



BC Division of Blue Cross Laboratories Pvt Ltd.

K-PIO (PIOGLITAZONE) AND DEMENTIA

Dementia is a syndrome characterized by a deterioration in the cognitive function beyond what is expected from the usual consequence of biological ageing.

It is characterized by progressive deterioration of memory and can result from either a vascular etiology or a neurodegenerative disease known as Alzheimer's disease.

Type 2 diabetes and related features such as insulin resistance represent an important risk group for cognitive impairment. In addition to the risk that type 2 diabetes presents in the development and progression of dementia, long-term use of certain classes of oral antidiabetic drugs too have been implicated in the same.

However, a certain class of oral antidiabetic drugs like thiazolidinediones (glitazones) like pioglitazone have shown to be protective in the development and progression of dementia through its unique action of PPAR- γ (Peroxisome proliferator-activated receptor gamma) agonism.

PATHOPHYSIOLOGY OF DEMENTIA

ALZHEIMER'S DISEASE DEMENTIA

The two hallmark pathologies implicated in the development and progression of Alzheimer's disease are:

Plaque deposits of β -amyloid peptide: In a healthy brain, these protein fragments are broken down and eliminated. However, when the plaques are formed, these are hard and clump together between the neurons and disrupt the cell function leading to development and progression of Alzheimer's disease.

Increased phosphorylation of Tau proteins: Increased phosphorylation of a specific protein called as the Tau protein, causes the abnormal accumulation of the same inside the microtubules of the neurons which help in transport of nutrients and molecules from the cell body to the axon and dendrites.

The abnormal phosphorylation of the Tau protein causes it to detach from the microtubules and stick to other Tau molecules forming threads called the neurofibrillary tangles which block the neurons transport system and harms the synaptic communication between the neurons.

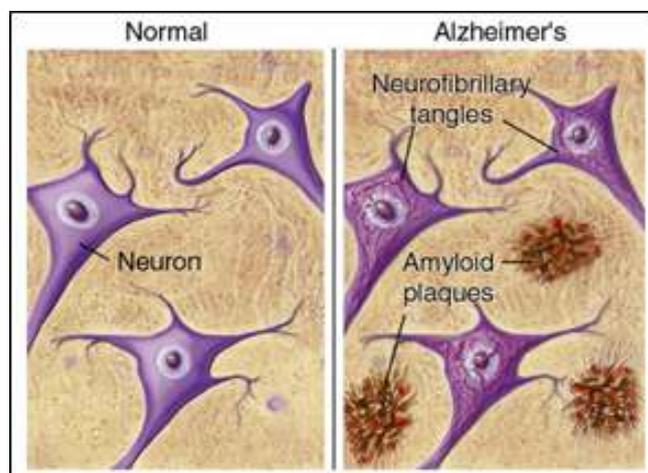
Other pathologies are also implicated in the development of Alzheimer's disease dementia.

Chronic inflammation: It has been suggested that chronic inflammation is caused by the build-up of glial cells that are normally meant to keep the brain free of debris.

The microglial cells and astrocytes engulf and destroys waste and toxins in the healthy brain and the malfunctioning of the same results in its collection around the neurons but a failure to perform its debris clearing function resulting in a release of chemicals causing chronic inflammation & damage to the neurons.

VASCULAR BRAIN INJURY DEMENTIA

Vascular dementia develops after a stroke which blocks the artery in the brain or from other conditions that damage the blood vessels and reduce circulation, depriving the brain of oxygen and nutrients.



