Newer Drugs

Dr. Sangeetha Gopinath
Associate Professor, Pharmacology
SUT Academy of Medical Sciences, Thiruvananthapuram

IMEGLIMIN

Imeglimin is a novel tetrahydrotriazine compound first introduced in Japan as an oral agent for the treatment of Type II Diabetes Mellitus

Mechanism of Action

Imeglimin Novel oral antidiabetic drug with dual mechanism of action. The two mechanisms of action are:

(a) It amplifies glucose-stimulated insulin secretion (GSIS) and preserves β-cell mass, and

(b) It enhances insulin action, including the potential for inhibiting hepatic glucose output and improving insulin signalling in both the liver and skeletal muscle

At a cellular and molecular level correction of mitochondrial dysfunction is suggested. Mitochondrial dysfunction is a prominent feature of Type II Diabetes Mellitus pathology that contributes to both β-cell defects and insulin resistance).

Use

Imeglimin is used as an oral anti diabetic drug for the treatment of Type II Diabetes Mellitus

Adverse Reactions

Imeglimin is a relatively safer drug well tolerated by most of the patients. It has only a low risk of developing hypoglycaemia. The common side effects noticed are:

- Nausea
- Abdominal pain
- Vomiting.

DOSE

The usual adult dose of Imeglimin is 1 – 2 g per day, orally, in two divided doses

Conclusion

The unique mechanism of action of Imeglimin is expected to provide it a new niche in the treatment of type II diabetes mellitus. Well tolerated by most of the patients including elderly with low risk of developing hypoglycaemia, this agent may evolve as an effective treatment option for controlling Type II Diabetes Melllitus

POLMACOXIB

Polmacoxib is a novel NSAID that was introduced in South Korea for the treatment of Osteoarthritis

Mechanism of Action

Polmacoxib has a dual mechanism of action: it inhibits COX-2 and carbonic anhydrase.

Inhibition of COX-2 in endothelial or vascular smooth muscle cells is believed to contribute to cardiovascular risks due to the reduction in the production of PG I2, leading to an increased tendency for thrombosis

and hypertension.

Polmacoxib's greater affinity for carbonic anhydrase compared to the COX-2 enzyme is thought to potentially reduce the risk of NSAID-induced hypertension and associated cardiovascular issues. This is because carbonic anhydrase levels are high in these sites, causing Polmacoxib to bind more strongly to carbonic anhydrase and less to COX-2. Given that carbonic anhydrase is abundant in the cardiovascular system, there is a theoretical possibility that Polmacoxib's dual action mechanism may mitigate the adverse cardiovascular effects of COX-2 inhibition, although conclusive clinical evidence is currently lacking.

Use

Polmacoxib can be used for the treatment of idiopathic osteoarthritis of the hip and knee.

Adverse Reactions

- GI: Nausea, abdominal pain, and vomiting are the most common side effects.
- **Due to water retention:** Generalized edema, peripheral edema
- Headache, somnolence, and depression.
- It is postulated to have attenuated cardiovascular risk compared to selective COX2-inhibiting NSAIDs

DOSE

The usual adult dose of Polmacoxib is 2 mg per day orally to be administered after meals

Conclusion

Pulmacoxib demonstrates a greater affinity for carbonic anhydrase (CA) than for COX2. Consequently, in tissues with a high concentration of COX-2, such as the GI tract, blood, and kidney, its binding to COX2 is less pronounced. This postulates a significant reduction in the gastrointestinal (GI) and cardiovascular (CVS) side effects of Pulmacoxib when compared to other COX2 inhibitors. Furthermore, Pulmacoxib is well-tolerated and clinically effective in the treatment of osteoarthritis pain.

ESAXERENONE

Esaxerenone is a novel nonsteroidal MR blocker (MRB) introduced in Japan for the treatment of hypertension.

Mechanism of Action

Esaxerenone is a non-steroidal, selective mineralocorticoid receptor antagonist. Studies have shown that esaxerenone elicits renoprotection independent of its antihypertensive effect.

In contrast, spironolactone, which has a steroidal structure, acts as an inhibitor at the testosterone receptor and an agonist at the progesterone receptor (PR). Consequently, its use can be associated with sex-steroid-related adverse effects, including gynecomastia, loss of libido, menstrual irregularities, and the aggravation of breast fibrocystic changes

Use

Esaxerenone can be used for the treatment of Hypertension and for the treatment of chronic kidney disease (CKD)in individuals with type 2 diabetes (T2D).

Adverse Reactions

- Dizziness • Hyperkalemia
- Hyperuricemia

Dose

The usual adult dose of Esaxerenone is 2.5 -5 mg per day orally

Conclusion

Esaxerenone is a more selective, efficient, and potent mineralocorticoid receptor antagonist (MRA) compared to spironolactone and eplerenone. Experimental studies have shown that both spironolactone and eplerenone exhibit a greater affinity for the kidneys than the heart (kidneys > heart), whereas esaxerenone displays a balanced distribution between cardiac and kidney tissues (kidneys = heart). This balanced distribution likely explains its more efficient reduction in cardiac hypertrophy, pro-B-type natriuretic peptide (pro-BNP) levels, and proteinuria compared to eplerenone and spironolactone. To date, there is no evidence suggesting that esaxerenone is associated with a lower risk of incident hyperkalemia compared to spironolactone or eplerenone. Esaxerenone has demonstrated efficacy as an antihypertensive drug and is associated with fewer side effects related to sex hormones than spironolactone.