

TREATMENT OF PREGNANCY INDUCED HYPERTENSION

WITH NIFEDIPINE (ADALAT)

THESIS

submitted in partial fulfillment for the degree of

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BY

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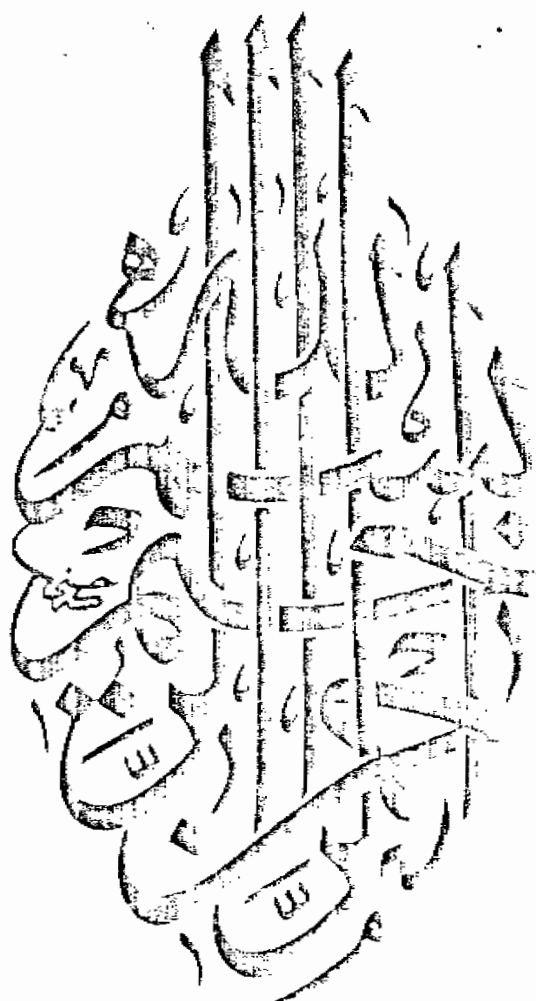
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AIM OF THE WORK

The aim of the work is to evaluate the results of management of hypertensive disorders of pregnancy in Ain Shams Maternity Hospital by sublingual Adalat and is to study the effect of Adalat as a new modality in the treatment of pregnancy induced hypertension with its rapid onset of action.

HYPERTENSION :

It is defined as a diastolic blood pressure of at least 90 mmHg. or systolic blood pressure of at least 140 mmHg. or rise in the former of at least 15 mmHg., or the later of 30 mmHg., the blood pressure cited must be manifest on at least two occasions 6 hours or more apart.

PROTEINURIA :

It is defined as more than 0.3 gm per liter in 24 hours collection, or greater than 1 gm per liter in at least two random urine specimens collected 6 hours or more apart.

PRE ECLAMPSIA :

It is the development of hypertension with proteinuria, oedema, or both induced by pregnancy after the 20 th Week of gestation, and sometimes earlier when there is extensive hydatiform changes in the chorionic villi.

ECLAMPSIA :

It is occurrence of convulsions, not caused by any coincidental neurological disease such as epilepsy, in a woman whose condition also fulfills the criteria for pre eclampsia.

SUPERIMPOSED PRE ECLAMPSIA AND ECLAMPSIA:

It is the development of pre eclampsia or eclampsia in a woman with chronic hypertensive vascular or renal disease.

CHRONIC HYPERTENSIVE DISEASE :

It is the presence of persistent hypertension, of whatever the cause, before the 20th week of gestation in the absence of neoplastic trophoblastic disease, or persistent hypertension beyond 6 weeks postpartum.

GESTATIONAL HYPERTENSION :

It is hypertension that develops during the later half of pregnancy or during the first 24 hours after delivery. It is not accompanied by other evidence of pre eclampsia or hypertensive vascular disease, and it disappears within 10 days following parturation. Gestational hypertension is most likely to be a variety of pre eclampsia.

GESTATIONAL OEDEMA :

It is the generalized accumulation of fluid of greater than " one plus " pitting oedema after 12 hours bed rest or a weight gain of 5 pounds or more in a week.

GESTATIONAL PROTEINURIA :

It is the proteinuria during pregnancy in the absence of hypertension, oedema, renal infection or known renovascular disease, the existence of such entity is questionable.

CHRONIC HYPERTENSIVE DISEASE

DEFINITION:

more than It is the presence of persistent hypertension (140/90 or more), of whatever the cause, before the 20th week of gestation, in the absence of neoplastic trophoblastic disease, or persistent hypertension beyond 6 weeks postpartum. (Pritchard - Mac Donald, 1980)¹.

CLASSIFICATION :

Sims (1970)⁷ has proposed the following classification, which is presented here with slight modifications :

I) Hypertensive disease :

- 1- Essential hypertension (hypertensive vascular disease) :

It is the most common disease, which may be mild, moderate, severe or malignant (accelerated).

- 2- Renal vascular hypertension (renovascular hypertension).
- 3- Coarctation of the aorta.
- 4- Primary aldosteronism.
- 5- Pheochromocytoma.