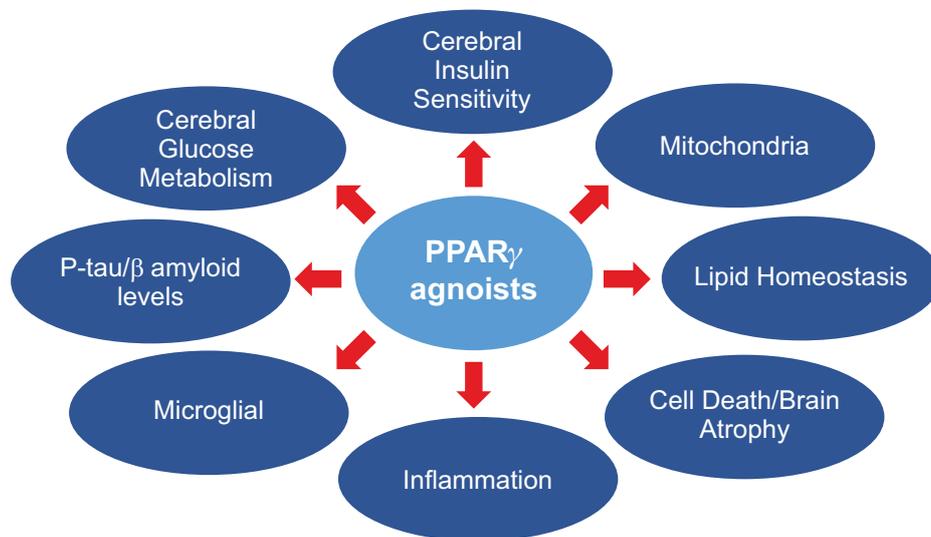
K-PIO[®]

Pioglitazone 15 mg. / 30 mg. Tablets

NEUROPROTECTIVE EFFECT OF PPAR- γ AGONISM

PPAR- γ is the dominant isoform in the microglia in the CNS and is expressed in low levels in the brain under physiological conditions playing a beneficial role in lipid metabolism, neural cell differentiation and death, inflammation and neurodegeneration. Apart from the function of PPAR- γ stimulation in improving glucose tolerance and insulin sensitivity in type 2 diabetes, the activation of PPAR- γ receptors through the action of PPAR- γ agonists is known to have a positive influence in the pathology of dementia.

- In case of Alzheimer’s disease dementia, it represses the secretion of proinflammatory molecules, enhances mitochondrial function and increases the processing of β -amyloid peptide and reducing Tau protein levels.
- In case of vascular brain injury dementia, the activation of PPAR- γ receptors exhibits antioxidant, anti-inflammatory, anti-acetylcholinesterase and neuroprotective actions.



PROTECTIVE EFFECT OF PIOGLITAZONE IN DEMENTIA

Pioglitazone, which is a member of the thiazolidinedione class of drugs, is a potent and highly selective PPAR- γ agonist which has made it a potential therapeutic intervention in neurodegenerative disorders.

Pioglitazone is shown to improve many pathophysiological determinants involved in dementia.

- Pioglitazone regulates the production of β -amyloid peptides and its activation of PPAR- γ significantly reduces the β -amyloid plaques.
- Pioglitazone also inhibits the phosphorylation of Tau proteins and preserves the synapses.
- It blocks the synthesis of proinflammatory molecules like IL-1, IL-6, TNF α , etc.
- Apart from these effects, pioglitazone improves cerebral blood flow and enhances cerebral glucose uptake and disposal and reduces cerebral insulin resistance.
- PPAR- γ agonists like pioglitazone also ameliorate mitochondrial dysfunction by inhibiting β -amyloid peptide production, limit oxidative damage by inhibiting ROS generation and exert a positive effect on neuronal energy balance.

To conclude, Pioglitazone represents “polypharmacy in a pill” and improves multiple etiopathology determinants of dementia including inflammation, oxidative stress, microglial defects, development of amyloid plaques and neurofibrillary tangles, impaired cerebral glucose consumption and mitochondrial dysfunction.

Several longitudinal cohort studies have shown that pioglitazone reduces the risk and delays the onset of dementia in type 2 diabetes and its effect was time and dose dependent. These results are consistent with small scale, pilot studies in T2DM cases that showed pioglitazone increased cerebral blood flow as well as delayed the onset of dementia.

These findings make pioglitazone a promising therapeutic intervention and a preferred oral antidiabetic agent in preventing the development and slowing the progression of dementia in type 2 diabetes.

Source: Sagheddu C et al. Pharmaceuticals 2021; 14(10): 1025; Heneka MT et al. Curr Neuropharmacol 2011; 9(4): 643-650; Saunders AM et al. Front Neurosci 2021; 15: 666958.

BLUVIT-D3 DROPS (VITAMIN D) SUPPLEMENTATION IN CHILDREN WITH ASTHMA

Asthma is a chronic inflammatory condition & is a highly complex, immune mediated inflammatory disease. It is a leading cause of chronic illness in children with approximately 8% of the children affected in India in the year 2022.

