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The impact of uric acid level on the daily functioning of elderly people

Wpływ stężenia kwasu moczowego na codzienne funkcjonowanie osób w wieku podeszłym

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Abstract

Introduction. *High levels of uric acid can lead to oxidative stress, a process that damages cells, proteins, and DNA. This in turn triggers inflammation, which is the basis of many chronic diseases. Taking into account the above information, it is justified to attempt to determine the influence of uric acid on the resulting functional disorders.* **Material and methods.** *A literature review was conducted using online databases. The literature was searched for the review based on key words.* **Results.** *The results of studies on the effect of hyperuricemia on cognitive functions remain contradictory. Caution should be exercised when lowering uric acid levels in the case of hyperuricemia, because rapid attempts to lower it may cause a decrease in the level of independence or an increase in the risk of developing depression in old age. The diet itself has not been shown to be of particular importance in lowering uric acid levels.* **Conclusions.** *The main direction of further research should be the effect of uric acid levels on cognitive functioning, because the results of studies obtained so far are often contradictory. Studies in this area should take into account numerous variables that may distort the results of studies occurring in people of advanced age. (Gerontol Pol 2025; 33; 3-9) doi: 10.53139/GP.20253305*

Keywords: *old age, uric acid, cognitive functions, independence, nutritional status, depression*

Streszczenie

Wstęp. *Wysokie stężenie kwasu moczowego może prowadzić do stresu oksydacyjnego, procesu, który uszkadza komórki, białka i DNA. To z kolei wyzwala stan zapalny, który jest podstawą wielu chorób przewlekłych. Biorąc pod uwagę powyższe informacje, uzasadnione jest podjęcie próby określenia wpływu kwasu moczowego na powstałe w wyniku tych procesów zaburzenia czynnościowe.* **Materiał i metody.** *Dokonano przeglądu literatury korzystając z internetowych baz danych. Literaturę wyszukiwano do przeglądu na podstawie słów kluczowych.* **Wyniki.** *Wyniki badań na temat wpływu hiperurykemii na funkcje poznawcze pozostają sprzeczne. Należy z ostrożnością obniżać stężenie kwasu moczowego w przypadku stwierdzenia hiperurykemii, ponieważ gwałtowne próby jego obniżenia może wywoływać obniżenie poziomu samodzielności czy zwiększenie ryzyka rozwoju depresji wieku podeszłego. Nie wykazano, aby sama stosowana dieta miała szczególne znaczenie w obniżaniu stężenia kwasu moczowego.* **Wnioski.** *Głównym kierunkiem dalszych badań powinien być wpływ stężenia kwasu moczowego na funkcjonowanie poznawcze, ponieważ dotychczas otrzymywane wyniki badań często są ze sobą sprzeczne. Badania w tym zakresie powinny uwzględniać liczne zmienne mogące zaburzać wyniki badań, występujące u osób w wieku zaawansowanym. (Gerontol Pol 2025; 33; 3-9) doi: 10.53139/GP.20253305*

Słowa kluczowe: *wiek podeszły, kwas moczowy, funkcje poznawcze, samodzielność, stan odżywienia, depresja*

Introduction

Uric acid is the end product of purine metabolism, chemical compounds that occur naturally in living organisms, both in food and in body cells, where they play a key role in biochemical processes such as DNA and RNA synthesis. Their breakdown produces uric acid, which is normally excreted from the body mainly through the kidneys. Uric acid can be present in the body in a dissolved form (in the blood) or in the form of crystals that can be deposited in various tissues, especially in the joints. This phenomenon leads to the development of

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gout, a disease characterized by inflammation of the joints. In a healthy body, the concentration of uric acid in the blood remains at a level of 3.5-7.2 mg/dl. When its level exceeds 7.2 mg/dl, hyperuricemia occurs [1].

