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REVIEW ON ANTIDIABETIC DRUGS

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ABSTRACT

Diabetes insipidus is the disorder that causes an imbalance of water in the body. The major complication is the dehydration leads to electrolyte imbalance. Following drugs desmopressin, vasopressin and hydrochlorothazide are prescribed to control the disease. Among them desmopressin is more effective to the patients and show less side effect to patient when it is compared with other drugs.

Diabetes Insipidus: Diabetes insipidus is one of the rare disorders that occur when a person's kidneys are no longer able to control the excretion water.

Etiology

- Antidiuretic hormone (ADH) controls the amount water that is excreted in urine. ADH is also known as vasopressin.
- It is made in the part of the brain known as the hypothalamus. Then it is stored and secreted by the pituitary gland which lies just beneath the base of the brain.
- DI that is occurred by the lack of ADH is known as central diabetes insipidus. When DI occurred by the failure of kidneys to respond towards ADH, this particular condition is known as nephrogenic diabetes insipidus.

Treatment

It is controlled by following drugs

1. Desmopressin
2. Vasopressin
3. Estriol.

Desmopressin: Desmopressin is a synthetic octapeptide, and an analogue of human hormone arginine vasopressin a with Antidiuretic and coagulant acivities.

- Desmospressin binds toV2 receptors in renal collecting duct which leads to excytosis of von Willebrand factor (VWF) and tissue plasminogen activator (t-PA) from Weibel-palade bodies, therby increasing water resorption.
- This agent also increases nitric oxide (NO) production via activation of endothelial NO synthase, thereby induces a afferent arteriolar vasodilation. Furthermore, desmopressin simulates the release of factor VIII from endothelial cells mediated through V1a receptor, thereby promotes blood coagulation.

Dosage Form

Intranasally from 10 to 40 micro gram

Intravenously from 2 to 4 micro gram

For its hemostatic effect, a single infusion of desmopressin at a dosage of 0.3 micro gram per KG.

Drug Ineraction: Although the pressor activity of *DDAVP* is very low compared to its Antidiuretic activity, large doses of *DDAVP tablets* should be used with other pressor agent only with careful patient monitoring. The concomitant administration of drugs that may increase the risk of water intoxication with hypoantremia, (e.g. tricyclic antidepressants, selective serotonin re-update inhibitors, chlorpromazine, opiate analgesics, NSAIDs, lamotrigine and carbamazepine) should be performed with caution.

Side Effects

- Headache, nausea, upset stomach, or flushing of the face may occur. If any of these effects persist or worsen, tell your doctor or pharmacist promptly.
- Many people using this medication do not have serious side effects.
- Desmopressin can rarely cause a low level of sodium in the blood, which can be serious and possibly life-threaning.
- Severe nausea.
- Vomiting.
- Severe headache.
- Muscle weakness etc.

A very serious allergic reaction to this drug is rare.

Vassopressin

Vasopressin has three main effects

• Increasing the water permeability of initial and cortical collecting tubules (ICT & CCT), as well as outer and inner medullary collecting duct (OMCD & IMCD) in the kidney, thus allowing water reabsorption and excretion of more concentrated urine, i.e.,antidiuresis. This occurs through increased transcription and insertion of water channels (Aquaporin-2) into the apical membrane of collecting tubule and collecting duct epithelial cells. [12] Aquaporins allow water to move down their osmotic gradient and out of the nephron, increasing the amount of water re-absorbed from the filtrate (forming urine) back into the bloodstream. This effect is mediated by V2 receptors. Vasopressin also increases the concentration of calcium in the collecting duct cells, by episodic release from intracellular stores. Vasopressin, acting through cAMP, also increases transcription of the aquaporin-2 gene, thus increasing the total number of aquaporin-2 molecules in collecting duct cells.

• Increasing permeability of the inner medullary portion of the collecting duct to urea by regulating the cell surface expression of urea transporters,[13] which facilitates its reabsorption into the medullary interstitium as it travels down the concentration gradient created by removing water from the connecting tubule, cortical collecting duct, and outer medullary collecting duct.

