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FETAL OUTCOME IN EPILEPTIC MOTHERS ON ANTI EPILEPTIC DRUG THERAPY

Neurology

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ABSTRACT

AIM: To study the fetal outcome in Epileptic mothers on Anti Epileptic Drug therapy.

METHODS: This is a prospective study done in the epilepsy division on GMK medical college, Salem, Tamilnadu, India. From January 2016 to December 2017

Inclusion Criteria: Antenatal mothers suffering from epilepsy, on Anti Epileptic Drug Therapy are included and monitored to study the fetal outcome.

Exclusion Criteria: Antenatal mothers are taking drugs for other medical illness are excluded.

RESULTS: This study is done in 100 Antenatal mothers on Anti Epileptic Drug Therapy. Patients were studied into mono and poly therapy groups. The fetal outcome was studied as miscarriage, preterm delivery, intra uterine death, intra uterine growth retardation (IUGR), congenital malformation, Statistical analysis revealed statistically significant unfavorable fetal outcome in epileptic patients on poly therapy (<p 0.0001), All patients on sodium valproate showed poor fetal outcome, Phenytoin. Carbamazepine, phenobarbitone. Showed statistically significant unfavorable pregnancy outcome with polytherapy(P<0.0001). This study revealed statistically significant incidence of intra uterine death (<p 0.0001), Preterm delivery (<p 0.0001), IUGR (<p 0.0001) in polytherapy, Epileptic Antenatal mothers treated with Levetiracetam had good fetal outcome.

KEYWORDS

Pregnancy. Epilepsy, AED therapy, fetal Outcome

INTRODUCTION

Pregnancy may lead to worsening of epilepsy especially in labor where lack of sleep, hyperventilation may precipitate seizure. Approximately 0.5% of pregnant women may suffer from epilepsy. Recurrent seizures may cause hypoxic injury to the fetus or spontaneous abortion. Anti epileptic drugs are mostly teratogenic, however they should be continued whenever needed to avoid adverse fetal and maternal outcome due to epilepsy. Monotherapy is favored since it is less teratogenic than polytherapy.

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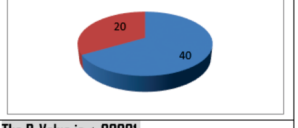
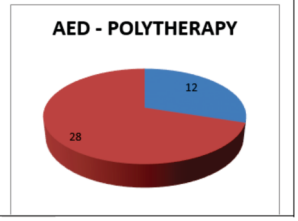
Monotherapy	20/60	P< 0.0001
Miscarriage	2	
IUGR	10	
Preterm	4	
Anomaly	2	
IUD	2	



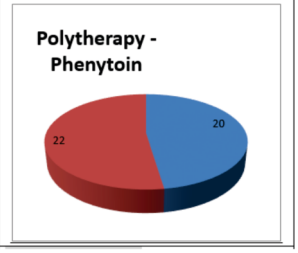
Polytherapy	28/40	P< 0.0001
IUGR	14	
Preterm	2	
Anomaly	2	
IUD	8	
Neonatal death	2	

The P-Value is < .00001.



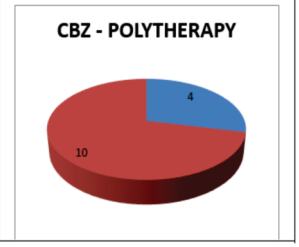
Phenytoin	78
Monotherapy	36
• Preterm	4
• IUGR	8
Polytherapy	42
• IUGR	12
• IUD	8
• Preterm	2

P<0.0001

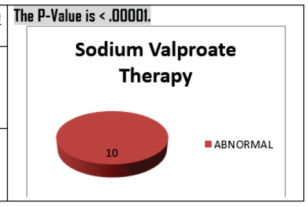


Carbamazepine	22	P< 0.0001
Mono	8	
Poly	14	
• IUGR	8	
• IUD	2	

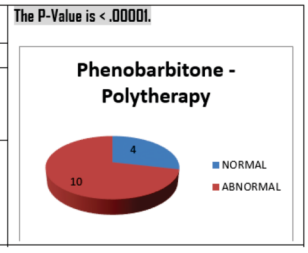
The P-Value is < .00001.