Hyperuricemia can result from two main mechanisms: overproduction of uric acid or impaired renal excretion. In many cases, both factors coexist. There are many reasons why uric acid levels can increase, such as excessive production of purines, eating large amounts of purine-rich foods (red meat, offal, seafood, alcohol), or certain genetic diseases (e.g. Lesch-Nyhan syndrome). In the case of kidney diseases (such as chronic renal failure), uric acid may be less excreted from the body, which leads to its accumulation in the blood [2].

Uric acid, although it plays an antioxidant role in the body, becomes harmful in excess and leads to many negative health effects, especially in the context of metabolism. Its effect on metabolism is multifaceted.

High levels of uric acid can lead to oxidative stress, a process that produces reactive oxygen species (ROS) that can damage cells, proteins, and DNA. This in turn triggers inflammation, which is the basis of many chronic diseases, including atherosclerosis, heart disease, diabetes, and neurodegenerative diseases such as Alzheimer's disease. Oxidative stress contributes to damage to the walls of blood vessels, which leads to the development of hypertension and heart disease. As a result, the risk of developing a heart attack and stroke increases [3].

Studies show that people with elevated levels of uric acid in their blood are more likely to suffer from insulin resistance. Chronic hyperuricemia can also lead to damage to the beta cells of the pancreas, which produce insulin, which impairs the body's ability to regulate glucose levels [4].

Uric acid also influences the development of obesity and lipid disorders. Excess uric acid affects lipid metabolism, causing increased triglyceride levels and decreased HDL cholesterol levels [5].

Taking into account the above information, it is justified to attempt to determine the influence of uric acid, both in the form of deficiency and excess, not only on the development of metabolic diseases but also on the resulting functional disorders.

Material and methods

A literature review from 2007 to 2025 was conducted using the following online databases: PubMed, Google Scholar, Index Copernicus, MedlinePlus, and Mendeley. The literature was searched for review based on the following keywords: old age, uric acid, cognitive functions, independence, nutritional status, depression.

Results

Uric acid and cognitive functions in the elderly

The effect of uric acid on cognitive functions is ambiguous despite many studies and meta-analyses.

Long-term hyperuricemia causes oxidative stress and subsequent structural and functional damage to neurons and cerebral vessels, increasing the risk of cerebral ischemia. In the context of Alzheimer's disease, it damages the endothelium of cerebral vessels and impairs clearance of amyloid beta across the blood-brain barrier. In addition, hyperuricemia inhibits AMP-activated protein kinase, which promotes inflammation and atherosclerosis, which is associated with vascular dementia and other neurodegenerative diseases [6].

Euser et al. showed that elevated serum uric acid levels improve cognitive functions and reduce the risk of dementia independently of cardiovascular risk [7], while in the study by Verhaaren et al. hyperuricemia was associated with white matter atrophy and thus poorer cognitive performance [8].

Uric acid may have dual properties, both potentially harmful in the context of vascular diseases such as stroke or cerebrovascular disease, and antioxidant effects, protecting neurons from damage and reducing the risk of neurodegenerative diseases in other situations [9]. Studies show a neuroprotective effect of uric acid in both Alzheimer's disease and Parkinson's disease. The effect of hyperuricemia in patients with vascular dementia is ambiguous. Some studies suggest that high concentrations of uric acid may negatively affect the course of the disease in vascular dementia [10], while others show the opposite effect, which is why it has been suspected that depending on its concentration and the origin of dementia, it may affect cognitive functions in different ways [11].

The meta-analysis by Alrouji et al. showed that patients with neurodegenerative diseases had lower serum uric acid levels, while also drawing attention to studies showing its adverse effects, including impairing cognitive functions, worsening memory, and causing white matter atrophy [12]. In a study of 4618 participants, higher uric acid levels calculated for cardiovascular risk and vascular disease markers were associated with a lower risk of dementia [13].

The influence of uric acid on the independent functioning of the elderly

Experimental studies have shown that hyperuricemia is associated with endothelial dysfunction, increased oxidative stress, thrombus formation, and elevated levels of circulating inflammatory mediators. Paradoxically, one method of preventing or reducing the disability associated with aging may be to maintain uric acid at a moderately high level but still within the normal range.