Recent studies have reported an association between vitamin D deficiency and an increased risk of asthma occurrence and exacerbations with studies capturing lower levels of vitamin D with an increased asthma markers like IgE & eosinophils.

VITAMIN D SUPPLEMENTATION IN CHILDREN WITH ASTHMA

It is believed that vitamin D deficiency may cause lung compliance to be insufficient and cause immune function disorders.

Meta-analyses of multiple studies have reinforced these hypotheses as the findings that children with asthma have a lower vitamin D status as compared to healthy children. The findings have also shown that asthmatic children treated with vitamin D supplements reduced the asthma recurrence rate & had a positive co-relation with the clinical control of asthma and lung function.

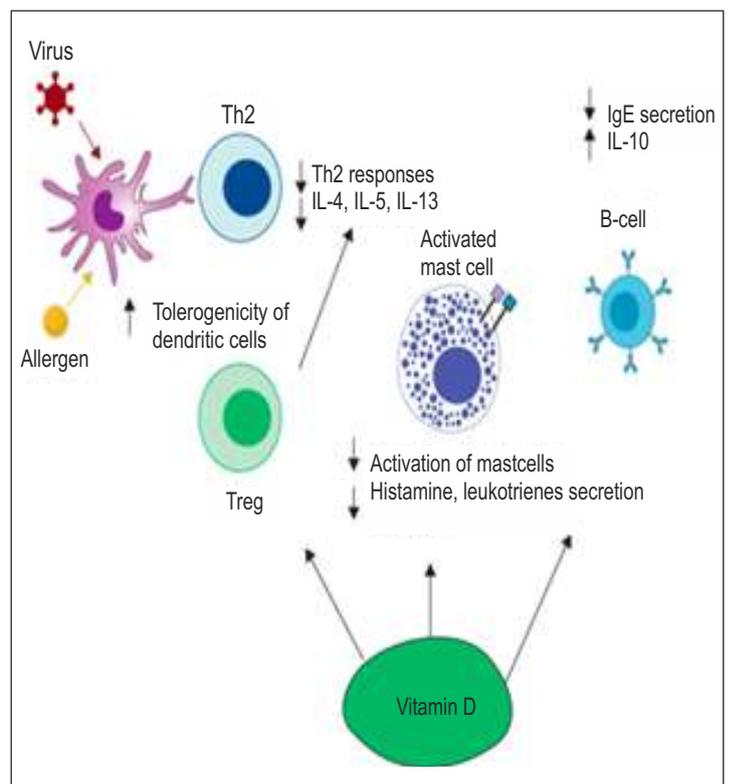
Vitamin D3 is a highly metabolically active product with hormone-like characteristics that can increase the anti-inflammatory effect of glucocorticoids & help relieve asthma.

Childhood asthma is a complex, multifactorial chronic disease caused by environmental and genetic factors. It has the clinical characteristics of infiltration of mast cells and eosinophils regulated by Th2 cells, resulting in high airway response, inflammation, and airway obstruction.

Th2 cell immune response produces IL-4, IL-5, IL-9, and IL-13, which may be related to the increase of IgE and eosinophils induced asthma.

Studies have shown that vitamin D metabolites are an important hormone for regulating immunity, which can suppress allergic respiratory diseases mediated by Th2.

Moreover, the immunomodulatory function of vitamin D exists in other immune cells such as macrophages and dendritic cells and plays an important role in regulating innate immune function and adaptive immune function.



