D-R HASAN EFRAIMOV

PRE-ECLAMPSIA AND ECLAMPSIA

2016

PRE-ECLAMPSIA
AND ECLAMPSIA
D-R HASAN EFRAIMOV, ***author***

Bulgarian, First Edition
2016
Editor: Rose Vassileva
Artist Cover: Filiz Tindzharova

Ковачев - Silistra
ISBN: 978-954-8198-91-2

ETIOLOGY

Pre-eclampsia and eclampsia are disorders of human pregnancy only. There is no reliable data on their occurrence in other species. A major role in the etiology of pre-eclampsia and eclampsia perform factors leading to a reduction of the glomerular filtration rate through the kidneys.

The decrease of the glomerular filtration rate during these diseases is an irrefutable fact. E. Petri1 /1983/ reports that the glomerular filtration rate in pre-eclampsia and eclampsia decreases 32 % compared with normal pregnancy levels. There are similar reports by other authors, too, however, they all assume the reduction of the glomerular filtration rate as a consequence, and not as a cause for the development of pre-eclampsia and eclampsia.

There exist ideal conditions for a reduction of the glomerular filtration rate during human pregnancy. They are contingent upon the pressure exerted on the kidneys and their tubular apparatus, the anatomical features of the pregnant woman, the length of pregnancy, as well as upon a variety of physiological and pathological states. The etiology of pre-eclampsia and eclampsia is complex. These disorders do not develop due to the influence of only one factor, but under the impact of multiple factors and the complex interaction between them. The end result of this interaction is the reduction of the glomerular filtration rate through the kidneys.

These factors include:

I. Upright walking posture of man.

II. Gravid uterus of a large volume.

III. Reduced spatial conditions in the abdominal cavity.

IV. Other factors decreasing the glomerular filtration rate.

V. Pre-existing kidney diseases.

VI. Length of human pregnancy.

I. UPRIGHT WALKING POSTURE

1. Pre-eclampsia and eclampsia, as a typical human phenomenon, appeared way back in the time when humans made their first steps in an upright position. With that they changed the position of the gravid uterus from horizontal to vertical toward the ground.

The advantage of the horizontal position of the uterus is that its weight falls onto the abdominal wall. The kidneys, together with their tubular system, remain on top of the wall, where they are not subject to compression influence by the gravid uterus and so their functioning remains normal.

In humans, the gravid uterus grows and exerts pressure in the abdominal cavity, on kidneys and ureters including, and, with the pregnancy progress, the kidneys function is affected on account of the mechanical compression by the gravid uterus.

2. The upright walking posture resulted in a reduction of space in the abdominal cavity due to retraction of the abdominal wall in the direction of

the spine, resulting in less space for the growth of the gravid uterus.

3. The upright walking posture led to the development of the physiological lordosis of the spine, which further reduced the space in the abdominal cavity.

4. Man is the only animal that lies and sleeps on their back. This position of the body creates ideal conditions for compression on the kidneys and their tubular system by the gravid uterus.

This is the reason why:

a/ blood pressure is higher in lying than in standing position, N.Gant2 /1980/

b/ diurnal rhythm of blood pressure has its peak in the late hours of the day, C. Redman3/1976/.

c/ the glomerular filtration rate is 25% lower at night.

d / in bed rest/left lateral position of the body in the bed/, the weight of the gravid uterus falls to one side. The kidneys and their tubular system are eased of the burden, the glomerular filtration rate increases, the swelling reduces and the blood pressure tends to drop.

5. In comparison to other species, the pregnancy period of human beings is much longer and the compression on the tubular system of the kidneys is more prolonged in result.

II. GRAVID UTERUS OF LARGE VOLUME

1. Pre-eclampsia begins to develop during the second half of the pregnancy when the gravid uterus has grown enough to exert compression effects on the kidneys and their tubular system.

There is a "critical volume" of the gravid uterus bellow which the development of pre-eclampsia is virtually impossible.

This "critical volume" is different for each pregnant woman. It depends on many factors – height of the pregnant woman, prolonged bed rest on her back, prior kidney diseases and many others. The taller the pregnant woman, the larger this "critical volume" is and vice versa – the shorter the pregnant person, the smaller the "critical volume" is, hence less space in the abdominal cavity.