Studies indicate that moderate elevation of uric acid contributes to better physical fitness, muscle strength, and overall functioning in older people. This is evidenced by a pilot study that investigated whether regular physical activity increases serum uric acid levels. The study included 424 older people at risk of physical disability. Participants were divided into two groups: to participate in a 12-month physical activity program (PA group) and to participate in a 12-month educational program on healthy aging (SA group). The PA intervention (physically active group) resulted in an average increase of 2.1% +/- 1.4% by the end of 12 months, while the SA intervention (health education group) resulted in a decrease of uric acid levels by 1.7% +/- 1.9%. After adjusting for gender, baseline uric acid level, BMI, diabetes, baseline status, and change in creatinine, the results of a randomized controlled trial provide evidence that a 1-year PA intervention modestly increases systemic uric acid levels in individuals at risk of physical disability [14].

The next included study aimed to clarify how uric acid may affect activities of daily living in patients after acute ischemic stroke. Serum uric acid levels and activities of daily living were measured during hospitalization and at discharge in women and men. Activities of daily living were assessed using the Rankin scale, where a score of 3 or higher indicated poor activities of daily living.

Characteristics of each group included age, sex, previous stroke, smoking, alcohol consumption, hypertension (systolic/diastolic blood pressure), diabetes (blood glucose at admission, HbA1c), dyslipidemia (triglycerides, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol), creatinine clearance (CLcr), and stroke subtype. A U-shaped relationship was observed between serum uric acid levels and ADL impairment in both men and women. Lower serum uric acid levels at the onset of ischemic stroke were associated with significantly worse ADL outcomes during hospitalization and at discharge in both men and women. Multivariate analysis showed that the first and fourth quartiles of serum uric acid levels were associated with significantly worse ADL outcomes during hospitalization compared with other groups in men. These results indicated that men may be more susceptible to dramatic changes in uric acid levels than women [15].

There was also a study looking for the relationship between oxidative stress and neuroinflammation in the context of fatigue and depression in patients with multiple sclerosis (MS). The study focused on two main biomarkers: uric acid (UA) and C-reactive protein (CRP), which are supposed to indicate the presence of oxidative stress and inflammatory processes. The study was conducted on 98 MS patients (in the relapse and remission phase) and 35 healthy controls. MS patients were divided into those in the relapse phase and those in the remission phase. UA and CRP blood measurements were performed, as well as assessment of depression severity using the Beck Depression Inventory (BDI) and fatigue using the Fatigue Severity Scale (FSS). It was shown that UA levels were significantly lower in MS patients compared to the control group. In patients in the relapse phase, UA levels were even lower than in patients in remission. Lower UA levels were associated with depressive symptoms, such as sadness and disruption of daily activities. The authors suggest that the decrease in UA, an antioxidant, may be a defensive response of the body to the oxidative stress associated with MS. In turn, CRP protein in patients in the relapse phase reached higher levels than in patients in remission, which indicates an increased inflammatory process during relapses. Reduced UA levels may be a marker of an increased risk of depression [16].

A correlation between uric acid levels and gait disturbances in Parkinson's disease has also been demonstrated. The Unified PD Rating Scale (UPDRS) III and Hoehn and Yahr (H and Y) were used to assess disease severity, and the Frontal Assessment Battery (FAB) and Montreal Cognitive Assessment (MoCA) were used to assess cognitive function. The study suggests that low serum UA levels are associated with gait disturbances in Parkinson's disease [17].

The antioxidant effect of uric acid on the level of functioning in older adults has also been studied. Functioning was assessed using a standardized questionnaire and performance measures. The Short Physical Performance Test (SPPB) assessed walking speed, standing balance, and ability to rise from a chair. Each physical performance test was graded into a five-level score, where 0 indicates inability to perform the test and 4 indicates the highest level of performance. The study found that participants with moderately high uric acid levels, between 4.8 and 5.3 mg/dl, tended to have less disability in daily activities and greater physical function than those with uric acid levels higher or lower than this range [18].