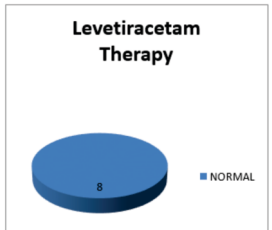
Sodium Valproate	14 - 100% Adverse Outcome
Mono	4
• Preterm	2
• IUGR	2
Poly	10
• IUD	10



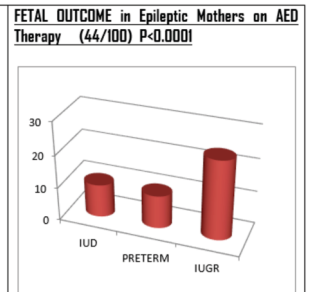
Phenobarbitone	18 P< 0.0001
Monotherapy	4
Polytherapy	14
• IUGR	8
• Preterm	2



Levetiracetam 8 100% Normal



No adverse outcome



DISCUSSION

Epilepsy includes the group of neurological disorders manifest as epileptic seizures. It may vary from brief seizure episode to long period of vigorous shaking.

The cause of epilepsy in most cases is unknown. It may be due to trauma, tumors, infections, birth defects and genetic mutations. Epileptic seizures are the result of excessive and abnormal neuronal hyperactivity in the cerebral cortex.

Seizures are treated with medication in 70% of epilepsy patients. In those patients who do not respond to medication, epilepsy surgery, neuro stimulation and dietary changes may be considered.

Preconception counseling is must, it includes information of the risk for both mothers and the fetus. Consultation with the neurologist helps in selecting the least teratogenic anti epileptic drug therapy.[3,4]

Pregnancy causes dramatic changes in the drug pharmacokinetics, absorption, metabolism and protein binding. Monitoring AEDs level during pregnancy and postpartum period helps in adjusting the drug dosage.[3,4]

AEDs can produce anatomical or behavioral teratogenisis. Several theorys have been postulated. Although the exact mechanism are not known, proposed mechanisms include AEDs induced apoptosis, ischemia and neuronal suppression.[5]

Epileptic mothers on AED therapy are more prone to preterm delivery, small for gestational age babies. women with epilepsy are more prone to give babies with low apgar score.[6,7,8]

In utero exposure to some AED is associated with increased risk of major congenital malformation, adverse obstetric outcome, adverse fetal outcome, impair behavioral development and impair cognitive development in the child.[6,7,8]

During pregnancy epilepsy patients should be screened for fetal anomalies such as neural tube defects, facial deformities or cardiac deformities.[6]

This study done in 100 epileptic mothers on anti epileptic drug therapy, patients were treated with Phenytoin, phenobarbitone, carbamazepine, Sodium valproate, and levetiracetam. Patients on polytherapy (40%), patients on monotherapy (60%). Fetal outcome was compared between mono and polytherapy. Polytherapy patients had statistically significant adverse fetal outcome in the form of Miscarriage, preterm delivery, intrauterine growth retardation, intra uterine death, fetal congenital malformations. Patients treated with sodium valproate had significant adverse outcome in the form of intra uterine death, preterm delivery, intra uterine growth retardation. Patients on Phenytoin, phenobarbitone, carbamazepine had significant adverse outcome with poly therapy.

Monotherapy is preferred in epileptic mothers than polytherapy to avoid the significant incidence of adverse fetal outcome.[7]

In this study 10% of patients had sodium valproate as polytherapy all patients had adverse fetal outcome in the form of intra uterine death of the fetus.[7]

North American studies revealed monotherapy is favorable than polytherapy. Sodium valproate has adverse fetal outcome[5]. It should be avoided in pregnancy whenever possible. European studies revealed women with epilepsy has adverse fetal outcome[9]. Australian studies revealed polytherapy patients had low birth weight and intra uterine growth retardation[1,2]. Asian studies reveals adverse outcome in polytherapy[10,11].

Patients who were treated with phenobarbitone as polytherapy had chances of fetal congenital malformations.[6,7]

Patients treated with Phenytoin showed higher incidence of preterm delivery and IUGR in polytherapy.[6,7] Patients treated with carbamazepine as monotherapy had safe fetal outcome than polytherapy.[6,7]

Patients treated with Levetiracetam therapy had safe fetal outcome.[6,7]

CONCLUSION

In our study epileptic mothers had poor fetal outcome when compared with normal mothers. Patients who were on anti epileptic drug monotherapy had favorable fetal outcome. Patients who were treated on sodium valproate had significant unfavorable outcome in both mono and poly therapy. Hence sodium valproate therapy in pregnancy should be avoided whenever possible. Patients who were treated with levetiracetam during pregnancy had good fetal outcome. So levetiracetam as monotherapy should be advised during pregnancy according to this study. Large scale multi centre study in the globe can give adequate evidence to improve the fetal outcome in epileptic pregnant mothers.

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