

## Brief Communication

### Women and epilepsy

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Epilepsy affects about 45 million people worldwide. Incidence is highest among young children and the elderly, and men are affected slightly more often than women (1.5:1) <sup>(1)</sup>. In the United States, age-adjusted annual incidence rates based on 1990 census figures range from 31 to 57 per 100,000 population <sup>(2)</sup>. Cause and seizure type vary with age. Excluding febrile seizures or those related to an acute illness, the lifetime likelihood of someone experiencing at least one seizure is about 10%. The risk of epilepsy development, however, is lower, about 3 to 4% emphasizing that not all seizures lead to epilepsy <sup>(3)</sup>. In fact, about 30% of persons with unprovoked seizure types, such as absence, myoclonic, and complex partial, are virtually always recurrent by time a physician is consulted <sup>(4)</sup>. Because people with a single seizure do not have epilepsy and may not require long term antiepileptic drug treatment, it is important to determine whether a first unprovoked seizure is likely to lead to further attacks. Unfortunately, the ability to do this is not always easy <sup>(5,6)</sup>. Persons with epilepsy have increased mortality rates compared with the general population. Most of this increased risk occurs in patients with symptomatic epilepsy in whom mortality relates to the underlying condition. In patients with idiopathic or cryptogenic epilepsy, the increased risk of death is related mainly to accidents, especially drowning although sudden unexpected death can occur. Autopsy and clinical series have demonstrated an increased risk of sudden unexplained death among epileptic patients <sup>(7)</sup>.

#### Obstetric complications associated with epilepsy

1. Increase the risk of vaginal bleeding
2. Anaemia
3. Hyperemesis gravidarum
4. Abrupto placentae
5. Eclampsia
6. Premature labour
7. Spontaneous abortion
8. Stillbirth and perinatal death rates are slightly increased when compared to women without epilepsy <sup>(8,9)</sup>.
9. Foetal congenital malformation

Women with epilepsy who are or intend to become pregnant should be treated with special care. Almost 90% of pregnant women with epilepsy tend to deliver without any complications. Seizure frequency may increase during pregnancy especially in the third trimester, the exact cause of this is unknown but it may be due to the fact that third trimester is associated with high plasma hormones, hypomagnesemia, fluid retention and low level of antiepileptic which may be due to fluid retention, impaired absorption and increase clearance of the drugs due to enhance hepatic microsomal induction. Repeated attacks of convulsion can cause high maternal and foetal mortality <sup>(10,11)</sup>.

The treatment goal is to prevent seizures without producing harmful or intolerable side effects of the drugs. When feasible, the lowest effective dose of single antiepileptic drugs (AEDs) should be utilized. Optimal treatment requires knowledge of the patient's age, medical history, current seizure

type and cause, if possible as well as familiarity with available AEDs and their pharmacokinetic profiles, action spectra, and side effects<sup>(12-14)</sup>.

**Phenytoin** is a commonly prescribed anticonvulsant used to treat most types of seizure disorders and status epilepticus, with the exception of absence seizures. Phenytoin toxicity can affect the mother and the fetus; for the mother in addition to the famous side effects like gingival hypertrophy it can aggravate the symptomatology of hyperemesis gravidarum, it can cause folate deficiency anaemia and osteomalacia. For the fetus phenytoin can cause fetal congenital abnormalities, fetal hydantoin syndrome is manifested by broad nasal bridge, wide fontanelle, low hairline, cleft lip/palate, epicanthal folds, short neck, microcephaly, low-set ears, small or absent nails, dislocated hip, hypoplasia of distal phalanges, impaired growth, and congenital heart defects. Measurement of phenytoin plasma serum level will be of value to avoid the complications and to detect drop of serum level during third trimester<sup>(15)</sup>.

**Phenobarbitone** like phenytoin is cheap and available, it can be used in the treatment of generalized epilepsy and as second line in the treatment of secondary generalized epilepsy. The most adverse effect following administration of phenobarbitone is sedation, but this often becomes less marked with continued administration. Like some other antiepileptic agents, phenobarbitone may produce subtle mood changes and impair mental depression may occur. Prolonged administration may occasionally result in folate deficiency or hypocalcaemia; rarely, megaloblastic anaemia or osteomalacia has been reported and all these factors can affect pregnancy. Neonatal drug dependence and symptoms resembling vitamin K deficiency have been reported in infants born to mothers who received phenobarbitone during pregnancy. Congenital

malformations have been reported in children of women who received phenobarbitone during pregnancy but the causal role of the drug is a matter of some debate<sup>(16)</sup>.

