Uric acid

- Machine learning-based prediction of diabetic peripheral neuropathy: model development and clinical validation
- Serum uric acid is associated with shunt dependent hydrocephalus of aneurysmal subarachnoid hemorrhage patients
- Metabolomics: a new frontier in neurodegenerative disease biomarker discovery
- The serum γ-Glutamyltransferase Level is Associated with the Development of Hypertension in Alcohol Infrequent Drinkers but not in Frequent Drinkers
- Uric Acid Stroke Cerebroprotection Transcended Sex, Age, and Comorbidities in a Multicenter Preclinical Trial
- Association between uric acid/high-density lipoprotein cholesterol ratio and testosterone deficiency in adult American men: findings from the national health and nutrition examination survey 2011-2016
- Serum metabolomic profiling uncovered metabolic shifts in individuals upon moderate-altitude exposure and identified the potentiality of beta-alanine to ameliorate hyperuricemia
- Neuroprotective strategies in acute ischemic stroke: A narrative review of recent advances and clinical outcomes

Abstract

Uric acid, a compound generated during the metabolic breakdown of purines, plays a pivotal role in various physiological processes within the human body. It is not only a normal component of urine but also a crucial antioxidant that safeguards cells against oxidative stress. Uric acid's intricate relationship with human health extends beyond its role in metabolism, as its levels in the bloodstream can significantly impact well-being. This introduction sets the stage for an exploration of uric acid, delving into its formation, functions, health implications, and its emerging relevance in contemporary medical research. From its association with conditions like gout and cardiovascular health to its potential neuroprotective properties, uric acid's multifaceted nature underscores its significance in both metabolic pathways and clinical contexts.

Introduction

Uric acid is a product of the metabolic breakdown of purine nucleotides, and it is a normal component of urine.

Uric acid is primarily excreted by the kidneys in the form of urine. It plays an essential role in the body's metabolism.

Key points

Formation: Uric acid is formed when the body breaks down purines, which are found in foods like organ meats, certain seafood (e.g., anchovies and sardines), beer, and high-fructose corn syrup.

Function: Uric acid is an antioxidant, and it helps protect the body's cells from damage caused by

oxidative stress. It also has a role in certain enzymatic reactions.

Blood levels: Uric acid levels in the blood can vary, and elevated levels can lead to health issues, including gout and kidney stones. Normal uric acid levels in the blood typically range between 3.5 and 7.2 mg/dL (milligrams per deciliter).

Health conditions: High levels of uric acid (hyperuricemia) can lead to gout, a painful form of arthritis, as well as kidney stones. It is also associated with certain medical conditions like metabolic syndrome and kidney disease.

Diet: Diet plays a crucial role in managing uric acid levels. Reducing the consumption of foods high in purines, alcohol, and fructose can help lower uric acid levels in the blood.

Medication: In cases where diet and lifestyle changes are not sufficient to control uric acid levels, medications may be prescribed. These drugs, such as allopurinol, can help lower uric acid production or increase its excretion.

Uric acid (URIC), a water-soluble antioxidant discovered in human body, has been recognized in numerous recent studies to exert a crucial part in neuroprotection.

Reviews

Uric acid (UA) is a strong endogenous antioxidant that neutralizes the toxicity of peroxynitrite and other reactive species on the neurovascular unit generated during and after acute brain ischemia. The realization that a rapid reduction of UA levels during an acute ischemic stroke was associated with a worse stroke outcome paved the way to investigate the value of exogenous UA supplementation to counteract the progression of redox-mediated ischemic brain damage. The long translational journey for UA supplementation recently reached a critical milestone when the results of the multicenter NIH stroke preclinical assessment network (SPAN) were reported. In a novel pre-clinical paradigm, six treatment candidates including UA supplementation were selected and tested in six independent laboratories following predefined criteria and strict methodological rigor. UA supplementation was the only intervention in SPAN that exceeded the pre-specified efficacy boundary with males and females, young mice, young rats, aging mice, obese mice, and spontaneously hypertensive rats. This unprecedented achievement will allow UA to undergo clinical testing in a pivotal clinical trial through a NIH Strokenet Thrombectomy Endovascular Platform (STEP) created to assess new treatment strategies in patients treated with mechanical thrombectomy. UA is a particularly appealing adjuvant intervention for mechanical thrombectomy, as it targets the microcirculatory hypoperfusion and oxidative stress that limits the efficacy of this therapy. This descriptive review aims to summarize the translational development of UA supplementation, highlighting those aspects that likely contributed to its success. It includes having a well-defined target and mechanism of action, and an approach that simultaneously integrated rigorous pre-clinical assessment, with epidemiological and preliminary human intervention studies. Validation of the clinical value of UA supplementation in a pivotal trial would confirm the translational value of the SPAN paradigm in pre-clinical research [1)].