The influence of uric acid on nutritional status

Both elevated uric acid levels (hyperuricemia) and low uric acid levels (hypouricemia) in older people have a significant impact on health and functioning, particularly on nutritional status. Uric acid is a product of purine metabolism and, when excreted incorrectly or produced excessively, it can accumulate in the body, leading to inflammation and gout-related symptoms. The effects of hyperuricemia can also indirectly affect the nutritional status of older people, as a result of dietary restrictions and pain that limits activity.

A cross-sectional study examining the relationship between dietary patterns and hyperuricemia showed that the direct effect of diet on hyperuricemia is small, while obesity itself has the greatest effect, which is confirmed by the research results. This knowledge may be useful during therapy lowering uric acid levels, because according to the results, thanks to the use of an additional slimming diet, it is possible to obtain better therapeutic effects [19].

A meta-analysis of randomized controlled trials showed a significant reduction in serum uric acid levels after treatment with orlistat, a drug for obesity in adults [20]. Furthermore, a meta-analysis of 20 cohort studies assessing the association of bariatric surgery with gout and serum uric acid levels showed that uric acid decreased on average by 0.73 mg/dl 3 months after bariatric surgery and 1.91 mg/dl 3 years after surgery [21]. The 2020 ACR Gout Treatment Guidelines also recommend that people with gout who are obese or overweight should follow a weight loss program [22].

It has been shown that nutritional patterns for weight loss can be an effective way to prevent and treat hyperuricemia. Therefore, diets such as Mediterranean, DASH (Dietary Approaches to Stop Hypertension), Nordic, vegan, and vegetarian are recommended to facilitate weight loss [23].

In a study of the relationship between serum uric acid levels and nutritional status in hemodialysis patients, it was shown that patients with hyperuricemia were better nourished. On the other hand, patients with normouricemia were more susceptible to malnutrition and cachexia. The results suggest that in patients with hyperuricemia, the need for restriction of purines and proteins in the diet should be assessed individually. This is due to the possible beneficial effect of UA on antioxidant balance and nutrition [24].

The role of high uric acid levels in the development of depression

Depression is a common and widespread health problem in older people, affecting 17,1% of people over the age of 75 [25]. The pathogenesis of depression is complex and multifactoral. An additional risk in this age group includes biochemical mechanisms that cause ageing of the body, especially oxidative stress [26]. Uric acid due to its antioxidant and neuroprotective effects [27] and high correlation of plasma uric acid levels with cerebrospinal fluid levels [28] is considered promising in studies of psychiatric and neurological disorders.

Research suggests strong correlations between serum uric acid levels and the occurrence of depression symptoms. Data from American National Health and Nutrition Examination Survey (NHANES) revealed a negative correlation between an increased serum uric acid levels and depressive symptoms and it is more significant in women than in men and also in the population over 60 years of age. The results revealed specific association between serum uric acid levels and depressive symptoms: when the serum uric acid level is lower than 319.72 μmol/, the risk of depressive symptoms decreases by 21.7% for every 100 μmol/l increase of uric acid levels. However, when serum uric acid level exceeds 319.72 μmol/l the risk of depressive symptoms decreases by 2% for every 100 μmol/l increase of serum uric acid level [28]. Data from The Korean National Health and Nutrition Examination Survey revealed a negative correlation between serum uric acid levels and depressive symptoms, especially in women over 60 years of age. The results suggest that this correlation is stronger in women than in men, which may be due to relatively lower serum uric acid levels in women than in men and due to the susceptibility of women to oxidative stress, which may be related to a decline in estrogen [29]. Study by Chen J. et al. found an inverse relationship between serum uric acid levels and depressive symptoms in postmenopausal women, while this relationship was less pronounced in premenopausal women [30]. Conversely, the study by Li Y. et al. also revealed an inverse correlation between serum uric acid levels and depressive symptoms, yet this correlation was exclusively observed in men and not in women [31]. This finding indicates the necessity for further research that incorporates aspects of sex and age in a more comprehensive manner with focus on the ageing process.

