INTRODUCTION

Carbamazepine (CBZ) is an anticonvulsant used in the treatment of epilepsy and neuropathic pain along with it also having an activity of anticholinergic, antineuralgic, anti-diuretic, muscle relaxant, antinamic, antidepressive, antiarrhythmic properties. Carbamazepine has a lot of therapeutic uses but along with it there is occurrence of adverse reactions (ADRs) to CBZ can negatively impact the quality of life of patients, as well as, increase health care costs. Thus, knowledge of CBZ-induced ADRs is important to achieve safer treatment outcomes. CBZ is developed by Schindler in 1953, was first applied as a treatment for depressions and psychosis. Shortly after the approval, first side effects were observed including cutaneous ADRs. The mechanism of action of the drug is to stabilize inactivated state of sodium channels, thereby making neurons less excitable. May reduce activity of nucleus ventralis of the thalamus or decrease synaptic transmission or summation of temporal stimulation leading to neuronal discharge. Absorption Bioavailability: 85% (oral suspension) Peak serum time: 4.5 hr (immediate-release tablets); 3-12 hr (extended-release tablets); 1.5 hr (oral suspension) Distribution Protein bound: 90% Vd: 1.5 L/kg

Carbamazepine inhibits sodium channel firing, treating seizure activity. Animal research studies have demonstrated that carbamazepine exerts its effects by lowering polysynaptic nerve response and inhibiting post-tetanic potentiation. In both cats and rats, carbamazepine was shown to decrease pain caused by infraorbital nerve stimulation. A decrease in the action potential in the nucleus ventralis of the thalamus in the brain and inhibition of the lingual mandibular reflex were observed in other studies after carbamazepine use. Carbamazepine causes the above effects by binding to voltage-dependent sodium channels and preventing action potentials, which normally lead to stimulatory effects on nerve.
Dr. K. Lakshmisurekha, Dr. Naga Subrahmanyam S and Dr. P. Parasankumar, Carbamazepine Induced Cutaneous Reactions

(neonates); 1.9 L/kg (children); 0.59-2 L/kg (adults) Metabolism Via hepatic CYP3A4 Metabolites: Carbamazepine 10,11-epoxide Enzymes induced: CYP1A2, CYP2C9, CYP3A4 Elimination Half-life: 25-65 hr (initial dosing); decreases to 10-20 hr after auto induction; 35-40 hr (extended release) Excretion: Urine (72%); feces (28%)

Pharmacogenomics
HLA-B*1502
It is estimated that 1 in 20 patients with HLA-B*1502 will have a severe dermatologic reaction (eg, TEN, SJS) when taking carbamazepine

HLA-A*3101
Retrospective case-control studies in patients of European, Korean, and Japanese ancestry have found a moderate association between the risk of developing hypersensitivity reactions and the presence of HLAA*3101, an inherited allelic variant of the HLA-A gene, in patients using carbamazepine; these hypersensitivity reactions include Stevens Johnson syndrome and toxic epidermal necrolysis

HLA-A*3101 is expected to be carried by more than 15% of patients of Japanese, Native American, Southern Indian (eg, Tamil Nadu)[2]

Case Report
A child of age 12 years was admitted in the hospital with chief complaints of fever since 1 day, 2 episodes of vomiting, redness of both eyes, oral ulcers, swelling of lips and skin rashes since 2 days. Patient in past medical history identified with 2 episodes of tonic clonic seizures and on medication 500mg of carbamazepine PO BD since 2 months. On examination patient was conscious and coherent. On physical examination temp 103°F, PR: 82 beats/min, RR: 18 cycles/min, CVS: S1,S2+ on laboratory investigation Hb 11.2g/dl, WBC 12,900 cells/cu.mm in differential count P40,L45,E, platelets 2.40 lakhs, blood urea 22mg/dl, serum creatinine 0.8mg/dl. Based on the above information suspected it as probable ADR (swelling of lips, oral rashes, skin rashes, redness of eyes) patient is referred to dermatology department to confirm the ADR. On analysis of case carbamazepine is the drug given 500mg BD literature support the above ADR. To know the effect we advised challenge test i.e drug was withdrawn from treatment regimen and prescribed Tab.fexofenidine 120mg BD, mositurex soft cream, kenocort and oral paste, soframycin cream, Moxifloxacin eye drops.

Causality Assessment
To evaluate the relation between the drug and reaction we performed causality assessment by using scales like WHO causality assessment scale, Naranjo’s scale and observed ADR [7,8]

Table 1 causality assessment of suspected ADR

<table>
<thead>
<tr>
<th>adr scale</th>
<th>who- cas</th>
<th>naranjo’s scale</th>
<th>Assessment</th>
<th>Probable</th>
</tr>
</thead>
</table>

Table 2 Analysis of observed ADR

<table>
<thead>
<tr>
<th>severity assessment</th>
<th>moderate level 4(a)</th>
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</thead>
<tbody>
<tr>
<td>Preventability</td>
<td>Probably preventable</td>
</tr>
<tr>
<td>Predictability</td>
<td>Type - A</td>
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</tbody>
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DISCUSSION
The cutaneous reaction are mostly induced by multiple etiologies and commonly triggered by viral infections but also having the common cause due to use of medications. The increases number of prescriptions of carbamazepine for the control of pain, seizures may be the reason for the increased frequency of SJS/TEN to Carbamazepine [9]. The patients usually develop hypersensitivity reaction to the drug carbamazepine between 2 and 12 weeks [10]

The symptoms experienced by the patient on questioning understandable that adverse reaction in terms of pharmacokinetics, narrow therapeutic index and individual variability in metabolism and elimination, prolonged use of the medication at high dose. The patient developed adverse reaction after prolonged use of medication for 8 weeks. The patient was presented with symptoms of swelling of lips, oral rashes, skin rashes, redness of eyes after 8 week treatment with the carbamazepine. Carbamazepine adverse reaction in patient tested with certain genotype, SNPs but we haven’t done due to cost consideration of the patient. The patient was improved after withdrawal of carbamazepine and given with the supportive care for the adverse drugs reaction.

During the treatment course as a clinical pharmacist we have identified adverse reaction as follows: the patient under the medication with carbamazepine adverse drug reaction has been identified based on literature reviews, on examination and other investigations we concluded the condition due to drug carbamazepine performed causality assessment, severity, preventability, predictability. After identification we withdrawn the drug carbamazepine and provided appropriate treatment along with supportive care.

CONCLUSION
In recent years there is increased number of carbamazepine prescriptions. The case report there is probable relation between the carbamazepine and cutaneous reactions. The case report is to highlight the use of carbamazepine and also to create awareness regarding the cutaneous reactions and careful management of all the patients who receives the drug carbamazepine. Better pharmacovigilance can also prevent the above adverse drug reactions.

Reference
6. Kuo CC, Chen RS, Lu L, Chen RC: Carbamazepine inhibition of neuronal Na+ currents: quantitative distinction from phenytoin and possible therapeutic

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