

Pellagroid Dermatitis due to Phenytoin Medication Error in an adult woman with Generalized Epilepsy

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ABSTRACT

Background: Phenytoin is a drug commonly used for treatment of generalized tonic clonic seizures and partial seizures. It has very narrow therapeutic index. Its therapeutic range is 10-20 mcg/dL above which signs of toxicities appear. Pellagroid Dermatitis is a rare adverse drug reaction of phenytoin with incidence of 23 cases among 57,792 cases of ADR due to Phenytoin in VIGLaccess.

Case report: A 25 years female, having epilepsy since 1 month was prescribed phenytoin 100mg thrice a day. She, due to misunderstanding; took 3 tablets of 100mg, together at bed time and plasma level of phenytoin was elevated to 33.44mcg/dL along with Pellagroid Dermatitis, Diarrhea and Giddiness. Rashes were distributed bilaterally, on the exposed areas of back of hands up to rim of sleeves (Pellagra Gloves). Area involved in legs is up to the edge of trousers or skirt. As Tab. Phenytoin was withdrawn, diarrhea and giddiness improved. She was given Tab. Niacinamide 250mg twice a day. Patient was shifted to tab. Valproate 200mg thrice a day orally

Discussion: Phenytoin elimination is dose dependent. At low blood levels 10-15mcg/dl, it follows first order kinetics; as the blood level rises above 20mcg/dl, liver enzymes get saturated and plasma level rises rapidly. Peak plasma level reaches within 3-12 hours of oral administration. Plasma levels in individual's shows emergence of dose-related side effects. **Conclusion:** Phenytoin may contribute to niacin deficiency at higher concentration that can manifest as pellagra. As the drug has narrow therapeutic index, therapeutic drug monitoring along with counseling of patient for proper use of medicine must be done.

Keywords: Phenytoin, Pellagroid dermatitis, medication error

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INTRODUCTION

Phenytoin is a drug commonly used for treatment of generalized tonic clonic seizures and partial seizures. It has very narrow therapeutic index. Its therapeutic range is 10-20 mcg/dL above which signs of toxicities appear. Pellagroid Dermatitis is a rare adverse drug reaction of phenytoin with incidence of 23 cases among 57,792 cases of ADR due to Phenytoin in VIGLaccess.

CASE DETAILS

STUDY DESIGN

A female patient(A.S.) aged 26 years was admitted to Civil Hospital Rajkot with chief complaints of increased frequency of stools since 3 days, Blackening of hands and feet since 3 days and giddiness since 2 days.

The patient had past history of generalized tonic clonic seizures since last 1 month for which she was taking phenytoin 3 tablets (each tablet of 100mg) altogether at bedtime instead of divided doses as prescribed by physician. There was no any other significant personal/family history.

There was no history of any other medications. No history of hypertension or diabetes mellitus. No history of fever, bleeding or trauma. No any other significant personal or family history.

Patient had one female child 10 years back and patients last menstrual period was 20 days before admission to hospital.

On admission, patients' temperature was normal, pulse rate was 96/min. Blood pressure was 110/80 mmHg, SPO2 was 97%, Random blood sugar of patient was 90 mg/dL. Patients' respiratory sounds were normal and bilaterally similar. Cardiovascular examination was also normal. Patient was conscious and oriented to time, place and Patient was conscious and oriented to time, place and person but was lethargic and was feeling very much fatigue. Muscle tone was normal in all four limbs. Planter reflexes were decreased bilaterally.

Local examination of all four limbs showed hyper pigmented lesions in both hands and feet. Lesions were distributed on back of hands and forearms up to the rim of sleeves (Pellagra Gloves) and in feet and legs up to the edge of trousers or skirt. The rashes were characterized by clear zone of demarcation between affected and

normal skin. Hyper pigmented Erythematous patches were accompanied by itching, scaling and exfoliation.

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On laboratory examination, peripheral examination showed hypochromic microcytic picture with some macrocytic RBCs and mild degree of anisopoikilocytosis. Patients serum phenytoin level was 33.44 mcg/dL. Hemoglobin was 8.1 (normal range 12.5-16 gm/dL) Hematocrit was 28.5 (Normal range 40.5 – 41.5). RBC count, Total Leukocyte count, Differential count and platelet count were normal.

Serum Niacin level and estimation of urinary metabolites N1-methylnicotinamide and 2-pyridone could not be done because of financial constraints.

Treatment Details:

Day 1: On admission, patient was given ORS and Tab. Domstal twice a day. After shifting to the ward Patient was given Inj. Multivitamin and Inj. Cynocobalamine along with rehydration therapy intravenously 8 hourly. She was also prescribed Tab. Folic acid once a day once an day.

Day 2: According to opinion from pharmacology department of medical college, phenytoin was withdrawn and patient was shifted on Tab. Sodium Valproate 200mg thrice a day.

Day 3, 4: Same treatment was continued.

Day 5: Dermatology consultant opinion was taken and Tab. Niacinamide 250mg twice a day, Tab. B complex, Tab. Folic acid was given. Betamethasone cream and emollient was given for local application.

All the medications were given for 1 month and follow up was planned after one month.

To evaluate the relationship between the drug and reaction, we have performed causality assessment.

The suspected ADR was “probable (as per Naranjo’s and WHO causality assessment scale) and “level - 4 severity” as per Modified Hartwig and Siegle scale.^{[4][5][6]} The ADR was “probably preventable” by using Modified Schumock and Thornton scale.

DISCUSSION

Phenytoin elimination is dose dependent. Initially at low blood levels (up to 10-15 mcg/dL) it follows first order kinetics; as the blood level rises above 20mcg/dL, liver enzymes get saturated and plasma level rises rapidly. This threshold for shift from first order to zero order kinetics depends on many factors such as patients’ genetic factors, weight, other concomitant drugs etc. After oral administration peak plasma levels reaches within 3-12 hours, so FDA recommends it to be prescribed as 100mg thrice a day sustained release tablets. Steady state plasma level is achieved after 7-10 days so therapeutic drug monitoring should be done between 10-15th day of starting the therapy. Plasma levels in individuals show emergence of dose related side effects.

CONCLUSION

Phenytoin may contribute to niacin deficiency at higher concentration that can manifest as pellagra. As the drug has narrow therapeutic index, therapeutic drug monitoring along with counseling of patient for proper use of medicine must be done.

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Fig 1- Photographs