This review provides a compelling case for the therapeutic potential of uric acid supplementation in the context of ischemic brain damage. It outlines the promising journey of uric acid from its

antioxidant properties to successful pre-clinical testing, emphasizing the importance of rigorous research and a well-defined translational approach. The potential application of uric acid supplementation as an adjuvant intervention for mechanical thrombectomy highlights its relevance in improving ischemic stroke treatment outcomes. However, the ultimate validation of uric acid's clinical value will depend on pivotal trials, which will confirm the significance of this translational research in practical medical settings.

The depletion of adenosine-derivatives within the purine cycle is expected to result in a compensatory increase in oxopurines (uric acid precursors) and secondarily increased uric acid, observed in both bipolar mania and epilepsy. Cortisol-based inhibition of purine conversion to adenosine-derivatives may be reflected in observed uric acid increases and the well-established contribution of cortisol to both bipolar mania and epilepsy pathology. Cortisol-inhibited conversion from IMP to AMP as precursor of both ATP and adenosine may represent a mechanism for treatment resistance common in both bipolar mania and epilepsy. Anti-cortisol therapies may therefore augment other treatments both in bipolar mania and epilepsy. Evidence linking (i) adenosine deficit with a decreased need for sleep, (ii) IMP/cGMP excess with compulsive hypersexuality, and (iii) guanosine excess with grandiose delusions may converge to suggest a novel theory of bipolar mania as a condition characterized by disrupted purine metabolism. The potential for disease-modification and prevention related to adenosine-mediated epigenetic changes in epilepsy may be mirrored in mania. Evaluating the purinergic effects of existing agents and validating purine dysregulation may improve diagnosis and treatment in bipolar mania and epilepsy and provide specific targets for drug development [2)].

It is crucial to recognize that this hypothesis remains largely theoretical and requires substantial empirical validation. The complexity of these psychiatric conditions suggests that multiple factors are likely at play, and purine metabolism is just one facet of a much larger picture. While the proposed connections are intriguing, they should be considered within the broader context of ongoing research into the causes and treatments of bipolar mania and epilepsy.

Febuxostat and allopurinol are the most commonly used uric acid-lowering medications, and their safety is of great concern, especially the cardiovascular adverse reactions associated with febuxostat. We propose to study the cardiovascular toxicity of febuxostat and allopurinol using the FDA Adverse Event Reporting System (FAERS) database.

Methods: A total of 64 quarters of FAERS data were downloaded from 2004 to 2019. Febuxostat- and allopurinol-related cardiovascular adverse events were extracted after data cleaning. Signal detection was conducted by reporting odds ratio (ROR) and proportional reporting ratio (PRR).

Results: There were 2939 and 25,219 reports of febuxostat- and allopurinol-related cardiovascular adverse events (CVAEs), respectively. The most frequent CVAEs with febuxostat and allopurinol were edema peripheral (14.38%) and peripheral swelling (8.76%), respectively. In elderly gout patients, febuxostat is associated with an increased risk of heart failure, ischemic heart disease, hypertension, and cardiomyopathy. Febuxostat in combination with acetic acid derivatives nonsteroidal anti-inflammatory drug (NSAIDS) also increases the risk of cardiovascular adverse events.

Compared with allopurinol, febuxostat may increase cardiovascular toxicity in patients with gout [3)].

The review contributes to the understanding of the cardiovascular safety of uric acid-lowering medications. It highlights the potential risks associated with febuxostat, especially in certain patient populations. However, it is crucial to recognize the limitations of the FAERS database, the need for further research to confirm these findings, and the importance of individualized risk-benefit assessments when prescribing these medications for gout management.

It has been shown that low levels of uric acid may be a risk factor for the development of Parkinson's disease. We aimed to investigate the relationship between uric acid and improvement of motor symptoms in patients with Parkinson's disease after subthalamic nucleus deep brain stimulation.

Methods: We analyzed the correlation between serum uric acid levels in 64 patients with Parkinson's disease and the rate of improvement of motor symptoms 2 years after subthalamic nucleus deep brain stimulation.

Results: A non-linear correlation was observed between uric acid levels and the rate of motor symptom improvement after subthalamic nucleus deep brain stimulation, during both the drug-off and drug-on periods.

Conclusions: Uric acid is positively associated with the rate of motor symptom improvement in subthalamic nucleus deep brain stimulation within a certain range [4].

Complications

High blood concentrations of uric acid can lead to gout and are associated with other medical conditions, including diabetes and the formation of ammonium acid urate kidney stones.

Hyperuricemia in adolescence was not only associated with the overweight or obesity in BMI, but with the combination of overweight or obesity in BMI and central obesity in WHtR. However, in boys and girls, the increased risk of hyperuricemia associated with elevated body mass index was significantly better than that of waist height ratio [5]

Uric acid in trigeminal neuralgia

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