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Convulsive syndrome in eclampsia and epilepsy in parturition under 30 years of age

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ABSTRACT

The convulsive syndrome in eclampsia and epilepsy is often a major complication in obstetrics. If eclampsia is a pathology of gestation, epilepsy is a pre-existing pathology of pregnancy. Epilepsy can be aggravated by the presence of preeclampsia and eclampsia in both terms of fetal-placental units, frequency of convulsions. Obstetrical behaviour at birth by caesarean surgery or vaginal delivery with or without applying forceps should be chosen so as not to delay maternal and fetal prognosis. Epileptic patients have a higher risk of developing complications in pregnancy, by increasing maternal morbidity due to seizures, coma, birth bleeding or caesarean section, pelvi-genic hematoma, infections. The extraction of the fetuses was performed by caesarean surgery and forceps application. The immediate maternal and fetal, vital and functional prognosis was good. We recommended ablation in epileptic patients and administration of anticonvulsant treatment.

The objective of the paper is represented by the study of the neuro-convulsive syndrome in eclampsia, epilepsy and in the association of the preeclampsia – epilepsy, the difference between the three entities and the therapeutic medical and obstetrical attitude for a good materno-fetal prognostic.

Keywords: eclampsia, epilepsy, convulsive seizures, caesarean section, forceps application

INTRODUCTION

The convulsive syndrome in eclampsia and epilepsy is often a major complication in obstetrics. If eclampsia is a pathology of gestation, epilepsy is a pre-existing pathology of pregnancy. Epilepsy may be aggravated by the presence of preeclampsia and eclampsia both in terms of fetal-placental unit and seizure frequency, which

in half of the patients can increase, in a quarter of cases may remain unchanged and in the remaining 25% of parturients had been reduced. Chronic antiepileptic treatment in pregnancy with teratogenic implications is the old generation of phenytoin and phenobarbital, valproic acid and carbamazepine, which causes facial dysmorphies, impairment of distal phalanges and nails, cardiac malformations, spina bifida.

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The same cannot be said for new generation antiepileptics (gabapentin, tiagabine, oxcarbazepine, levetiracetam, zonisamide), which has been found to have no incidence of malformations greater than in the general population (1-5). Obstetrical behaviour at birth by caesarean surgery or vaginal delivery with or without forceps should be chosen so as not to delay maternal and fetal prognosis (6).

Eclampsia along with uterus-placental apoplexy, uterine rupture and HELLP syndrome are major gestational accidents (7,8). Eclampsia occurs on the background of untreated severe preeclampsia and is predominantly manifested by tonic-clonic convulsion. In 50% of cases, antepartum occurs, in 25% in labor and the remaining 25% in postpartum (9,10). Eclampsic access occurs as a consequence of cerebral edema, secondary HTA and mimics epileptic access. The convulsive episode may be unique, especially when it occurs during advanced labor or after birth, sometimes convulsions occur in 2-3 intervals or even more (11,12).

Convulsions in epilepsy are defined as involuntary movements, the result of paroxysmal dysfunction of the central nervous system, characterized by a neurological discharge with or without loss of consciousness. Epilepsy comprises several syndromes whose common character is the predisposition for spontaneous convulsions through the hyper excitability of epileptogenic diencephalic center. In epilepsy in pregnant women, convulsive syndrome may occur in both normotensive and gestational hypertension, preterm, labor, or postpartum. After headache, convulsive disorders are the most common type of neurological disease seen in pregnant women. Confusional disorders in pregnant women are associated with intrauterine growth retardation and may complicate pregnancy evolution (10,13-15).

The objective of the paper is represented by the neuro-convusive syndrome in eclampsia, epilepsy and in the association of preeclampsia – epilepsy, the difference between the three entities and the therapeutic medical and obstetrical attitude for a good materno fetal prognostic.

MATERIAL AND METHODS

The study was performed over a 2-year period (2015-2016) and focused on solving 19 cases, namely: 14 cases of severe preeclampsia, complicated with eclampsia and 5 cases of epilepsy, admitted to the maternity of the Emer-

gency County Clinical Hospital, Craiova. The attendants were aged between 15 and 30 years old. Some were highlighted and performed sporadic medical checks (clinical examination, haematological and urinary investigations, maternal-fetal ultrasound), others were not highlighted. Seizures have occurred at home, in ambulance or in hospital.

The positive diagnosis of admission was established based on the general and obstetrical clinical examination. In most cases, the anamnesis data was not known, sometimes it was being provided only by family entourage. Of the 5 cases of epilepsy, 2 were known by the family. In the epilepsy cases it was observed the sfincterian incontinence.

