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VISION

To emerge as one of the premier pharmacy colleges in the country and produce pharmacy professional of global Standards.

MISSION

- To deliver quality academic programs in Pharmacy and empower the students to meet industrial standards.
- To build student community with high ethical standards to undertake R&D in thrust areas of national and international standards.
- To extend viable outreach programs for the health care need of the society.
- To develop industry institute interaction and foster entrepreneurial spirit among the graduates

DOOR SYNDROME- A RARE DISEASE

E Niranjani, Pharm D V yr

Background:

Door syndrome is a rare genetic disorder and it is an acronym for characteristic abnormalities associated with the syndrome stands for deafness due to a defect of the inner ear or auditory nerve (sensorineural hearing loss); onchodystrophy that refers to the various abnormalities in the nail; osteodystrophy stands for the dystrophic growth of the bones; and mild to profound mental retardation. It is a inherited autosomal recessive fashion. Most of people with DOOR syndrome have profound hearing loss caused by changes in the inner ears misshapen or absent of fingernails. Dystrophic growth may consist of an extra small bone in the thumbs and bones in other fingers or toes.

Epidemiology:

DOOR syndrome is a rare disorder ; its prevalence is unknown . Approximately 50 affected individuals have been described in the medical literature. This syndrome mainly appears to affect males and females in equal numbers.

Signs and Symptoms:

DOOR syndrome is a rare genetic disorder characterized by deafness at birth (congenital) due to the inner ear or auditory nerve; (sensorineural hearing loss). The various abnormalities in the finger nails and toes (onchodystrophy), dystrophic growth of the bones (oestodystrophy) of the fingers and toes and mental retardation. This syndrome may be associated with seizure disorder.

The syndrome may consists of the same of the additional features i.e.., polyhydramnios stands for the increased amniotic fluid during pregnancy and increased nuchal fold during pregnancy ; specific facial features such as a large nose, severe and sometimes refractory seizures, abnormalities on the magnetic resonance imaging of the brain, increased 2-oxoglutaric acid in the blood and urine, fingers like thumbs visual impairment and peripheral neuropathy stands for the nerves conducting sensation from the extremities to the brain and insensitivity to pain.

Infants with DOOR syndrome also have typically have characteristics abnormalities f the structure feature and color of the fingernails and toe nails. Such abnormalities may include misshapen, discolor or absent finger nails. Dystrophic bone growth may consists of extra small bone in thumbs and bones in the other fingers and toes.

Causes:

DOOR syndrome is inherited as an autosomal recessive trait. It can be caused by the mutations in the TBC1D24 gene. This gene provides instructions for making a protein whose specific function in the cell is unclear. The protein may have several roles in the cells.

TBC1D24 gene mutations that cause DOOR syndrome are thought to reduce or eliminate the function of the TBC1D24 protein but the specific mechanism by which loss of TBC1D24 function leads to the signs and symptoms of the door syndrome.

Inheritance:

This syndrome is inherited in an autosomal recessive pattern which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the conditions.

Other Variants:

- Autosomal recessive deafness onychodystrophy syndrome.
- Deafness, onychodystrophy – osteodystrophy and mental retardation syndrome.
- Deafness- onychodystrophy- osteodystrophy- intellectual disability syndrome.
- Deafness- onchyoosteodystrophy intellectual disability syndrome.
- Digitorenocerebral syndrome.
- DOOR syndrome.
- DRC syndrome.
- Eronen syndrome.

Diagnosis:

DOOR syndrome may be suspected shortly after birth by the identification of certain characteristic physical features (i.e.., bone, dermatoglyphic and nail abnormalities). A diagnosis of DOOR syndrome may be confirmed based upon a through clinical evaluation, a detailed patient history and specialized testing, such as x-ray studies. X-ray studies may reveal the presence of an extra bone in the thumbs and/ or great toes as well as underdevelopment of bones in other fingers and/ or toes. Per the medical literature, infants with these characteristics abnormalities should be tested for sensorineural deafness.