A review of the research conducted on the correlation between serum uric acid levels and symptoms of depression reveals the potential of serum uric acid levels as a promising biomarker for assessing the

risk of depression in adult patients [28,29]. This assertion is supported by the documented negative correlation between the increase in serum uric acid level in serum and the occurence of depression symptoms [30,31]. Furthermore, testing for pharmacological or dietary interventions should be considered in patients with high risk of developing depressive symptoms and low serum uric acid levels.

Discussion

As described by Min-Gu Kang et al., uric acid may have clinical significance in the daily functioning of older people. Hyperuricemia increases the risk of frailty, which in turn may accelerate aging. According to Min-Gu Kang et al., uric acid can be used as a marker of frailty and be a valuable tool in assessing the risk of loss of physical, cognitive, and social functions [32].

Nafija Serdarević and co-authors from the conducted studies and observations noted the clinically significant significance of hyperuricemia in cerebrovascular diseases, including ischemic strokes and vascular dementias. They observed that hyperuricemia may indicate advanced vascular atherosclerosis and tissue hypoxia. This may affect the deterioration of cognitive functions [33].

Research by Laixi Kong and co-authors shows that higher uric acid levels are associated with the risk of low muscle mass in older women, which was not found in older men. They showed that the association between high uric acid levels and low muscle mass in women is statistically significant, so controlling uric acid levels in older women may be helpful in preventing sarcopenia. [34]

The article written by Huan Li and co-authors showed a positive correlation between the waist index adjusted for body mass (WWI) and serum uric acid levels. Higher uric acid levels may be associated with eccentric obesity. A greater tendency was observed in women. Health problems resulting from abdominal obesity, i.e. improper distribution of fat tissue, can lead to, among others, heart disease and diabetes, which are among the most common chronic diseases in the elderly. Huan Li and co-authors in their results suggest that it is important to monitor uric acid levels, especially in older women, because in this way it is possible to reduce the risk of developing abdominal obesity [35].

Jayprakash Mishra et al. proved in their publication that serum uric acid concentration ≥7 mg/dl in patients with sepsis increases the risk of therapeutic failure, prolonged treatment time of patients, and therefore prolonged hospitalization, which may be associated with an increased risk of hospital infections. This may be related to increased oxidative stress, which may lead to organ damage, including kidneys [36].

NA Kunicka and co-authors showed that higher levels of uric acid may have potential health benefits due to its antioxidant properties. They may thus support cognitive functions in the elderly. They described that higher levels of uric acid may delay the progression of Alzheimer's disease or Parkinson's disease by performing neuroprotective functions. On the other hand, low levels of uric acid may have an impact on accelerating these types of diseases. They also showed that high levels of uric acid in vascular dementia negatively affect cognitive functions. It can be concluded that the role of uric acid in neurodegenerative diseases depends on the type of dementia [37].

According to Hongjiang Liu and co-authors, hypouricemia appears to be associated with increased mortality in seniors with lung diseases. Patients with hypouricemia also have increased levels of inflammatory markers, including CRP and LDH, suggesting that reduced uric acid levels have an impact on inflammation. They also showed that patients with hypouricemia have low levels of lymphocytes and higher levels of neutrophilia in the blood, and therefore a weakened immune system [38].

Conclusions

The results of studies on the effect of hyperuricemia on cognitive functions remain contradictory. Further studies are needed in this area, taking into account numerous variables that may distort the results of studies, occurring in the elderly. Uric acid concentration should be reduced with caution in the case of hyperuricemia. It has been shown that the best functionality was maintained by patients with uric acid concentration remaining in the upper limits of the norm. At the same time, rapid attempts to reduce it may cause a decrease in the level of independence or an increased risk of developing depression in old age. Obese body structure influences the development of hyperuricemia, but it has not been shown that the diet itself has any special significance. Commonly used methods of reducing body weight simultaneously lead to a decrease in uric acid concentration. Studies indicate that uric acid may be a potential laboratory marker of frailty syndrome, as well as the risk of death due to infectious diseases.

Konflikt interesów/Conflict of interest
Brak/ None

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