Acute increase of sodium absorption across the ascending loop of henle. This adds to the countercurrent multiplication which aids in proper water reabsorption later in the distal tubule and collecting duct.

Dosage

5 to 10 units (0.25 to 0.5 mL) IM or subcutaneously repeated 2 or 3 times a day as needed.

Interaction

1) The following drugs may potentiate the antidiuretic effect of vasopressin when used concurrently: carbamazepine; chlorpropamide; clofibrate; urea fludrocortisone; tricyclic antidepressants.

2) The following drugs may decrease the antidiuretic effect of vasopressin when used concurrently: demeclocycline; norepinephrine; lithium heparin alcohol. 3) Ganglionic blocking agents may produce a marked increase in sensitivity to the pressor effects of vasopressin.

Side Effect

- chest pain or tight feeling.
- severe or pounding headache, severe drowsiness, feeling very weak.
- slow heart rate, weak pulse, fainting, slow breathing.
- loss of color in your lips or around your mouth.
- numbness or tingling in your hands or feet; or.
- pain or loss of feeling anywhere in your body.

Hydrochlorothiazide

Hydrochlorothiazide may also be used to treat patients with diabetes insipidus and to prevent kidney stones in patients with high levels of calcium in their blood. Hydrochlorothiazide belongs to thiazide class of diuretics. It reduces blood volume by acting on the kidneys to reduce sodium (Na^+) reabsorption in the distal convoluted tubule. The major site of action in the nephron appears on an electroneutral NaCl co-transporter by competing for the chloride site on the transporter. By impairing Na^+ transport in the distal convoluted tubule, hydrochlorothiazide induces a natriuresis and concomitant water loss. Thiazides increase the reabsorption of calcium in this segment in a manner unrelated to sodium transport.[14] Additionally, by other mechanisms, HCTZ is believed to lower peripheral vascular resistance.

Usual adult dose of hydrochlorothiazide for diabetes insipidus

Initial: 50 mg orally once daily.

Maintenance dose: May increase to 100 mg orally daily.

Drug Interaction: Thiazide diuretics given concurrently with antidiabetic drugs [such as oral agents and insulin Apidra, Exubera,Humulin 70-30, Humalog Mix 50-50, Humalog 75-25, Humulin R, Humulin N, Humulin 50-50, Velosulin, Humalog,Lantus, Levemir, Novolog, Novolog Mix 50/50, Novolog Mix 70/30)] causes a decreased blood level of antidiabetic drugs, hence doses of antidiabetic drugs may need to be increased Diuretics are often prescribed with other medications for high blood pressure and heart disease. This may increase the effects of these medications, potentially causing electrolyte abnormalities (such as reduced levels of potassium).

Side Effect

- weakness

- low blood pressure
- light sensitivity
- blurred vision
- impotence
- nausea
- abdominal or stomach pain
- constipation
- electrolyte disturbances
- pancreatitis
- yellow skin or eyes (jaundice)
- severe allergic reaction (anaphylaxis)

DISCUSSION

Diabetes insipidus is disease whre kidney fail to control the excretion of water. It has more specific antiuresis with less adverse reaction.its selective antidiurtic activity is used with advantage In the treatment of nocturnal enuresis and as diagnostic test of tubular function. Dosage -10-40 microgram (intranasally) 2-4 microgram (intravenously).

Vasopressin is the most frequently utilized treatment of diabetes insipidus, the occurenc of occasionally allergic, irritative, or vasoconstrictive reaction.

Thiazide , antidiurtic effect appear to be the result of mild sodium depletion with an increase in proximal salt and water reabsorption and consequently decrease I the delivery of fluid to diluting segment of nephron.

CONCLUSION

The drugs such as vasopressin and thiazide have some serious side effect when it is administrated for longer period of time. Hence, DESMOPRESSIN is the drug which had less side effect.

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