Emergency paraclinical investigations were: complete blood count, blood group, Rh, blood glucose, urea, creatinine, uric acid, hepatic transaminase, coagulogram, serum and urine ionogram, proteinuria, complete urinalysis. To these analyzes was added the obstetrical ultrasound for the fetal biophysical profile and the status of fetal annexes - placenta, amniotic fluid. Also, blood pressure was measured and electrocardiography and cardiology, neurological, ophthalmic and nephrology examinations were performed.

Two epilepsy parturients had convulsive syndrome during the first half of pregnancy and were admitted to the neurology clinic. Anticonvulsant treatment was given on this occasion. They did not continue treatment during pregnancy.

Of the 5 cases of epilepsy, pregnancy development in 3 parturients was complicated by severe preeclampsia and eclampsia, not being epileptic, with convulsive seizures attributable to eclampsia. Later in postpartum, the epilepsy diagnosis of these parturients was established.

RESULTS

At the objective clinical examination, we found edema of the inferior limbs (Fig. 1), at the level of the fingers of the hand (Fig. 2), edema of the face, eyelid edema, in the 14 preeclampsia patients and in the 3 preeclampsia and epilepsy (Table 1). Blood pressure values oscillated between 160/100 mm Hg and 220/120 mm Hg. Edema is suggestive for diagnosis especially when it occurs in the last 48 hours. These have typically been associated with an increase in systolic and diastolic blood pressure over 160/100 mm Hg, with oliguria and proteinuria.



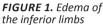




FIGURE 2. Edema of the fingers of the hand

TABLE 1. Pathology associated to the pregnancy

| Patology | Eclampsia | Eclampsia and epilepsy | Epilepsy |
|-----------|-----------|------------------------|----------|
| Nr. cases | 14 | 3 | 2 |

On haematological and urinary investigations performed, we did not detect changes in hemoleucogram and liver samples, but there were changes in renal markers: increase in serum creatinine over 1.2 mg/dl, uricemia increase over 5.7 mg/dl.

In all these circumstances, we found a decrease in fibrinogen below 400 mg/dl, a platelet decrease below 100.000/mm3, an increase in fibrin degradation products over 16 micrograms/ml. These changes in haemostasis are those that lead to severe preeclampsia at hemorrhagic high risk, both in parturition and postpartum, in birth by natural way, forceps extraction, or extraction of the foetus through caesarean surgery. In the cases we studied found: thrombocytopenia, haemolysis, high prothrombin time, low fibrinogen, fibrin degradation products and fibrin monomers increased. In seven severe cases, we found hemoglobinuria and proteinuria over 0.3 g/l urine/24 hours, with 2 cases reaching 5 g/l/24 hours and 7g/l/24 hours (Table 2).

Emergency fetal ultrasound revealed the presence of 17 live fetuses in the cranial presentation and, in 2 cases, in transversal presentation. The placenta was quasi-normal eco-structure, amniotic fluid in normal amount. The fetal biophysical profile was 10 in three cases, ranged from 6 to 8 in twelve cases, in four cases it was under 6 and associated with placental insuffi-

ciency and intrauterine growth retardation (Table 3).

TABLE 2. Clinical and paraclinical changes in pregnant women with preeclampsia

| Parameters | Values |
|-----------------|--------------------------|
| edema | + |
| TA | 160/100 mmH |
| Oligury | 500-1000 ml (10 cases) |
| | < 500 ml (7 cases) |
| Proteinury | < 0,3 g/l/24h (10 cases) |
| | 0,3 g/l/24 h (7 cases) |
| Hemoglobinury | + (7 cases) |
| Creatininemia | 1,2 mg/dl |
| Uricemia | 7 mg/dl |
| Na ⁺ | 160 mmol/l |
| Fibrinogen | \downarrow |
| Nr. Trombocites | \downarrow |
| PDF | \uparrow |
| Quick Time | ↑ |

TABLE 3. Repartition of the cases by the biofizic fetal score

| Biophysic fetal score | Nr. cases |
|-----------------------|-----------|
| 8-10 | 3 |
| 6-8 | 12 |
| < 6 | 4 |

The ophthalmologic examination revealed spasm of retinal arterioles, retinal edema, retinal haemorrhages and a case of retinal decollation. In these cases, the patients presented intense headache, diplopia, decreased visual acuity to amaurosis.

In severe preeclampsia, neurological examination was found the setting of violent headache, which has often been reported to be the imminence of neurological complications through severe visual disturbances, cerebral spasms, speech and hearing disorders, and in severe cases, cerebral hemorrhages that are the origin of hemiplegia and often exitus.