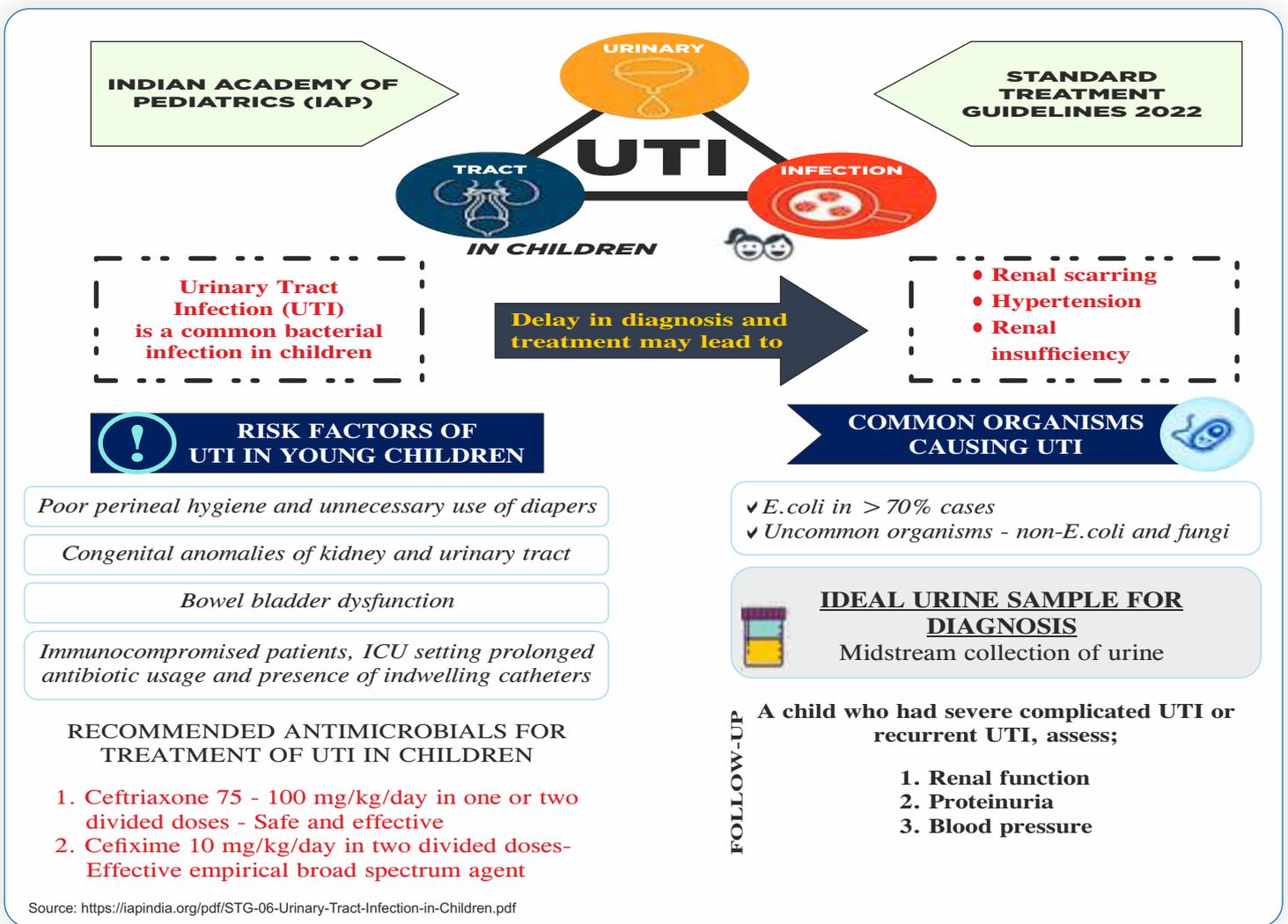
In conclusion, children with lower vitamin D status could be more at risk of developing asthma as well as increased recurrence and exacerbations of asthmatic symptoms.

Vitamin D supplementation can hence be a promising adjuvant therapeutic option in the management of asthma in children.

Source: Wang Q et al. J of Pediatric Nursing 2022; 62: E60-E68; Daniel R et al. Lung India 2022; 39(4): 357; Barragan M et al. Nutrients 2015; 7(9): 8127-8151.

URINARY TRACT INFECTION IN CHILDREN: INDIAN ACADEMY OF PEDIATRIC GUIDELINES

The Indian Academy of Pediatrics (IAP) has released Standard Treatment Guidelines 2022 for Urinary tract infection (UTI) in children. The below represents major recommendations of the guidelines;



In Urinary Tract Infections

Extacef[®]
Cefixime 50 mg. / ml.
DROPS

Extacef-P[®]
Cefixime 50 mg. / 5 ml.
DRY SYRUP

Extacef-DS[®]
Cefixime 100 mg. / 5 ml.
DRY SYRUP

Also available
Extacef[®]
Cefixime
200 mg. DT* 100 mg. DT*
***Dispersible Tablets**