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Antiepileptic Drug Therapy And Its Effects On Pregnant Women

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Date of submission: - 30th / June / 2018.

Abstract :-

Pregnant women with epilepsy constitute 0.5% of all pregnancies.

Proper seizure control is the primary goal in treating women with epilepsy.

The commonly used anticonvulsants are established human teratogens, factors such as epilepsy, anticonvulsant-induced teratogenicity, patient's genetic predisposition and the severity of convulsive disorder may attribute to adverse pregnancy outcome for the children of women with epilepsy

Anticonvulsant interaction with folic acid and phytonadione (vitamin K) metabolism may lead to an increased risk for neural tube defect and early neonatal bleeding.

Preconceptional counselling should include patient education to ensure a clear understanding of risks of uncontrolled seizures and possible teratogenicity of anticonvulsants. Genetic counselling should be performed if both parents have epilepsy or the disease is inherited. Seizure control should be achieved at least 6 months prior to conception and, if clinically possible, by the lowest effective dose of a single anticonvulsant according to the type of epilepsy.

The new anticonvulsants are not recommended in pregnancy and require further research to prove their safety in humans.

Folic acid 5 mg/day should be administered 3 months before conception and during the first trimester to prevent folic acid deficiency-induced malformations

Therapeutic drug monitoring should be performed monthly, or as clinically indicated.

In order to prevent convulsions during labour, proper seizure control should be achieved during the third trimester. Benzodiazepines or phenytoin are found to be effective for seizure cessation during labour and delivery

Phytonadione should be administered immediately after birth to the newborn. The neonate should be assessed carefully for epilepsy and anticonvulsant-associated dysmorphology

Advising the patient on postpartum management regarding contraception and breast-feeding will help maximise the best possible outcome for the newborn and mother. With proper preconceptional, antenatal and postpartum management up to 95% of these pregnancies have been reported to have favourable outcomes.

Introduction :-

Epilepsy is a chronic disorder that causes unprovoked, recurrent seizures which are a sudden rush of electrical activity in the brain.

A mild seizure may be difficult to recognize. It can last a few seconds during which you lack awareness.

Stronger seizures can cause spasms and uncontrollable muscle twitches, and can last a few seconds to several minutes. During a stronger seizure, some people become confused or lose consciousness. Afterward you may have no memory of it happening

The National Institute of Neurological Disorder and Stroke (NINDS) estimates epilepsy affects **1% of the United States population** (about 2.5 million people).

It is estimated that about 1/3-1/2 of women with epilepsy will have more frequent seizures during pregnancy.

The likely reason for the increase in seizures are the anticonvulsant [medications](#). Because anticonvulsant medications tend to work differently during pregnancy and therefore the injury risks for the baby and mother are increased.

In this report , different anticonvulsant medications and its effects on pregnant women will be discussed¹.

Discussion :-

❖ In The National Institute of Neurological Disorder and Stroke (NINDS) , The relation of epilepsy with gestation was studied in 59 patients through 153 pregnancies.

In patients with idiopathic epilepsy, 45% had more frequent fits during pregnancy, 50% were unchanged, and 5% were improved.

The results in patients with symptomatic epilepsy were similar. Patients with a high frequency of fits in the progestational state are likely to have an increased number when pregnant. Two cases of status epilepticus were treated successfully without interruption of pregnancy. Fourteen patients had true gestational epilepsy, 4 of whom had underlying organic disorders.

Congenital heart disease occurred in 2%, and cleft lip or cleft lip and palate in 1% of infants, all of these mothers on antiepileptic therapy. The rate was 4 and 10 times the rate in 69,000 consecutive births in the same area¹.

❖ At Department of Pediatrics, Tokyo Women's Medical University, Dr. M. Oguni conducted a multiinstitutional prospective study, analyzing 1,072 offspring born in Japan, Italy, and Canada. The incidence of congenital malformations in the offspring was 3.3% in mothers with monotherapy, 4.7% in those with two AEDs, 4.4% in those with three AEDs, and 8% in those with four AEDs.