Deafness may be suspected within the first few months of life and confirmed through a variety of specialized hearing (auditory) tests. Intellectual disability may also be present at birth but may not be detected until an affected infant is old enough to be thoroughly evaluated. In those who also experience seizures, such seizure episodes usually begin during the first year of life. Diagnostic evaluation may include electroencephalography (EEG) and certain advanced imaging techniques, such as computerized tomography(CT) scanning or magnetic resonance imaging (MRI).EEG records the electrical impulses produced by brain activity. During CT scanning, a computer and x-rays are used to create a film showing cross-sectional images of the brain's tissue structure structure.

According to reports in the medical literature, some individuals with DOOR syndrome may also have elevated levels of the organic acid 2-oxoglutarate in the urine and fluid portion of the blood(plasma). The implications of this finding are not fully understood .However, some investigations have suggested that elevated 2-oxoglutarate levels may potentially be associated with more severe symptoms, findings and disease course in some cases.

Recent whole exome sequencing research has identified the gene TBC1D24 as an important cause of the syndrome, although diverse phenotypes have been described. DOORS syndrome and cause diverse phenotypes. In cohort of 36 patients clinically diagnosed with DOOR syndrome, 13 individuals from 10 families had TBC1D24 mutations, while two patients had mutations in another gene known as SMARCB1, known to cause coffin- siris syndrome, which is associated with 2-oxoglutaric aciduria. There are several syndrome in the differential diagnosis of DOOR syndrome.

Standard Therapies:

The treatment of DOOR syndrome is directed toward the specific symptoms that are apparent in each individual. Treatment may require the coordinated efforts of a team of medical professionals, such as pediatricians, surgeons, specialists who assess and treat hearing problems, physicians who diagnose and treat neurological disorders (neurologists), and / or other health care professionals.

Hearing impairment should be assessed and treated as early as possible to help minimize possible speech difficulties or improve communication ability as an affected child ages. In addition, clinical evaluation should be conducted early in development and on a continuing basis to help determine the extent of intellectual disability.

In individuals with seizure episodes, treatment may include various medications that may help to prevent, reduce, or control seizures (anticonvulsants). Prolonged seizures accompanied by unconsciousness (status epilepticus) require immediate medical intervention. Early intervention is also important to ensure that children with DOOR syndrome reach their potential. Special services that may be beneficial include special remedial education, speech pathology, special social support, physical therapy, and other medical, social, and /or vocational services.

Genetic counseling will be of benefit for affected individuals and their families. Other treatment for this disorder is symptomatic and supportive.

PHENYTOIN TOXICITY- A REVIEW

Stephania, Pharm D IV yr

Introduction:

Drug toxicity refers to the level of damage that a compound can cause to an organism. The toxic effects of a drug are the dose - dependent and can affect an entire system as in the CNS or a specific organ like liver. Drug toxicity usually occurs at doses that exceed the therapeutic efficacy of a drug; however, toxic and therapeutic effects can occur simultaneously

Phenytoin:

It is sold under the brand name DILANTIN, it is an anti-seizure medication i.e the drug class is Anticonvulsant .It is useful for the prevention of tonic – clonic seizure (Grand Mal seizures) and focal seizures, but not absence seizures. It can be taken intravenously or by mouth.

Mechanism of Action:

Phenytoin is believed to protect against seizures by causing voltage- dependent block of voltage gated sodium channels. This blocks sustained high frequency repetitive firing of action potentials. This is accomplished by reducing the amplitude of sodium-dependent action potentials through enhancing steady-state inactivation.

What is Phenytoin Toxicity:

Dilantin, or phenytoin, toxicity happens when you have high levels of Dilantin in your body that become harmful. Dilantin is a medicine that is used to prevent and treat seizures. Dilantin toxicity can lead toa coma.

Phenytoin toxicity is rarely fatal, but can cause neurologic symptomsranging from nystagmus to ataxia to coma. Intravenous phenytoin administration may rarely be complicated by the Purple Glove Syndrome.