2. Pre-eclampsia starts to fade away immediately after parturition due to the elimination of the compression on the kidneys, quickly followed by increased diuresis, subsiding of swelling, and blood pressure normalization.

3. However, increased diuresis is observed as early as the end period of pregnancy when the front part of the foetus engages in the pelvis thus reducing the compression on the kidneys. From this moment on, pre-eclampsia shows a trend toward disappearance.

4. The term "hyperplacentosis" was coined by J. Scott4 and A. McFarlan to denote conditions

accompanied with a large placenta. The authors have also found a higher incidence of pre-eclampsia and eclampsia in these conditions compared to the cases with a normal size of the placenta.

The larger placenta represents a larger volumetric material, leading to an increase in the pressure of the gravid uterus on the kidneys and their tubular system, but there is something else which is common for these conditions: the larger volume of the uterus is not only on account of the larger placenta, but also of the larger foetus.

a/ this is the reason for the more frequent and earlier onset of pre-eclampsia in cases of twins, found by I. McGillivray5 as early as in 1958, because the gravid uterus increases its volume earlier and to a greater degree.

b / in case of Rh incompatibility pregnancy without hydrops fetalis, the incidence of pre-eclampsia is not different from the one in normal pregnancy. But in case of a large hydropic foetus, pre-eclampsia develops in up to 50% of the pregnant women /J. Scott 1958 /.

c/ the same relationship is observed with thalassemia:

- alpha-thalassemia major: large hydropic foetus – a higher incidence of pre-eclampsia.

- beta-thalassemia minor: lack of foetal hydrops - the frequency of pre-eclampsia is same as in normal pregnancy.

d / with diabetes in patients with no preliminary damage of the vessels, the following two cases are observed:

- diabetes with good control of the blood sugar and a foetus of normal size: the frequency of pre-eclampsia does not differ from the level in normal pregnancy.

- decompensated diabetes with poor glycemic control and a larger foetus: there is a higher incidence of pre-eclampsia.

e/ a small, slowly growing mola hydatidosa does not lead to development of pre-eclampsia, but a large, fast growing mola gives rise to pre-eclampsia in 70% of the cases, E.Page6 /1939/.

5. Hydramnios. The volume of the gravid uterus is larger in comparison to the one in normal pregnancy. After a spontaneous rupture of membranes, but no cervical dilatation shortly afterward, there follows increased diuresis and the swelling tends to subside.

III. REDUCED SPATIAL CONDITIONS IN THE ABDOMINAL CAVITY

1. Primapara

Pre-eclampsia is a disease common for primaparous mothers as their abdominal wall is tight, which results in reduced spatial conditions in the abdominal cavity.

In multiparous mothers, the pressure in the abdominal cavity is lower because of the loose abdominal wall. In order to exert the same compression onto the kidneys and their tubular system, the gravid uterus should have a larger volume, i.e. the “critical volume” is bigger.

That is the reason why a previous pregnancy does not prevent the development of pre-eclampsia in the case of twin pregnancy.

A simple measurement of the abdominal girth can prove this fact. In pregnant women with pre-eclampsia, the largest abdominal measurement is found in multiparous mothers with more than one child, followed by multipara bearing a second child, and the smallest one is measured in primapara – the smallest girth yet with developed symptoms of pre-eclampsia.

2. Teenagers

The greater incidence of pre-eclampsia in this group is related to the uncompleted growth process and the anatomical immaturity. As a result, the spatial conditions in the abdominal cavity are relatively limited. Therefore, a uterus of a small volume is likely to exert compression on the renal function, i.e. the "critical volume" is smaller. Generally the pregnant teenagers with pre-eclampsia are short sized, while in the tall ones even the swelling is rare and most often it is in relation to other diseases.

3. Obesity

S. Fukunaga7 and T. Miyazaki8 /1985/ report for a higher incidence of pre-eclampsia in obese women.

The accumulation of fat results in a reduction of the spatial conditions in the abdominal cavity. On the other hand, the higher weight requires higher blood flow to the kidneys and higher glomerular filtration.