**Carbamazepine** is a drug of choice for partial and secondary generalized epilepsies, in women of childbearing potential, carbamazepine should, whenever possible, be prescribed as monotherapy, because the incidence of congenital abnormalities in the offspring of women treated with more than one antiepileptic drug e.g., valproic acid plus carbamazepine plus phenobarbitone and/or phenytoin is greater than in those women receiving a single antiepileptic. Minimum effective doses should be given and the plasma levels monitored. If pregnancy occurs in a woman receiving carbamazepine, or if the need for initiating carbamazepine arises during pregnancy, the drug's potential benefits must be weighed against its hazards, particularly during the first 3 months of pregnancy. Carbamazepine should not be discontinued or withheld from patients if required to prevent major seizures because of the risks posed, to both mother and fetus, by status epilepticus with attendant hypoxia. The possibility that carbamazepine, like all major antiepileptic drugs, increases the risk of malformation has been reported. There are rare reports on developmental disorders and malformations, including spina bifida, in association with carbamazepine<sup>(17)</sup>.

**Sodium valproate** is the drug of choice for most types of epilepsies, in pregnancy, the lowest effective daily dose in divided doses should be used and monotherapy should be used wherever possible. Folate supplementation throughout pregnancy whilst taking antiepileptics is recommended, to reduce the incidence of neural tube defects. There is also an increase of neonatal bleeding (related to hypofibrinaemia) and neonatal hepatotoxicity. The combination of sodium

valproate and lamotrigine should be avoided. Overall the expectant mother/ the woman wishing to become pregnant should be informed of all the risks and benefits of continuing sodium valproate therapy throughout pregnancy<sup>(18)</sup>.

Because the concentration of valproic acid found in breast milk is only 1-10% of that in the maternal plasma there is no contraindication to breast feeding.

The teratogenic effects of newer AEDs are unknown at this time<sup>(19)</sup>.

#### Management of epilepsy during pregnancy

The great majority of patients with epilepsy can be managed by a general practitioner. In a small minority who has exceedingly frequent seizures, treatment in hospital or residential care is necessary. There remains, however, a considerable social stigma attached to the diagnosis, an important fact to be considered when the nature of attacks of disturbed consciousness is uncertain. Present trends are to encourage pregnant women with epilepsy to lead lives as unrestricted as possible. Regarding epileptic pregnant women, it is better to be followed by obstetrician and neurologist<sup>(20,21)</sup>. Regular follow up to see whether the patient experience any attack of convulsion and to look for side-effects of the drugs on the maternal and fetal sides is recommended. Measurement of antiepileptic drugs level as baseline and to be repeated at 18 weeks and 35 weeks to adjust the dose is needed. Also, measurement of maternal serum alpha fetoprotein and abdominal ultrasound at 1 week will be of value to detect foetal neural tube defect<sup>(22,23)</sup>. Folate should be added to reduce the chance to develop neural tube defects which are believed to be due to the antifolate effects of antiepileptic drugs. During the last trimester, description of vitamin K to the mother (10mg daily oral dose) and one mg IM to the new born at the birth prevents the tendency to haemorrhage as a

result of deficiency of vitamin K dependent clotting factors which tends to occur as part of side effects of hepatic enzyme-inducing anticonvulsants. Most of epileptic women tend to deliver normally and 1-2% may experience an attack of convulsion during delivery which should be aborted by intravenous lorazepam and if not responding to the treatment Caesarian section will be the treatment of choice.

Since the amount of antiepileptic drugs excreted in the breast milk is negligible, infants can be breast fed safely.

Antiepileptics like carbamazepine, phenytoin, barbiturate and topiramate can cause contraceptive failure because they tend to cause hepatic enzyme induction. Sodium valproate has little interaction with oral contraception. So the best thing is to use sodium valproate or another alternative contraceptive method. As we know there is a well known relation between menstrual cycle and the tendency to develop seizure, this may be due to hormonal changes e.g. increase in the level of oestrogen decrease the threshold of epilepsy and increase the tendency to develop seizure<sup>(24-26)</sup>.

All these aspects concerning epilepsy in women have fundamental implications for antenatal care (ANC) and follow up of pregnant woman at the level of PHC facilities.

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