Cause of Toxicity:

Phenytoin toxicity can occur from an increase in the daily dose of phenytoin, changes in the formulations or brands as well as changes in the frequency of administration. It can also occur when patients are started on new medications that interact with the metabolism or binding capacity of phenytoin to plasma proteins.

Pathophysiology:

The nature of the toxicity depends on fundamental pharmacologic principles: the route of exposure (oral versus parenteral), duration of exposure (acute overdose versus chronic), dosage, and the nature of metabolism (or deficiency thereof). Phenytoin displays its main signs of toxicity on the nervous and cardiovascular systems. Overdose on oral phenytoin causes mainly neurotoxicity and only very rarely causes cardiovascular toxicity. On the other hand, cardiovascular toxicity is the main side effect of parenteral administration.

Symptoms:

- Fast, uncontrollable eye movements or double vision, Dizziness,drowsiness, or confusion
- Lack of coordination of fingers, hands, arms, legs, or body
- Slurred speech
- Nausea or vomiting
- Decreased appetite, decreased activity, abdominal bloating, or irregularjerky movements in children or the elderly

Diagnostic test:

The phenytoin test is used to optimize drug therapy, monitor the amount of phenytoin in the blood, determine whether drug concentrations are in the therapeutic range, and to monitor patient adherence. It may be ordered every few days when a person first begins taking phenytoin to help adjust the dose to the desired bloodlevel. The test is then ordered at regular intervals and as needed to monitor blood concentrations.

The test may also be ordered when a person experiences side effectsor exhibits symptoms that the healthcare practitioner suspects may be due to toxicity. Toxic symptoms can affect the mouth, cardiovascular and nervous systems, and the eyes and include:

- Swelling of the gums and/or lymph nodes
- Excess facial and body hair (hirsutism)
- Insomnia
- Confusion and irritability
- Difficulty swallowing
- Fatigue
- Fever
- Rashes Involuntary eye movement
- Abnormal heartbeat
- Low blood pressure
- Coma

Normal level:

Obtain a serum phenytoin level. The therapeutic range is 10-20mcg/ml.

Treatment / Management:

There is no specific antidote for phenytoin toxicity, and the hallmark of treatment is supportive care. The management of phenytoin toxicity should initially proceed along the lines of accepted treatmentof general overdoses. The airway should be assessed, and advanced airway management initiated in patients that cannot maintain their airway or respiratory drive. The circulation should be assessed and abnormalities in vital signs addressed. Hypotension can be treated with an initial bolus of isotonic solution. If unresponsive to fluid administration, vasopressors can be initiated with norepinephrine or dopamine being preferred.

Other symptoms of overdose can be managed according to standardsof care. Antiemetics can be administered in cases of nausea and vomiting. Seizures can be controlled by following the normal seizure protocols with benzodiazepines as the first like medications followed by phenobarbital or levetiracetam for persistent or recurrent seizures.

ZEGALOGUE (dasiglucagon) INJECTION – A NEWLY APPROVED DRUG FOR SEVERE `` HYPOGLYCEMIA IN PEOPLE WITH DIABETICS'

K.Harini, Pharm-D 3rd Year

BRAND NAME : **ZEGALOGUE.**

GENERIC NAME : **Dasiglucagon.**

MOLECULAR FORMULA : **C_{152} H_{222} N_{38} O_{50}.**

DRUG CLASS : **Glucagon Receptor Agonist.**

MANUFACTURING COMPANY : **Zealand Pharma, Denmark.**

DATE OF APPROVAL : **March 22, 2021**

Dosage Form & Strength: 0.6 mg / 0.6 mL Single dose auto injector.
0.6 mg / 0.6mL Single dose prefilled syringe.

Indication :

Zegalogue is indicated for the treatment of **severe Hypoglycaemia in paediatric & adult patients with diabetes aged, 6yrs & above**.