The incidence of congenital malformations in relation to the individual AED was 14.3% in PRM, 11.1% in VPA, 9.1% in PHT, 5.7% CBZ, and 5.1% in PB.

They recommended avoiding polypharmacy maintaining the serum concentration of VPA level below 70 µg/ml for the treatment of women of childbearing age with epilepsy to reduce the incidence of congenital malformations in the offspring, because the incidence of malformations is positively related to the VPA serum concentration, especially that >70 µg/ml

❖ In 2000 , Aprino et al. (24) prospectively studied teratogenic effects of AEDs among 8,005 cases with congenital malformations. They showed that the incidence of congenital malformations was twofold higher in women taking AEDs compared with that of the general population. In addition, the infants exposed in utero to VPA or to CBZ as monotherapy carried ~7 and 4 times higher risks of spina bifida than the general population, respectively.

- ❖ In 2001, Kozma (25) studied the teratogenic risk of VPA and recommended using the lowest effective dosage, dividing the daily dose into three or four equal doses so that the peak VPA level would be as low as possible. Diav-Citrin et al. (26) prospectively followed up 210 pregnancies exposed to CBZ during the first trimester. They showed a twofold increase in the rate of major congenital anomalies and a birthweight reduction, although no specific malformations were found, as there were to CBZ.
- ❖ In another study which is part of a prospective, observational, registration and follow-up study.

Suitable cases are women with epilepsy who become pregnant and who are referred before outcome of the pregnancy is known. The main outcome measure is the MCM rate. Outcomes were analysed against folic acid exposure, malformation type and drug group for the most commonly used monotherapy AEDs.

In 1935 cases reported to have received preconceptual folic acid, 76 MCMs (3.9%; 95% CI 3.1 to 4.9) and eight NTDs (0.4%; 95% CI 0.2 to 0.8) were identified. For 2375 women who were reported to have received folic acid but not until later in the pregnancy (n=1825) or not at all (n=550), there were 53 outcomes with an MCM (2.2%; 95% CI 1.7 to 2.9) and eight NTDs (0.34%; 95% CI 0.2 to 0.7)².

- ❖ In Department of Obstetrics and Gynaecology at Aarhus University Hospital, Denmark, Results of studies investigating the long-term effects of intrauterine exposure to antiepileptic drugs (AEDs) on cognitive functioning was performed to identify all original cohort studies that investigated cognitive functioning after *in utero* exposure to AEDs. Studies had to include at least one group exposed to an AED and one unexposed group.

Eleven studies met the inclusion criteria. Eight studies (three for valproic acid and five for carbamazepine) evaluated IQ as a measure of cognitive development. IQ was assessed by the Wechsler, Bayley or McCarthy intelligence scales, depending on age. One study investigated phenytoin and one study investigated phenobarbital (phenobarbitone).

The mean full-scale IQ (FSIQ), verbal IQ (VIQ) and performance IQ (PIQ) scores in children exposed to valproic acid *in utero* were 83.9 (95% CI 64.2, 103.6), 93.7 (95% CI 72.6, 114.7) and 88.3 (95% CI 69.9, 106.9), respectively. The mean FSIQ, VIQ and PIQ scores in the control group were 102 (95% CI 90, 116), 101 (95% CI 87, 114) and 99 (95% CI 90, 117), respectively. The mean FSIQ, VIQ and PIQ were all significantly lower in the valproic acid group compared with the unexposed group.

The FSIQ and VIQ of children exposed to carbamazepine were not statistically different from those of the unexposed control group. In a sub-analysis of carbamazepine exposure in three studies using the Wechsler intelligence scale, PIQ was significantly lower in children exposed to carbamazepine than in unexposed children³.

Conclusion :-

Epilepsy brings special issues for women, particularly in pregnancy, and While the majority of women with epilepsy can and do become pregnant, they may have certain risks that women without epilepsy don't have. These risks can affect their health and that of their babies. Yet if properly managed, the risks are very small

In fact over 90% of women with epilepsy who become pregnant have healthy babies.

References :-

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