EFFECT OF LEVETIRACETAM (LEV)VERSUS PHYNTOIN SODIUM(PHT) IN CONTROLLING OFCONVULSIONS CAUSED BY CARBOFURAN 3%CG INGESTIONAL POISON.

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ABSTRACT

Anti-epileptic drugs are commonly used for seizure prophylaxis after neurological injury. We noticed and observed a study (at Durga multispecialityhospital,Karimnagar) during treatment of controlling convulsions caused by the Carbofuran 3%CG (Furan 3G) poisonshowed effects on central nervous system. Intravenous IV Levetiracetam (LEV) to IV phenytoin (PHT) for controlling seizures in the carbofuran poisoning. Continuous EEG (cEEG) monitoring was performed for the initial 72 h; outcome data were collected. Our study is helpful and giving supports to the Research articleProspective, Randomized, Single-Blinded Comparative Trial of Intravenous Levetiracetam Versus Phenytoin for SeizureProphylaxisJerzy P. Szaflarski,Kiranpal S. Sangha, Christopher J. Lindsell, Lori A. Shutter. (1)

KEY WORDS: Carbofuran3%CG, Levetiracetam(LEV), Phenytoin (PHT) Sodium,Convulsions.

INTRODUCTION:

Agricultural development continues to remain the most important objective of Indian planning and policy. In the process of development of agriculture, pesticides/insecticides have become an important tool as a plant protection agent for boosting food production. Further, pesticides/insecticides play a significant role by keeping many dreadful diseases. However, exposure to pesticides/insecticides both occupationally and environmentally causes a range of human health problems. It has been observed that the pesticides exposures are increasingly linked to immune suppression, hormone disruption, diminished intelligence (CNS disorders), reproductive abnormalities and cancer. Currently, India is the largest producer of pesticides in Asia and ranks twelfth in the world for the use of pesticides. A vast majority of the population in India is engaged in agriculture and is therefore exposed to the pesticides used in agriculture(2).Intentional(suicidal) or accidentally ingestion /inhalation of insecticide poison cause major health hazards and even death occurs.

Carbofuran is one of the insecticide causing major potential health hazards like convulsions,coma even death occurs. Here one case report proved the concept of seizures control and prophylaxis of convulsions with the treatment levetiracetam (LEV) versus phenytoin sodiumwas occurred by ingestion of carbofuran 3%CGpoison.

Carbofuran (2,3-dihydro-2,2-dimethyl-7-benzofuranylmethylcarbamate) (see Fig. 1) is a carbamate insecticide used for the control of soil-dwelling insects in maize, oilseed rape, sorghum, sugar beet, sunflowers and vegetables. It is one of the metabolites of benfuracarb(3) (Fig. 1) and was detected in human fatal cases following benfuracarb ingestion (4). Carbofuran inhibits cholinesterase and is metabolized rapidly and completely by hydrolysis in rats and has been assigned a toxic class of WHO Ib. Carbofuran was introduced by Bayer AG and is widely used in many countries including Korea and Japan(5).Carbofuran is a reversible cholinesterase inhibitor. This product is highly toxic if swallowed, and has low dermal toxicity. It is expected to be highly toxic by inhalation. It is minimally irritating to the skin and practically non-irritating to the eyes, however, absorption through the mucous membranes of the eyes could be highly toxic.It elicits symptoms in humans typical of cholinesterase inhibition including headaches, light-headedness, weakness, abdominal cramps, nausea, excessive salivation, perspiration and blurred vision. More severe signs of cholinesterase inhibition include tearing, pin-point pupils, excessive respiratory secretions, cyanosis, **convulsions, generalized tremor** and coma. Excessive exposure may result in death. ***In humans, ingestion of large amounts of carbofuran has resulted in symptoms of reversible central nervous system depression including stupor, rapid breathing and heartbeat, profuse sweating and seizures.*** Atropine sulfate is antidotal. Use of oximes such as 2-PAM is controversial (6).Treatment is otherwise controlled removal of exposure followed by symptomatic and supportive care.

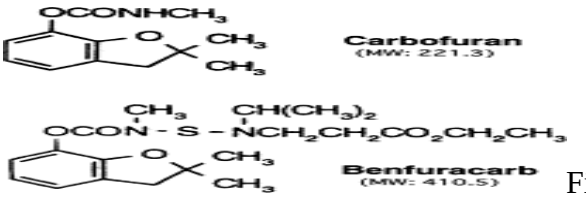

Fig:1Chemical structures of carbofuran and benfuracarb

Levetiracetam, marketed under the trade names Keppra among others, is a medication used to treat epilepsy(7).It is used for partial onset, myoclonic, or tonic-clonic seizures(8).It is the S-enantiomer of etiracetam.Levetiracetam reduces the release of presynaptic neurotransmitter including glutamate by binding to presynaptic vesicle protein(9).

