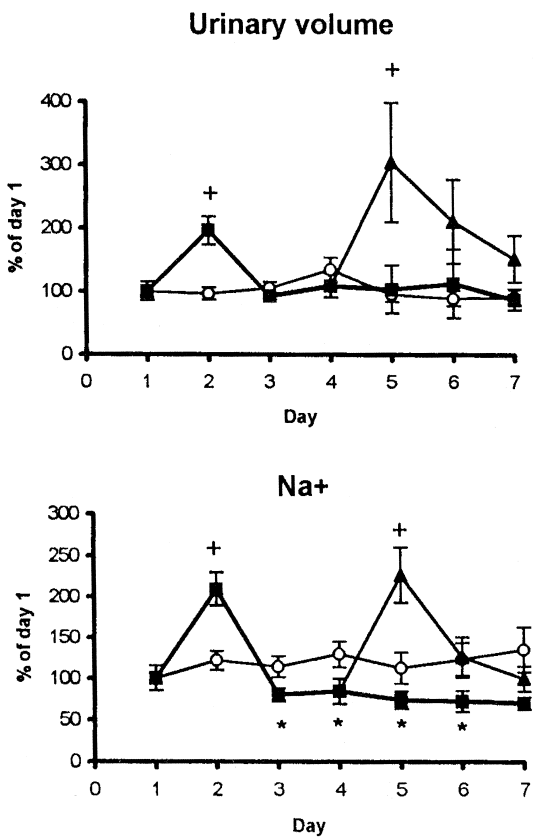


Fig. 1. Urine volume ($U \times V$) and urinary excretion of $Na^+$ in rats treated with vehicle (○) ($n = 10$), 0.5 mg/kg dexamethasone on day 2 (■) ($n = 6$) or 0.5 mg/kg dexamethasone on days 2 and 5 (▲) ($n = 5$). Values are expressed as percent of day 1. Results are means ± S.E. * Significantly different from day 1 (one way ANOVA); + significantly different from vehicle or one dexamethasone dose (two ways ANOVA).

excretion ($r = 0.51$; $p < 0.01$) across the entire group. In sham animals urinary volume and urinary excretions of $Na^+$ (Fig. 1), dopamine, DOPA, and DOPAC (Fig. 2) did not change significantly during the study.

In the 24 h following the first dexamethasone injection urinary volume increased about 100% (from $9.3 \pm 1.0$ to $21.4 \pm 1.9$ ml/24-h; $p < 0.05$). Urinary volume returned to day 1 values on day 3 and remained unchanged afterwards. $Na^+$ excretion also increased about 100% after dexamethasone injection (from $1.8 \pm 0.1$ to $3.6 \pm 0.2$ meq/24-h; $p < 0.05$). In the following days $Na^+$ excretion decreased about 30% ($p < 0.05$) when compared to the excretion of either sham or the day 1 excretion of treated rats (Fig. 1). Urinary excretion of dopamine increased slightly on the day of the first dexamethasone injection, decreased about 25% (from $56 \pm 5$ to $41 \pm 3$ nmol/24 h; $p < 0.05$) on days 3 and 4 and returned to day 1 levels thereafter. Urinary DOPA increased significantly

