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Original Research Article.

A Study to Know the Effect of Antiepileptic Drugs on Liver Enzymes

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ABSTRACT

Objective: To know the effect of antiepileptic drugs on liver enzymes.

Study Design: Cross sectional study.

Materials & Methods: The study was conducted on 108 patients at SIMS Hapur and G.S Medical College Hapur between Jan 17 to Dec 17. Patients divided into 3 groups, consisting of 36 patients in each group of phenytoin, carbamazepine and valproate.

Results: Total No. of Patients was 108, out of which 36 patients were there is each group of Phenytoin, Carbamazepine and valproate. Most of the patients 36 (33.33%) and 32 (29.62%) belongs to age group of >40 – 50 years and >50 year respectively. Regarding raised SGPT, it was seen in 5 (13.89), 3 (8.33) and 3 (8.33) in phenytoin, carbamazepine and sodium valproate group respectively. SGOT were raised in sodium valproate group respectively. Alkaline phosphatase were raised in 10 (27.78), 20 (55.56) and 22 (61.11) in phenytoin group, carbamazepine group, and sodium valproate group respectively.

Conclusion: From the present study we can conclude that sodium valproate is more hepatotoxic than carbamazepine which is more toxic than phenytoin. It is recommended that base line Liver Function Test (LFT) is essential before starting of AEDs and regular monitoring of LFT is also done between the course of treatment.

Keywords: Antiepileptic Drugs, Liver Enzymes, Alkaline Phosphatase.

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INTRODUCTION

Epileptic seizure is a medical emergency and characterized by a transient excessive, uncontrolled discharge of large number of neurons.[1]

Epilepsy is the most common chronic neurological disorder worldwide.[2] The liver plays an important role in the maintenance, performance and regulating homeostasis of the body. The main function of liver is metabolism of carbohydrate, protein, fat and detoxification. Liver also important role in drug metabolism and elimination of antiepileptic drugs and thus subjected to drug induced toxicity, this hepatotoxicity may be mild to fatal hepatic failure.[3]

For the AED, metabolic reactions are catalyzed predominantly by the cytochrome P $_{450}$ (CYP) UDP – glucuronyl transferase enzyme.[4]

Seven primary Isoenzymes are involved in hepatic metabolism of most of the drugs – CYP1A2, CYP2A6, CYP2C9, CYP2C19, CYP2D6, CYPP$_2$E, and CYP3A4.[5] The AED's like phenytoin, carbamazepine and sodium valproate have significant enzyme inducing properties and induction of immunoallergic reactions.[6,7] Phenytoin, valproate and carbamazepine is widely used antiepileptic drugs. Use of AED's may results in increase in gamma glutamyl transferase and to lesser extent in alkaline phosphatase due to enzyme inducing properties.[8] Even carbamazepine results in cholestatic hepatocellular injury and granuloma formation in liver.[9]

MATERIALS & METHODS

This study was conducted on 108 patients at SIMS Hapur and G.S Medical College Pilkhuwa, Hapur between Jan 17 to Dec 17. Patients divided into 3 group consisting of 36 patients in each group of phenytoin, valproate and carbamazepine.

In this cross sectional study patients were selected who were given antiepileptic drugs (carbamazepine, phenytoin and sodium valproate) from at least 6 months. The exclusion criteria were patients who have liver disease, on any other drugs and alcoholics.

Data's were collected in the in the form of age, gender, duration of treatment and daily dose of AED. Investigation was done in the form of alanine amniotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP).

Table I: Gender wise distribution

Gender	N=108
Male	68 (62.96%)
Female	40 (37.04%)

Table II: Age wise distribution

Age	Male (n=68)	Female (n=40)
20-30	8 (11.76)	6 (15)
>30-40	16 (23.53)	10 (25)
>40-50	24 (35.29)	12 (30)
>50	20 (29.41)	12 (30)
	68 (100)	40 (100)

RESULTS

Total numbers of patients were 108, out of which 68 (62.96%) were male and 40 (37.04%) were female. Most of the patients 36 (33.33%) and 32 (29.62%) belongs to age group of >40 – 50 years and >50 year respectively. In phenytoin group 20 (55.55%) and 16 (44.45%) were male and female respectively. In carbamazepine group 26 (72.22%) and 10 (27.78%) were male and female respectively. 22 (61.11%) and 14 (38.89%) were male and female in sodium valproate group respectively. Regarding raised SGPT, it was seen in 5 (13.89), 3 (8.33) and 3 (8.33) in phenytoin, carbamazepine and sodium valproate group respectively. SGOT were raised in sodium valproate group respectively. Alkaline phosphatase were raised in 10 (27.78), 20 (55.56) and 22 (61.11) in phenytoin group, carbamazepine group, and sodium valproate group respectively.

Table III: Distribution among groups

		Male (n=68)	%	Female (n=40)	%
Phenytoin Group I	**36**	20 (29.41)	55.55	16 (40)	44.45
Carbamazepine Group II	**36**	26 (38.24)	72.22	10 (25)	27.78
Sodium Valproate group III	**36**	22 (32.35)	61.11	14 (35)	38.11

Table IV: Serum Level of Liver Enzymes in deferent group

Liver Enzymes in U/L	Group I		Group II		Group III	
	Abnormal n (%)	Normal n (%)	Abnormal n (%)	Normal n (%)	Abnormal n (%)	Normal n (%)
SGPT	5 (13.89)	31 (86.11)	3 (8.33)	33 (91.67)	3 (8.33)	33 (91.67)
SGOT	8 (22.22)	28 (77.78)	3 (8.33)	33 (91.67)	5 (13.89)	21 (58.33)
Alkaline Phosphatase	10 (27.78)	26 (72.32)	20 (55.56)	16 (44.44)	22 (61.11)	14 (38.89)

DISCUSSION

In this study, there were 36 patients each in phenytoin, carbamazepine and sodium valproate group. Out of total 108 patients 68 were male and 40 were female. Regarding SGPT, it was raised in 5 (13.89%) patients on phenytoin, 3 (8.33) on carbamazepine and 3 (8.33) on sodium valproate. Regarding SGOT, it was raised in 8 (22.22), 3 (8.33) and 5 (13.89) in phenytoin, carbamazepine and sodium valproate group respectively. It was also observed in other study.

In phenytoin group, SGOT and Alkaline phosphatase were raised in 5 (13.89), 8 (22.22) and 10 (27.78) respectively. Other investigator also found the similar results.[10] It was suggested that enzymes induction by phenytoin is dose dependent. The investigator found that there was no significant correlation between serum levels of phenytoin and the risk for hepatotoxicity.[11] In carbamazepine group SGPT, SGOT and Alkaline phosphatase were raised in 3 (8.33), 3 (8.33) and 20 (55.56) patients respectively. Patients using carbamazepine has significantly higher Alkaline phosphatase than phenytoin group. The other Author reported that this higher level of Alkaline phosphatase is independent of dose.[12,13] In sodium valproate group, SGPT, SGOT and Alkaline phosphatase were raised in 3 (8.33) 5 (13.89) and 22(61.11) patient respectively. Our results are comparable with other study.[14] Most of the authors found that liver toxicity caused by Phenytoin, carbamazepine and sodium valproate is dose independent.[15,16]

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