IV. OTHER FACTORS REDUCING THE GLOMERULAR FILTRATION RATE

1. Decreased import of proteins.

Protein-rich food enhances blood flow to the kidneys and increases the glomerular filtration rate. The glomerular filtration rate is about 50% lower in vegetarians.

The mechanism of reduced glomerular filtration in hypoproteinemia is related to the change in the oncotic pressure of plasma.

W. Patterson9 /1982/ considers the hypoproteinemia a factor in the occurrence of pre-eclampsia.

2. Mental factors.

W. Wolcher and E. Holzer10 /1983/ highlight the role of psychological factors in the development of preeclampsia.

M. Pajnter11 /1981/ finds higher mental unrest in women with pre-eclampsia.

Many authors have published similar reports.

Psychological factors such as stress, depression, autonomic instability, lead to dominance of the sympathicus and hence to a reduction in the glomerular filtration rate. The mechanism of action is by means of changing the lumen of the vas afferens, vas efferens and vasa recta.

3. Individual peculiarities in the way of life of the pregnant woman, such as long bed rests on her back, also result in a decrease of the glomerular filtration rate because of the prolonged pressure on the kidneys and

their tubular system.

V. The development of pre-eclampsia depends to a great degree on the presence of pre-pregnancy kidney damage, such as pyelonephritis, glomerulonephritis, which – on account of the reduced glomerular filtration rate as a result of the decrease in the number of functioning nephrons - put the compensatory abilities of the kidneys to the test during pregnancy.

Ptosis and lower disposition of the kidneys lead to their earlier and stronger compression during pregnancy.

PATHOGENESIS

The main point in the pathogenesis of pre-eclampsia and eclampsia is the reduced glomerular filtration rate during pregnancy. The reduced glomerular filtration rate is a result of the complex effects of the above mentioned factors, and a crucial role plays the pressure of the gravid uterus on the kidneys and their tubular apparatus.

The glomerular filtration rate is a quantity that depends on many factors, namely:

1. The quantity, as well as the nature of the ultrafiltrate, depends primarily on the surface area and physical properties of the very membrane through which the ultrafiltration is performed.

2. Changes in the hydrostatic pressure of the glomerular capillaries through:

a. variations in the arterial blood pressure in the systemic circulation.

b. variations in the lumen of the vas afferens and vas efferens.

3. Changes in the intraglomerular pressure by:

a. impaired patency of the urethra.

b. pinching and swelling of the kidney.

4. Changes in the oncotic pressure of plasma by:

a. dehydration.

b. reduction of plasma proteins.

The mechanism of development of pre-eclampsia and eclampsia is as follow:

The first stage of the disease is a reduction in the glomerular filtration rate as a result of the above mentioned reasons. The glomerular filtration is a passive act, therefore any increase in the pressure in the tubular system of the kidneys due to pressure from the gravid uterus leads to its reduction in a natural way.

As a result of the reduced glomerular filtration, there occurs the first clinical symptom of pre-eclampsia: the edema.

The mechanism is completely identical to the primary hypervolemic nephritic edema, well known from the classic pathophysiology.

The acute increase in plasma volume as a result of the reduced glomerular filtration rate increases the

average hydrostatic capillary pressure on account of water and NA retention. The hydrostatic pressure moves the fluids to the interstitium and so the swelling builds up. The renin-angiotensin-aldosterone system is off.

The difference between these two types of edema is that in the case of the nephritic edema the decreased glomerular filtration rate is due to the reduction in the number of functioning nephrons, while in the case of pre-eclampsia it is of the obstructive type.

The complete clotting of the tubular system would lead to acute renal failure, but with preeclampsia it is not complete because there is some inhibition of urea, creatinine, and uric acid.

Basically, swelling occurs in most pregnant women. Therefore, many authors consider it normal during pregnancy. Furthermore, a correlation has been established that pregnant women with edema deliver bigger children /F. Paulin12 -1983/. On the contrary, it is just the opposite: edema is not the cause for bigger children, it is the bigger foetus - due to the larger volume of the gravid uterus - that leads to the development of edema.