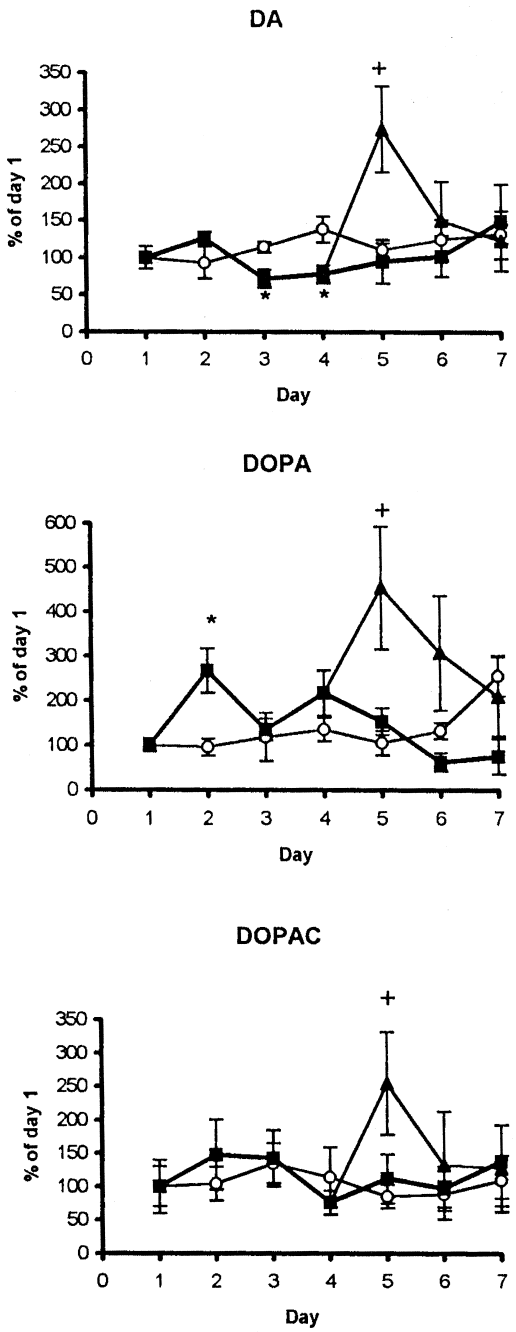


Fig. 2. Urinary excretions of dopamine (DA), DOPA and dihydroxyphenylacetic acid (DOPAC) in rats treated with vehicle (○) ($n = 10$), 0.5 mg/kg dexamethasone on day 2 (■) ($n = 6$) or 0.5 mg/kg dexamethasone on days 2 and 5 (▲) ($n = 5$). Values are expressed as percent of day 1. Results are means ± S.E. * Significantly different from day 1; + significantly different from vehicle or one dexamethasone dose.

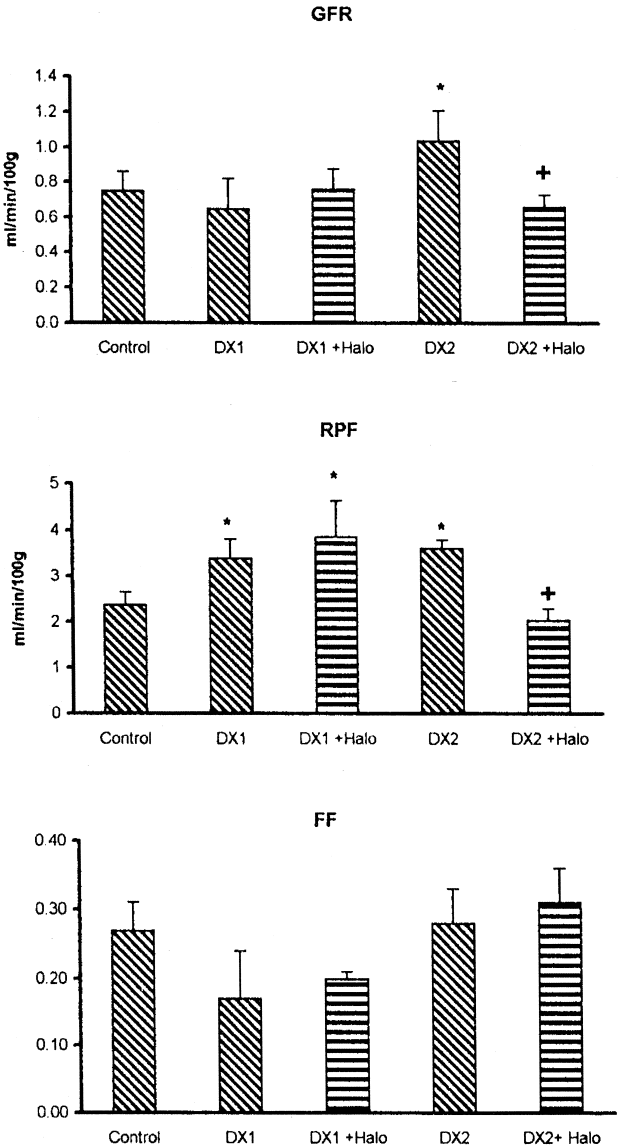


Fig. 3. Glomerular filtration rate (GFR), renal plasma flow (RPF) and filtration fraction (FF) in untreated animals (control) ($n = 8$), and animals treated with one dose of dexamethasone (DX1) ($n = 6$), one dose of dexamethasone and haloperidol (DX1 + Halo) ($n = 5$), two doses of dexamethasone (DX2) ($n = 5$) and two doses of dexamethasone and haloperidol (DX2 + Halo) ($n = 5$). For details of drugs administration see Section 2. Results are means ± S.E. * Significantly different from control; + significantly different from dexamethasone2.