The treatment consisted of hypotensives – Trivitrosan, Enap, and anticonvulsant – magnesium sulphate, diazepam. Anticonvulsants were administered both to patients with preeclampsia, eclampsia, and those with epilepsy. Magnesium sulphate, through anticonvulsant, hypotensive, sedative and spasmolytic action, has been a real maternal benefit, both by engaging convulsive seizures and by preventing underlying seizures.

The obstetrical attitude was decided upon stabilizing the general condition of the patients. The pregnancy was ended by obstetrical interventions and not by spontaneous birth. In 11 cases we applied the cesarian surgery of which

the segmental-transversal Fuchs-Dorffler method in 9 cases and the segmental-longitudinal Kronig-Beck in the case of 2 transversal presentations. We applied the forceps procedure to extract the fetuses in 8 cases.

There were no incidents or accidents in obstetrical interventions, the vital and functional maternal-fetal prognosis being good in all 19 cases. Cases of epilepsy were evaluated postpartum, in hospital, by the neurologist who indicated ablation, anticonvulsant treatment, ambulatory specialist consultation.

DISCUSSION

The incidence of epilepsy in women of reproductive age is on a second range, after headaches or migraine. Epilepsy, like eclampsia, has as a common symptom the seizures, and it is often difficult to differentiate it without a history. When uricemia rises above 60 mg/l, it means, according to most authors, a proportional increase in fetal risk in uterus. Increase in serum uric acid is proportional to anatomical damage to the kidneys, a few weeks before clinical signs appear. In severe preeclampsia and eclampsia, total body water exceeds 9 liters, the plasma volume increases over 2.5 liters, reaching in some cases over 5 liters in term. Sodium retention increases above 160 mmol/l, which we have also found on the analyzed cases.

The optimal management involves the collaboration between the obstetrician and the neurologist. The presence of the anesthetician is essential during labor and delivery to ensure analgesia or anesthesia. In the same time the presence of a neo-natologist is important to anticipate the needs of the newborn and to properly care for it.

Fetal asphyxia can appear after prolonged and repetitive seizures. During the tonic phase, the maternal respiratory muscles do not provide adequate oxygenation and prolonged apnea can cause fetal hypoxia. In the clonic phase, metabolic acidosis appears.

30 minutes after continuous electrical cerebral activity irreversible neural lesions can occur. The hippocampus and the amygdala are the most prone to injuries (16). The recurrent convulsions can cause: premature birth, spontaneous membrane rupture, abruptio placenta, acute fetal distress and fetal death in utero (17,18).

The tonic-clonic convulsions have an incidence of 1-2% in women in labor. Lorazepam or

Diazepam, short-acting benzodiazepines are the selective drugs that can combat epileptic seizures (19).

Magnesium sulphate is a calcium antagonist that inhibits the contraction of vascular smooth muscle as a vasodilator by decreasing the release of acetylcholine in the neuromuscular plaque; protects the blood-brain barrier and has an anticonvulsant effect, resulting in reduced maternal and fetal mortality and morbidity. Randomized studies have shown that magnesium sulfate would act as a competitive agonist at the level of N-methyl D-aspartate glutamate receptors, which have epileptogenic effect, with a direct effect in reducing the risk of eclapsis and preventing recurrences (20).

The antiepileptic doses should be monitored in postpartum, as their increase during pregnancy may cause inadequate serum levels for the after birth period, requiring their progressive decrease.

All the antiepileptics are excreted in the breast milk. The neonatal sedation may determine the obstetrician's decision to indicate ablation (21).

In neuro-convulsive syndrome caused by eclampsia and epilepsy, spontaneous birth is possible. In the cases analyzed by us, most of the patients were in labour, uncooperative, which is why the extraction of the fetuses was done via caesarean surgery and forceps application. The immediate maternal and fetal, vital and functional prognosis was good. I recommended ablation in epileptic mothers and administered anticonvulsant treatment recommended by the neurologist.

Regarding the opportunity for a new pregnancy in these patients, we agree with mechanical methods by using intrauterine devices (IUD) and less oral hormonal contraceptives. There have been situations where, at the request of the patients, I have proceeded to tubal sterilization.

CONCLUSIONS

The major risks of epilepsy in a pregnant woman are related to the coexistence of severe preeclampsia, the presence and increase of seizures, whether or not anti-epileptic treatment is performed. Epileptic patients have a higher risk of developing complications in pregnancy, by increasing maternal morbidity due to seizures, coma, birth bleeding or caesarean section, genital or pelvic hematoma, infections.