In each pregnancy there are more or less compression and excretion problems connected with the kidneys, so the swelling can not be normal for each and any pregnancy. It all depends on the existing conditions during each pregnancy. Where conditions are favorable, the kidneys function is eased for shorter or longer periods. A period of reduced urine output is followed by a period of intense diuresis. Swelling reduces or subsides, or at least it does not build up. In

the worst case, the proccess continues in the following manner:

Water retention continues. The existing hypervolemia (which is considered normal during pregnancy) is now supplemented with the second symptom of pre-eclampsia – the hypertension. This hypertension is volumetric and is characteristic of the early stages of pre-eclampsia. In the later stages, the nature of the hypertension changes.

Due to the increase of pressure in the systemic circulation there could appear certain increase in the glomerular filtration rate. In case this increase is appropriate, the process can be stopped again and a relative balance between water retention and its elimination can be sorted out.

In cases where the increase in the glomerular filtration rate is not adequate, changes in the physical properties of the glomerular membrane start.

Because of the increased compression from the side of vas afferens and the blockage of the ultrafiltrate flow from the tubular system, the pressure in the glomerulus increases and they begin to inflate, their podocytes flatten, the distance between them increases, their vascularization and trophic decrease.

The pressure in the tubular system increases, too, resulting in an acute expansion of the lumen of proximal tubules with a corresponding flattening of the epithelium thereof. The respective microscopic image of these changes is described in each authoritative guidance concerning pre-eclampsia.

As a result of these changes, the physical properties of the glomerular membrane are damaged and it begins

to lose proteins. In comes the third most characteristic symptom of pre-eclampsia - the proteinuria. At that moment, the situation turns into a circulus vitiosus.

Because of the upcoming hypoproteinemia, the glomerular filtration drops even further and the plasma loses its ability to retain fluids. Increasingly large quantities of it leave the vascular bed in the direction of the interstitium. The edematous syndrome deepens. The plasma volume continues to decrease. It is urgent for the compensatory mechanisms of the body to switch on in order to adjust the vascular walls to the reducing plasma volume. The volume receptors turn on. The generalized vasospasm, typical of pre-eclampsia, occurs. The vasospasm is the second real cause for the hypertension, which is characteristic of the later stages of pre-eclampsia. The body bathes in water and falls into hypovolemic shock. This is a unique phenomenon, specific of pre-eclampsia and eclampsia.

Rheological properties of blood are already damaged. The hematocrit increases. The test of the plasma ingredients without taking into account the hematocrit is not realistic. There remains only one step to the coagulation complications and the DIC syndrome.

Then comes the spasm of the small peripheral vessels. Retention of erythrocytes in them and their hemolysis, the increased blood clotting, which further includes fibrinolysis, plus injured homeostasis of the organism, make the risk of HELLP-syndrome quite real.

The microscopic picture described above is further accompanied by the final details typical of preeclampsia.

Due to the stasis, conditions for deposition of platelets, fibrin, and complement fractions on the glomeruli are created.

The process can still be stopped. It is necessary only to increase the glomerular filtration rate. The most reliable way has always been the cervical dilatation.

That is why the ideal treatment of pre-eclampsia is the cervical dilatation, rather than treating reasons related to the placenta trophoblast or other structures.

In cases where the glomerular filtration rate does not increase, eclampsia follows. The plasma is no longer able to retain water, the interstitial space is not able to absorb more water, too, as the process requires a certain amount of time. Here comes the pulmonary edema, brain edema and anasarca.

The clinical picture of the eclamptic seizure coincides with that of the water seizure described in the classical pathophysiology.

GUIDELINES IN THE PREVENTION AND TREATMENT OF PRE-ECLAMPSIA AND ECLAMPSIA

1. Magnesium and diazepam are not medications that cure eclampsia. They can only prevent the eclamptic seizure due to the reduction of the excitation threshold of the central nervous system.

2. The real treatment can be done only through an increase in the glomerular filtration rate. Any other treatment is symptomatic.

The bed rest is a very good method to increase the glomerular filtration rate. It must be mandatory for each and every pregnant woman in the third trimester.