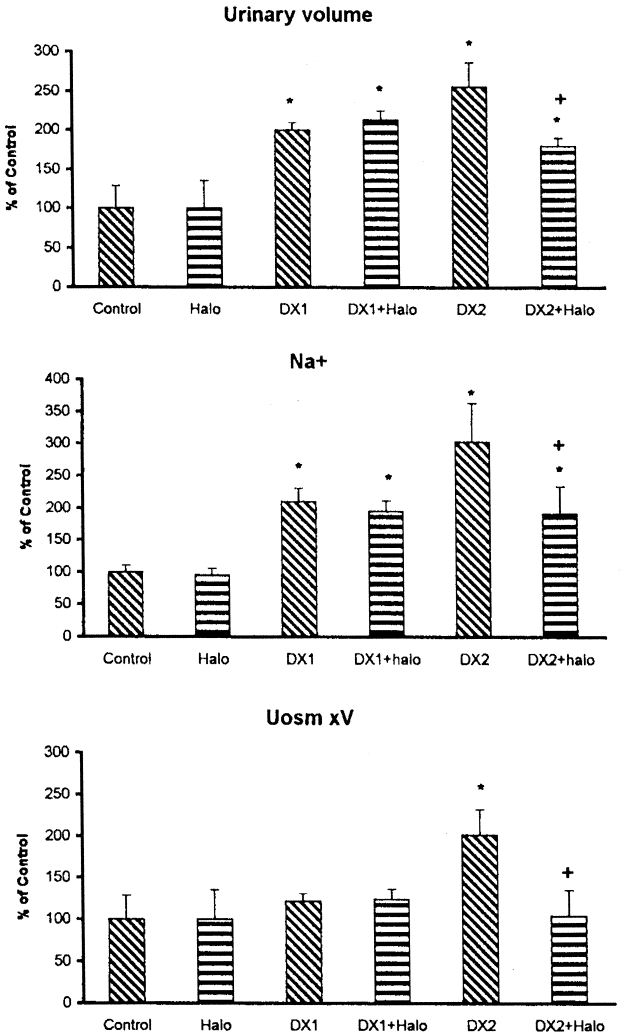


Fig. 4. Urinary volume, $Na^+$ excretion and $U_{osm} \times V$ responses to administration of vehicle (control) ($n = 10$), haloperidol (Halo) ($n = 5$); one dose of dexamethasone (OX1) ($n = 6$), one dose of dexamethasone and haloperidol (DX1 + Halo) ($n = 5$), two doses of dexamethasone (DX2) ($n = 5$) and two doses of dexamethasone and haloperidol (DX2 + Halo) ($n = 5$). For details of drugs administration see Section 2. Results are mean ± S.E. * Significantly different from vehicle; + significantly different from DX2.

on the day of dexamethasone injection (from $1.6 \pm 0.4$ to $5.0 \pm 0.5$ nmol/24 h; $p < 0.05$). Urinary DOPAC did not change significantly after one dexamethasone injection (Fig. 2).

Administration of one dose of dexamethasone did not produce any significant modification in glomerular filtration rate but increased significantly ($p < 0.05$) renal plasma flow and decreased, although not significantly, filtration fraction (Fig. 3). Osmolar excretion ($U_{osm} \times V$) increased slightly (from $19.5 \pm 0.81$ to $23.7 \pm 2.41$ mOsm/24 h) after one dose of dexamethasone.

Urinary volume and $Na^+$ excretion increased about 200% after administration of the second dexamethasone dose ($p < 0.02$). Both parameters were slightly higher than after one dexamethasone dose on days 6 and 7 (Fig. 1). Urinary dopamine and DOPAC also increased ($p < 0.03$) the day of the second dexamethasone dose (day 5). DOPA excretion increased in the two days following the second dose of dexamethasone (days 5 and 6; $p < 0.03$) (Fig. 2).