Mechanism of Action:

Dasiglucagon is a glucagon receptor agonist, which increases blood glucose concentration by activating hepatic glucagon receptors, thereby stimulating glycogen breakdown & release of glucose from the liver. Hepatic stores of glycogen are necessary for dasiglucagon to produce an **Anti-Hypoglycaemic effect.**

Adverse Drug Reaction:

Nausea, Vomiting, Headache, Diarrhoea, Injection site pain in adults & Paediatric and Hypersensitivity reaction.

Drug Interactions:

Patients taking **Beta blockers** may have a transient increase in pulse and **BP** when given Zegalogue. Zegalogue may increase the Anti-coagulant effect of **Warfarin.**

PHARMACOKINETICS:

Absorption:

Zegalogue absorption following SC injection of 0.6 mg resulted in a mean peak plasma concentration of 5110 Pg/mL at around 35 minutes.

Distribution:

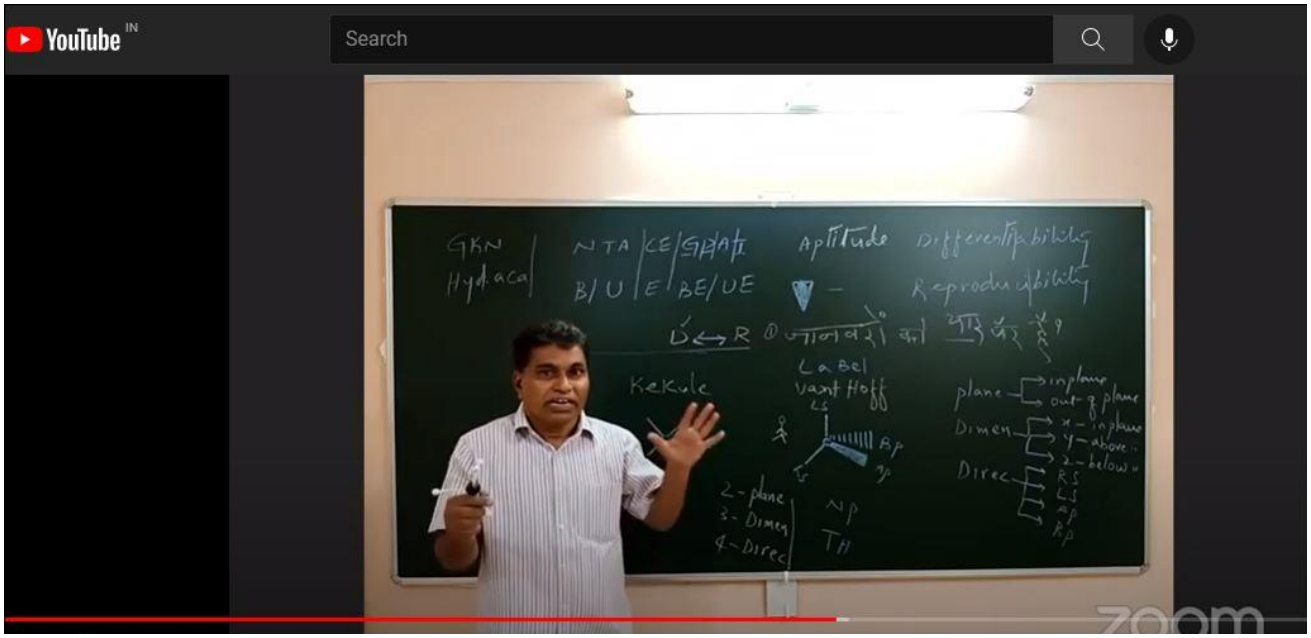
The mean apparent volume of distribution was 45L to 54L Following SC administration .

Metabolism:

Dasiglucagon is cleared like native glucagon through proteolytic degradation pathways in blood , liver & kidney.

Elimination:

The half-life time is approximately 30 minutes.



GPAT Awareness Programme

Awareness Programme on Disha App