II) Renal and Urinary tract disease :

- 1- Glomerulonephritis: more frequent than previously thought, it may be acute nephritis or nephrotic syndrome.
 - 2- Pyelonephritis.
 - 3- Lupus erythromatosus.
 - 4- Scleroderma with renal involvement.
 - 5- Periarteritis nodosa with renal involvement.
 - 6- Acute renal failure.
 - 7- Polycystic disease.
 - 8- Diabetic nephropathy.
-

PATHOLOGICAL CHANGES
IN PREGNANCY INDUCED HYPERTENSION

KIDNEY CHANGES :

The kidney is affected by marked reduction of plasma flow resulting in reduction of the glomerular filtration rate. The renal changes are probably of greatest significance, since they account directly for the proteinuria and for the salt and water retention.

Spargo and associates., 1959⁸ described a characteristic lesion peculiar to preeclampsia (glomerular - capillary endotheliosis). In this lesion there is enlargement of the glomerulus and wide spread swelling of intracapillary cells leading to occlusion of the capillary lumen and apparent avascularity of the glomerulus. The basement membrane is not thickened but there are characteristic subendothelial deposits of " fibrin - like " material which vary in electron density and appearance. These changes disappear rapidly after delivery.

Vassalli and Coworker., 1963⁹), on the basis of immunofluorescent staining considered this material

to be fibrinogen, or fibrinogen derivative and regarded its presence as a characteristic of preeclampsia.

This observation led to a theory that the renal lesions of preeclampsia, - eclampsia are the result of intravascular coagulation initiated by something, presumably, thromboplastin released from the placenta.

Altchek et al., 1968¹⁰ studied renal changes of 76 patients with preeclampsia, and reported on their renal biopsy. He described lesions that could be recognized by light and electron microscopy. These lesions comprised :

1. Glomerular lesions : glomeruli were slightly enlarged and cellular, all glomeruli appeared to be affected but the distribution within a single glomerulus was patchy . There was an increase in the number of cells between capillaries (mesangial cells).

The basement membrane was splitted due to increase in the mesangial matrix by electron microscope studies.

Bowman's capsule showed deposition of fibrillary protein strands within it.

2. Juxtaglomerular Hyperplasia : Juxtaglomerular cells were increased in number and size with cytoplasmic swelling and vaculation.
3. Lesions of Henle's loop : the epithelium of Henle's loop was severely desquamated with fragments of nuclei and cells. Swelling of the cytoplasm and vaculation were pronounced, in other areas regeneration was evident.
4. Afferent Arteriolar Spasm : Afferent glomerular arterioles showed marked vasospasm. After delivery these changes largely disappeared.

Fadel, Sabour et al., 1969 ¹¹ by pathological examination of renal biopsies found that patients with preeclampsia had a characteristic glomerular lesion described as glomerular capillary endotheliosis.

Thomson et al., 1972 ¹² Summarized the most important changes as follows :

- 1) Swelling and some proliferations of capillary endothelial cells.
- 2) Increased in mesangial cell and matrix.
- 3) Abnormal granular fibrillary and basement membrane like deposits between and within endothelial cells in the mesangial matrix and in continuity

with the endothelial aspect of the basement membrane.

Petruccio et al., 1974¹³), reported a deposition of Igm and IGg in the glomeruli after taking renal biopsies from seven preeclamptic patients out of eleven. They suggested an immunological mechanism in the production of the glomerular lesions.

Spargo et al., 1976¹⁴), in immunofluorescent studies on renal biopsy from 3 women with pregnancy induced hypertension showed that there was infrequent deposition of IGg and C₃ component of complement. After delivery, in the absence of underlying chronic vascular disease, complete recovery of renal function can be anticipated, except in rare cases where the major portion of the cortex of both Kidneys undergoes necrosis which develop oliguria or anuria and rapidly developing azotaemia. (Pritchard - Mac Donald, 1976¹⁵).

Mahran et al., 1978¹⁶) found that the serum uric acid is elevated in severe preeclampsia and that elevation was statistically significant. This phenomenon is related to decreased ability of the Kidney to excrete uric acid.

El Maraghi et al., 1982¹⁷) by immunofluorescent study of the Kidney from 2 toxæmic cases. Showed in one case immunofluorescent staining for Ig M in capillary loops of occasional glomeruli, C₃ was detected in few glomeruli with the same intensity, C₄ shown in many glomeruli but with more intensity, Diffuse fluorescent staining for fibrinogen in few glomeruli was detected. The tubules were dilated and show intracellular cytoplasmic fluorescent deposits in the lining cells and the interstitial tissue. In the 2nd case they showed positive fluorescence for Ig M, C₃, C₄ and fibrinogen but with more intensity of staining and extent of distribution but fibrinogen was not detected in the tubules as in the first case.

The results of their immunofluorescence studies on serum and placenta of toxæmic patients suggest that immune complex may be formed in sera of toxæmic patients as a result of damage to trophoplast by specific Ig M antibodies. This damage may liberate placental antigens into the maternal circulation, these antigens with their antibodies form complexes that may deposit in the renal glomeruli, where they produce glomerular injury through sequential activation of the