Administration of a second dose of dexamethasone increased significantly both glomerular filtration rate ($p < 0.05$) and renal plasma flow ($p < 0.05$) but had no significant effect on filtration fraction (Fig. 3). $U_{osm} \times V$ increased significantly ($p < 0.02$) to $39.3 \pm 12.5$ mOsm/24 h.

Haloperidol administered to untreated animals had no significant effect on urinary volume, $Na^+$ excretion and $U_{osm} \times V$ (Fig. 4) or urinary excretions of dopamine, DOPA and DOPAC (Fig. 5). Treatment with haloperidol had no significant effect on dexamethasone 1-induced modifications on urinary volume, $U_{osm} \times V$ and urinary excretions

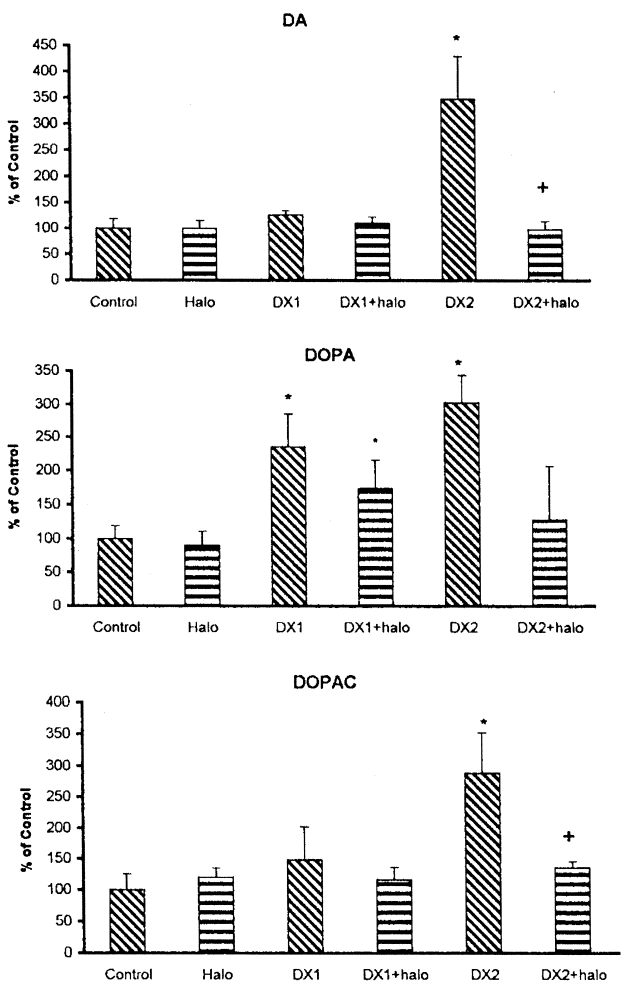


Fig. 5. Urinary dopamine (DA), DOPA and dihydroxyphenylacetic acid (DOPAC) responses to administration of vehicle (control), haloperidol (Halo) ($n = 5$); one dose of dexamethasone (DX1) ($n = 6$), one dose of dexamethasone and haloperidol (DX1 + Halo) ($n = 5$), two doses of dexamethasone (DX2) ($n = 5$) and two doses of dexamethasone and haloperidol (DX2 + Halo) ($n = 5$). For details of drugs administration see Section 2. Results are mean ± S.E. * Significantly different from vehicle; + significantly different from DX2.