Very good results are obtained when the pregnant woman lies on her stomach in a bed-trough that copies the shape of the abdominal wall. The diuresis increases, the swelling diminishes or subsides, RR normalizes.

3. Eclampsia can occur even when one of its main symptoms – proteinuria, is not present. This can happen in case of excessive water retention or its iatrogenic introduction.

Therefore, the inflow of aqueous solutions in case of pre-eclampsia and eclampsia should be prohibited or performed very carefully on strict indications.

4. Treatment with diuretics is not appropriate, because they extract water directly from the plasma, which is anyway reduced. However, the extraction of interstitial fluid takes time, and until that happens the volume receptors have already turned on due to the onset of hypovolemia.

5. The vasodilators question the compensatory abilities of the organism. Increased tone of the vessels and increased blood pressure are secondary. They are only a compensatory mechanism against the shock-like hypovolemia, in which the body has fallen into.

6. Treatment with protein solutions is essential for eclampsia. They heal and recover hypoproteinemia and restore the plasma volume, extracting water

from the interstitium, thus reducing the swelling. The recovered plasma volume eliminates the vasospasm and hypertension by turning off the volume receptors. The glomerular filtration rate increases.

7. Pregnant women with pre-eclampsia and eclampsia are at a particularly high risk of hemorrhagic shock and cannot tolerate blood loss. They are generally in a state of hypovolemic shock, and if it is accompanied with blood loss, the result can be fatal.

Hypoproteinemia correction and increased glomerular filtration rate should be the most important guidelines for the treatment of pre-eclampsia and eclampsia. The alternative is the cervical dilatation, after which the body copes on its own.

Preeclampsia and eclampsia are diseases for which a pathogenic treatment do not exist and will never exist. The main reason for their appearance is the "non-physiological" upright walking of man and the above mentioned consequences of this posture. In case the acceleration theory is correct, i.e. if the human height continues to grow with each successive generation, then after many years, when the height of man will have increased enough, the cases of preeclampsia and eclampsia will disappear or decrease in number. An evolution is in progress, an evolution which began with man walking upright and which has not yet finished.

REFERENCES

1. Petri, E. Niere bei Gestose. In: Book N 6, p. 124 – 129.

2. Gant, N., R. Warley. Hypertension in pregnancy. Concept and management. New York, Appleton-Century-Crofts, 1980.

3. Redman, C. et al. Variability of blood pressure in normal and abnormal pregnancy.

In: Book N 4, p. 53 – 59.

4. Scott, J. Pregnancy toxaemia associated with hydrops fetalis, hydatidiform mole and hydramnios. – J. Obstet. Gyanec. Brit. Emp., 65, 1958, 689.

5. Mac Gillivray, I. Some observations on the incidence of preeclampsia. – J. Obstet. Gyanec. Brit. Emp., 65, 1958, 586.

Mac Gillivray, I. Dixon. In Preeclampsia. London, Saunders Comp., 1983.

6. Page EW. The relation between hydatid moles, relative ischemia of the gravid uterus, and the placental origin of eclampsia. Am J Obstet Gynecol 1939, 37, 291

7. Fukunaga, S. et al. Obesity and obstetric complications during pregnancy. In: Book N 10, p. 247 – 250.

8. Miyazaki, T. et al. Body weight fluctuation in pregnant women (comparision between toxemic and normal gravida). In: Book N 10, p.251 – 254.

9. Patterson, W. How malnutrition, primarily of calcium deficiency and/or stress lead to edema proteinuria hypertension-gestosis: an hypothesis. Organis. Gestosis, Press, 1982.

10. Walcher, W, Holzer, E. The influence of psychosocial conflicts on the etiology of gestosis. in: H Janisch, E Reinold (Eds.) Proc Int Symp on Dilemmas in Gestosis.

11. Pajnter, M., J. Rojsek et al. Some psychodynamics of women with EPH-gestosis. In Book N 2, p. 102 – 103.

12. Paulin, F. et al. Is edema beneficial? I. Birth weight. In: "Dilemas…", p.54 – 55