Phenytoin (PHT)is an anti-seizure medication It is useful for the prevention of tonic-clonic seizures and partial seizures, butnot absence seizures. The intravenous form is used for status epilepticus that does not improve with benzodiazepines.It works by reducing the spread of seizure activity in the brain. Phenytoin is believed to protect against seizures by causing voltage-dependent block of voltage gated sodium channelsThe primary site of action appears to be the motor cortex where spread of seizure activity is inhibited(10).

Case report(11):

A 54 year oldmoderate obese female patient was presented to emergency department with chief complains of severe uncontrolled convulsions each episode last for 5-10 mins. On brief it shows she had alleged history of self consumptionof 150gm of carbofuran 3G with water and food at 3 pm on 6-4-2017 brought to ER at 3:20pm. During prehospital stage she became drowsy and throwing convulsions, frothing from mouth. On Examination in the hospital Patient became semiconscious, irritable, thrown fits,PR-48/min, B.P 60mmHg systolic only recordable,Heart-S_1^+,S_2^+,Lungs-Bilateral crepts were present,CNS-Pupils are pin pointed.SpO_2 is 59% on room air. Immediately patient airway was protected with adequate high flow oxygen inhalation with help of bag and mask ventilatation. Gastric lavage done with Ryle's tube insertion,treatment continued with Inj. Atropine sulfate antidote 2mg atropine intravenously and repeated with 0.4 - 2.0 mg atropine at 15 minute intervals until atropinization occurred (tachycardia, flushed skin, dry mouth, mydriasis),continuous infusion also given with 3ml/hr and maintained heart rate above 100/min. Ionotropic drugs support were given to maintain blood pressure.

In this event Recurrent episodes of convulsions seen which were not controlled with injlorazepam 2cc bolus or diluted midazolam 3cc bolus (5mg/ml concentration diluted with 1mg mixed with 4ml of normal saline in 5cc syringe) and given with 1gm of phenytoin sodium injection added in 100ml of normal saline fallowed by 100mg intravenously every 8thhourly. Continuous EEG monitoring for 72 hours done. Convulsions were controlled partially on day 1. Patient was kept on NIV and Saturation was maintained.Sample of blood collected from the patient for laboratory

investigations to evaluate any metabolic abnormalities and serum cholinesterase levels in the blood. The lab values of electrolytes werenormal; increase in WBC count, ABG shows respiratory acidosis while bicarbonates were normal range reported.On second day Patient was developed similar episodes of convulsions which were not controlled with Phenytoin sodium as dose 15mg/kg body weight. On expert advice Patient had given with 2gm of Inj. Levetiracetam added to 100ml of normal saline followed by 500mg of Inj Levetiracetam twice daily intravenously added to 100ml of normal saline infused. Treatment was continued until patient recovery from the poison effect. MRI brain epilepsy protocol was done to evaluate any brain damage but it showed age related cerebral atrophy changes. Patient stayed for 7 days but she had not been found with any episode of convulsions during the stay at hospital. Patient was discharged with medications added TabLevetiracetam500mg and advised review after 5 days. Patient bought tab Levetiracetam for three days only. After going home three days later patient met local doctor and he changed to phenytoin sodium 100 mg instead of Levetiracetam.She didn't come for review after 5 days from discharge date. She stopped Levetiracetam and started taking of Phenytoinsodium,two days later in the early morning she was developed convulsions and brought to primarlytreated hospital and their attenders described the incident about stoppage of medications. Immediately patient was continued with Levetiracetam and kept in observation for about 48 hours then no episode of convulsions had seen then discharged the patient with given instructions of continuing the Levetiracetam until further orders. After three months,she reviewed with no episode of convulsionsseen. During the treatment study, Neurologist, General physician, Intensivist, Emergency specialist, Anaesthetist opinion was consulted.

Conclusion:

Anti-epileptic drugs are commonly used for seizure prophylaxis after neurological injury. We performed a study comparing intravenous (IV) levetiracetam (LEV) to IV phenytoin (PHT) for controlling seizures in the carbofuran poisoning. Continuous EEG (cEEG) monitoring was performed for the initial 72 h; outcome data were collected.

This study of LEV versus PHT for seizure prevention in the NSICU showed improved long-term outcomes of LEV-treated patients vis-à-vis PHT-treated patients. LEV more preferable drug than PHT for seizure prophylaxis in this setting.

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9.*Levetiracetam improves symptoms of multiple chemical sensitivity: Case report*
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*11.*Case report shows Direct presentation of case in the ED at Durga multispeciality hospital karimnagar district.