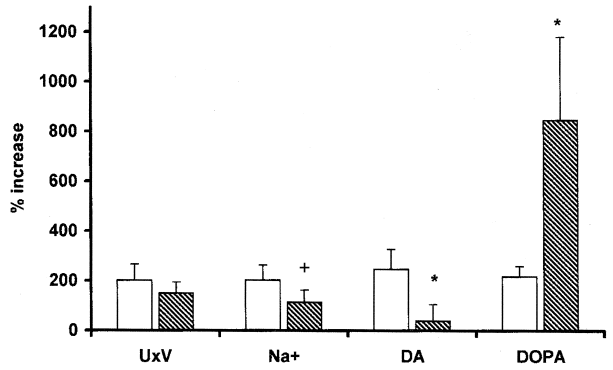


Fig. 6. Effect of Carbidopa (hatched bars) ($n = 4$) administered before the second dose of dexamethasone (open bars) ($n = 6$) on day 5 on the responses of urinary volume ($U \times V$), urinary $Na^+$, dopamine (DA) and DOPA. Results are mean ± S.E. and are expressed as percentage of day 1; $^+p < 0.05$; $^*p < 0.03$ significantly different from dexamethasone alone.

of $Na^+$ (Fig. 4), dopamine, DOPA and DOPAC (Fig. 5). It had also no significant effect on glomerular filtration rate, renal plasma flow or filtration fraction (Fig. 3).

However haloperidol decreased significantly both the volume increment (256 ± 31% vs. 151 ± 30%; $p < 0.02$), $U_{osm} \times V$ (201 ± 32% vs. 104 ± 20%, $p < 0.02$) and the natriuretic response (303 ± 60% vs. 191 ± 42%; $p < 0.05$) induced by the second dose of dexamethasone (Fig. 4). Haloperidol also abolished urinary dopamine response (230 ± 79% vs. 7 ± 16%; $p < 0.02$) and blunted urinary DOPA (302 ± 41% vs. 128 ± 71%) and urinary DOPAC (180 ± 60% vs. 36 ± 10%; $p < 0.02$) responses (Fig. 5). Moreover, administration of haloperidol abolished the increments on glomerular filtration rate and renal plasma flow (Fig. 3) induced by the second dose of dexamethasone.

Treatment with carbidopa reduced both the natriuretic response (from 203 ± 61% to 115 ± 48%; $p < 0.05$) and although not significantly the increase in urinary volume (from 200 ± 64% to 150 ± 45%) produced by the second dexamethasone dose. Carbidopa reduced significantly the increase in urinary dopamine brought about by the second dose (202 ± 77% vs. 40 ± 66%; $p < 0.03$) and increased significantly DOPA response to the corticoid (205 ± 41% vs. 898 ± 335%, $p < 0.03$) (Fig. 6).

## 4. Discussion

This study shows that renal dopamine production is affected by administration of glucocorticoids and strongly suggests that endogenously produced dopamine may mediate some of the effects of these hormones on renal hemodynamics and $Na^+$ handling.

Acute administration of dexamethasone acetate, a glucocorticoid having a long duration of action, especially following i.m. administration (Thomas and Keenan, 1986), had pronounced effects on diuresis, natriuresis and urinary excretion of DOPA but had no immediate effect on dopamine excretion. Acute administration of cortisol to rats is sometimes associated with a transient increase in glomerular filtration rate (Guant and Chart, 1962). The effects we have observed, however, appear to be independent from changes in the glomerular filtration rate since we were unable to demonstrate any significant modification in this parameter when it was determined either 8 h or 12 h (data not shown) after dexamethasone administration. The acute effects of dexamethasone administration on urinary volume, $Na^+$ excretion and urinary DOPA seem more likely to be derived from decreased tubular reabsorption as well as increased renal plasma flow with a concomitant decrease in medullary hypertonicity (Nashat et al., 1969).

In the days following the first administration of dexamethasone $Na^+$ excretion was decreased. This decrease was accompanied by a decrease in urinary dopamine that lasted for only two days. Urinary excretion of dopamine has been shown to closely parallel urinary excretion of DOPA in several experimental conditions (Goldstein et al., 1993; Armando et al., 1995). The lack of such a relation after acute dexamethasone suggests an impaired DOPA transport into the renal tubular cell that would be in line with the known effects of glucocorticoids on amino acid transport in the kidney as well as in other tissues (Beauwens and Crabbe, 1985). The analysis of the urinary dopamine to DOPA ratios along the study also suggests an impaired DOPA transport since these ratios were decreased for at least five days following dexamethasone administration. A decreased tubular uptake of DOPA would lead to decreased dopamine production (Lee, 1993; Armando et al., 1995).

