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A STUDY ON CUTANEOUS ADVERSE DRUG REACTIONS WITH MODEL DRUG LIKE PHENYTOIN

Tunuguntla K.N.V. Raja Kiranmai*, Atluri Jyothi, Poojitha Mandava, Pilli Sai Mounika
A.M. Reddy Memorial College of Pharmacy, INDIA.

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ABSTRACT

Phenytoin is a highly effective and widely prescribed anticonvulsant agent. Phenytoin is associated with both dose related side effects and hypersensitivity reactions. We report a case of phenytoin macular second degree rash, which was characterized by skin with high or spiking fever, increase in ALT, ALP and eosinophil's. Anticonvulsant Hypersensitivity Syndrome (AHS) is a delayed drug reaction associated with the use of anticonvulsant drugs majorly carbamazepine, phenytoin and phenobarbital. This uncommon, though potentially fatal, multisystem disorder appears to be a hypersensitivity reaction to arene metabolites of these drugs. The most common clinical presentation of this disorder includes fever, rash,abnormal liver function and lymphadenopathy. Onset generally occurs within 2-4 weeks of initiating therapy, but may take as long as 3 months.Discontinuation and replacement of another anti-convulsant drug is the remedy but in this case discontinuation of the drug was done.

Keywords: *Phenytoin, Carbamazepine, Phenobarbital and Hypersensitivity.*

INTRODUCTION

Drug-induced Cutaneousadverse effects are major health problem. Its main forms include macular rash, macula papular rash, Stevens - Johnson syndrome, toxic epidermal necrolysis, fixed drug eruption and urticaria. Phenytoin is an anticonvulsant agent which is used to control seizures. It works by slowing down impulses in the brain that cause seizures.

Adverse drug reactions (ADRs) are unwanted or unintended effects, which occur with use of drugs. Clinically important ADRs are diverse [1]. Any one organ system or several systems simultaneously can be the principal targets, but cutaneous ADRs are most common among the various adverse reactions and attributed by the drugs. Cutaneous drug rashes are most common type of adverse drug reactions are self-limiting and sometimes severe. Cutaneous ADR's occur in up to 10% of global population and in 2-3% of hospitalized patients [2]. Studies have found their incidence in developed countries as 1-3%, while the incidence in developing countries is supposed to be higher between 2 and 5%. The most frequently involved group of drugs are antibiotics (ofloxacin), anticonvulsant drugs (phenytoin, carbamazeineetc) [1].

When a patient admitted to the Emergency Department (ED) with skinfindings and unusual complaints after starting any newdrug, particularly antiepileptics, physical examination and appropriate diagnostic testing should be performedto detect systemic involvement. Initial testing shouldinclude a CBC with differential and peripheral smear, LFT, serum creatinine, chest X-ray, and urinalysis.

A phenytoin level was 5.4 (therapeutic 10–20) and basic to levetiracetam was described just last year. Most cases of phenytoin ADR occur within 8 weeks of exposure, but one case report occurred 4 months after initiation of carbamazepine [1].

CASE REPORT

A 30yrs Old Male Patient was admitted in the hospital with,

Chief Complaints: Fever without chills since 9 days, Rash on hands since 7 days, Nausea, Oral ulcer, Shortness of breath, Oliguria, Pain in abdomen.
Past History: Head injury 1 month back, seizures since 6 months and is on regular medication of drug Eptoin.

His vitals on admission:

Temperature: febrile

B.P- 110\60mmHg
P.R- 106/min
CVS- S1+S2+
R.S – B/LAE +

Advice: 2D ECHO, Urine analysis, Blood analysis, LFT.

Laboratory Investigation:

Table No. 1: Haematology

EXAMINATION	OBSERVED VALUE
HAEMOGLOBIN	14.5gm%
RBC	4.3m/cumm
WBC	7500 c/cumm
LYMPHOCYTES	26%
EOSINOPHILS	12%
NEUTROPHILLS	61%
MONOCYTES	01%
PCV	45%
MCV	81.8fl
MCH	28pg
MCHC	32.3gm%
ESR	5 mm/1sthr

Table No. 2: Biochemistry Examinations

EXAMINATION	OBSERVED VALUE
RBS	78mg/dl
S.CREATININE	1.0mg/dl
NA+	136meq/l
K+	3.6meq/l

***Corresponding author:**
Tunuguntla K.N.V. Raja Kiranmai
A.M. Reddy Memorial College of Pharmacy,
INDIA. Cell.No:9014258717
**E-Mail: kiranmaiammai@gmail.com*

No. 3: Liver Function tests

EXAMINATION	OBSERVED VALUE
Total bilirubin	0.7mg/dl
Direct bilirubin	0.4mg/dl
Indirect bilirubin	0.3mg/dl
Total proteins	6.8gm/dl
ALT	131U/L
ALP	287 U/L
Serum albumin	4.1gm/dl

Table No. 4: Urine Analysis

EXAMINATION	OBSERVED VALUE
Ph	6.0
Proteins	Trace
Pus cells	2-3hpf
Epithelial cells	1-2hpf
R.b.c	Nil

ECHO: Normal

Diagnosis: MACULAR 2°RASH

Treatment: He is treated with following Medications:

Table No. 5: Treated with following Medications

DRUG	DOSE	ROA	Frequency	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Inj. cefoperazone + sulbactam	1gm	I.V	1-0-1	✓	✓	✓	✓	✓	✓	✓
Inj.Dexamethasone	8mg	I.V	1-1-1	✓	✓	✓	✓	✓	✓	✓
Inj.Pantoprazole	40mg	I.V	1-0-0	✓	✓	✓	✓	✓	✓	✓
Inj.Levitiracetem	500mg	I.V	1-0-0	✓	✓	✓	✓	✓	✓	✓
Inj.paracetamol	125mg/5ml	I.V	SOS	✓	✓	✓	✓	✓	✓	✓
Syp.corex		P/O	1-1-1	✓	✓	✓	✓	✓	✓	✓
Dermo calm lotion				✓	✓	✓	✓	✓	✓	✓
Candid mouth paint				✓	✓	✓	✓	✓	✓	✓

Drug Related Problems:

Due to the use of drug phenytoin (eptoin) development of macular 2°rash was observed on hands on day 20.

Based upon the past medication history information Indicates drug induced macular rash due to the drug phenytoin.

Discontinue Medicine and Provide General Supportive Measures:

Treatment resolves the symptoms by discontinuation of the drug, addition of topical cortico-steroids and anti-histamines to decrease the intensity of the cutaneous rash. Systemic corticosteroids are often used to resolve only skin rash but not systemic symptoms.supportive care should be given to the patient .Regular Monitoring of Haemotological, LFT is important. Relapse is often seen [4].

Patients who have experienced AHS should avoid arene oxide anticonvulsants (carbamazepine, phenytoin and phenobarbitone) in the future. All cases of AHS should be reported to the Centre for Adverse Reactions Monitoring.

CONCLUSION

AHS is a rare phenomenon but may have fatal consequences due to the presence of aromatic benzene anticonvulsants such as (carbamazepine, phenytoin, phenobarbital). Signs, symptoms may vary from person to person. It is more prevalent in african-american population. In this case Discontinuation of drug was done.

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