It is required the monitoring of the patients with convulsive syndrome from the point of view of the general state of the patient, of the frequency of the convulsive crises and of the doses of the anti epileptic medication both ante partum, during gestation, in parturition and postpartum.

The most efficient treatment of the eclampsia proved to be the magnesium sulphate. To these it has to be added the monitoring of the intrauterine fetus and of the fetal annexes having in view the extraction of the fetus in good, viable conditions.

REFERENCES

- Carbuapoma F.R., Tomlinson M.W., Levine S.R. Neurologic Disorders. In: James D.K., Weiner C.P., Steer Ph.J., Gonik B. (Eds): High Risk Pregnancy. Elsevier. *Philadelphia Pennsylvania*. 2006:1061–1066.
- Braila Anca, Braila M.B., Dira L.M., Vaduva C. Normal Twin Pregnancy to Term Three Years after a Girl with Siamese Twins. Conference Proceedings of the 5th Congress Of The Romanian Society Of Ultrasound in Obstetrics and Gynecology, 2017; 137.
- Eadie M.J. Antiepileptic drugs as human teratogens. Expert Opin Drug Saf, 2008; 7:195.
- Pilo C., Wide K., Winbladh B. Pregnancy, delivery and neonatal complication after tratament with antiepileptic drugs. Acta Obst Gynecol, 2006; 85:643.
- Milgard-Nielsen D., Haid A. Newer generation antiepileptic drugs and risk of major birth defects. *JAMA*, 2011; 303(19):1996.
- 6. Brăila M., Neacşu A., Velea R., Brăila A.D. Caesarian Section And The Forceps Use 5 Year Study In Craiova SCJU Maternity Section. The 13th Conference Proceedings of the Romanian-German Society of Obstetrics and Gynecology, 2017; 91-94.

- Brăila A.D., Krastev B.M., Mihai-Zamfir E., Caraveţeanu D.C., Al Krayem N., Brăila M., Velea R., Neacşu A. Uteroplacental apoplexy associated with invasive cervical neoplasm, Rom J Morphol Embryol, 2017; 58(4):1465-1470.
- Brăila A.D., Gluhovschi A., Neacşu A., Lungulescu C.V., Brăila M., Vircan E.L., Cotoi B.V., Goganau A. Placental abruption. Etiopathogenic aspects, diagnostic and therapeutic implications, RJME, 2018; 59(1).
- Cunningam F.G., Leveno K.J., Bloom S.L., Hauth J.C., Rouse D.J., Spong C.Y. Williams Obstetrics. McGraw-Hill. 2010: 362 – 364.
- Cunningam F.G., Leveno K.J., Bloom S.L., Spong C.Y., Dashe J.S., Hoffman B.L., Casey B.M., Sheffield J.S. Williams Obstetrics. McGraw-Hill. 2014: 637 – 652.
- Georgescu Braila M., Berceanu S. Obstetrica. vol II, partea II. AIUS. 1997: 5-62.
- Crisan N., Nanu D. Aspecte de conduita in formele severe de HTA indusa de sarcina. Obstetrica si Ginecologia, 1994; 3:103-106.
- **13. Borthen I., Eide M.G., Daltveit A.K.**Obstetrics outcome in women with epilepsy:
 A hospital based retrospecting study *BJOG*, 2011; 118(8):956.

- 14. Mawer G., Briggs M., Baker G.A. Pregnancy with epilepsy: Obstetric and neonatal acollet study. Seizure. 2010; 19(2):112.
- 15. Brodie M.J. Management of epilepsy during pregnancy and lactation. *Lancet*, 1990; 426–427.
- Donaldson J.O. Neurologic emergencies in pregnancy. Obstet Gynecol Clin North Am 1991; 18: 199-211.
- Yerby M.S., Devinsky O. Epilepsy and pregnancy. Adv Neurol. 1994; 64: 45-63.
- 18. Brăila A.D., Forţofoiu C., Mihai Zamfir E., Velea R., Brăila M.B. Eclampsia And Epilepsy. Differential Diagnosis. Associated Diagnosis. The 13th Conference Proceedings of the Romanian-German Society of Obstetrics and Gynecology, 2017; 84-87.
- Delgado-Escueta A.V., Jantz D.
 Consensus guidelines: Preconception counseling, management and care of the pregnant women with epilepsy. *Neurology*, 1992; 42:149-160.
- 20. Conea I.M., Nanu D. Drug treatment in hypertension induced by pregnancy. *RJMP*. 2011; 4(24):337-341
- Committee On Drugs: The transfer of drugs and other chemicals into human milk. *Pediatrics*, 1994; 93:137-150.