In comparison with the first, the second dose of dexamethasone had a greater effect on diuresis, natriuresis and urinary DOPA, increased $U_{osm} \times V$ and produced clear increments in glomerular filtration rate and renal plasma flow while the filtration fraction was unaltered. The effect on DOPA excretion of this dose could be attributed not only to a tubular effect but also to the increase in glomerular filtration rate since DOPA in the urine derives from DOPA filtered from the plasma (Grossman et al., 1992; Lee, 1993). Administration of a second dexamethasone dose also increased markedly urinary dopamine. A similar effect on urinary excretion of dopamine has been reported in a patient on chronic corticosteroid therapy and attributed to increased renal production (Schoors et al., 1990). It has been shown that renal dopamine synthesis is dependent on $Na^+$ delivery to proximal tubular cells (Lee, 1993). It is thus possible that the previous $Na^+$ retention triggered an increase in renal dopamine synthesis that occurs gradually as it has been shown by salt-loading experiments, another situation accompanied by $Na^+$ retention (Grossman et al., 1991).

Our finding of increased glomerular filtration rate and renal plasma flow without changes in the filtration fraction is in agreement with that reported by Baylis and Brenner

(Baylis and Brenner, 1978) showing that in rats chronically treated with methylprednisolone the increase in single nephron glomerular filtration rate was produced by significant reductions in the resistance of both the afferent and efferent arterioles without variations in other determinants of glomerular filtration. The mechanisms involved in the increase in glomerular filtration rate induced by glucocorticoids are not clearly understood (Maddox and Brenner, 1996). Volume retention and alterations in eicosanoid production have been reported not to be involved in this effect (Garcia et al., 1987; Baylis et al., 1990).

Administration of carbidopa together with the second dose of dexamethasone blunted but did not suppress completely both the natriuretic and the diuretic response. The large increase observed in urinary DOPA reflected the inhibitory action of carbidopa on aromatic-L-aminoacid decarboxylase. The blunting of the natriuretic effect suggested an involvement of dopamine in this response.

Administration of haloperidol, a dopaminergic receptor blocking agent also decreased the natriuresis and the diuresis. The effects of the second dexamethasone dose on glomerular filtration rate and renal plasma flow were completely antagonized by blocking dopaminergic receptors with haloperidol. Interestingly, the blockade of the effects on glomerular filtration rate decreased the natriuresis and the diuresis to the levels observed after one dexamethasone dose suggesting that both the natriuresis and the diuresis produced by the second dexamethasone dose depend on hemodynamic as well as tubular effects. These results reinforced the suggestion of an involvement of dopamine in both the diuretic and the natriuretic response to the second dexamethasone dose. Haloperidol administration antagonized completely the effects of the second dexamethasone dose on glomerular filtration rate and renal plasma flow but had no effect whatever on any of the parameters measured either in control animals or in those administered one dose of dexamethasone. Blockade of dopaminergic receptors affected glomerular filtration rate only when renal production of dopamine was increased suggesting that dopamine is involved in the mechanism by which corticoids increase or maintain glomerular filtration rate high. This would suggest that dopamine may have a role as a paracrine regulator of renal microcirculation probably, as proposed by Lee (1993), through activation of dopamine receptors on the macula densa inhibiting renin release from the juxtaglomerular apparatus and promoting a decrease in the tubuloglomerular feedback (Schnermann et al., 1990).

One possible explanation for the different effects of the first and the second dose of dexamethasone is that the difference arises from the differences in $Na^+$ handling. When the second dose is given animals are in negative $Na^+$ balance (i.e., $Na^+$ retention). Previous $Na^+$ retention may be the triggering factor for increased dopamine production. This will in turn increase or maintain the increase in glomerular filtration rate that will ultimately result in increased DOPA availability to the proximal tubule and sustain the increase in dopamine production. If this hypothesis holds true it will also provide an explanation for the variable effects on natriuresis and glomerular filtration rate reported after acute administration of glucocorticoids.

In conclusion, our results show that modifications in renal dopamine production produced by corticoids may contribute to the effects of these hormones on $Na^+$ balance and diuresis and suggest that regardless the factor that promotes an increase in renal perfusion and glomerular filtration rate during long term administration of glucocorticoids, a dopaminergic mechanism is actively involved in the maintenance of these hemodynamic changes.

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