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Review/Praca poglądowa

Cognitive disorders in kidney diseases

Zaburzenia procesów poznawczych w chorobach nerek

Wojciech Rakoczy *

Specialist Hospital – Subcarpathian Oncology Center in Brzozów, Neurology Department with Stroke Unit, Brzozów, Poland

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ABSTRACT

Objectives: The presence of cognitive dysfunctions in patients with impaired renal function is emphasized in the article. A review of relevant research studies is aimed at identification of neuropsychological assessment methods that may be useful in this category of patients. **Overview:** Cognitive impairments are frequently associated with kidney disease severity. Patients with chronic kidney disease (CKD), and especially those with end-stage renal disease (ESRD) are prone to cognitive decline, particularly if additional risk factors such as diabetes or cardiovascular disease are present. Cognitive disorders can be seen also in patients treated with hemodialysis or peritoneal dialysis. However, kidney transplant recipients often show improvement on neuropsychological tests measuring cognitive skills. **Conclusions:** A number of studies on cognitive functioning in patients with impaired renal function are reviewed. The author discussed the prevalence and severity of cognitive deterioration in CKD and ESRD patients, emphasizing cognitive performance improvement after kidney transplantation. Renal patients show cognitive deficits in such domains as memory (in various modalities), attention, concentration, psychomotor skills, and executive functions. Global cognitive decline is observed especially among ESRD patients. Dialysis patients may also suffer from cognitive deficits (affecting memory, language, attention).

Introduction

Kidney diseases have become one of the major healthcare problems. The prevalence of kidney dysfunction is systematically increasing, particularly that of chronic kidney disease (CKD) [1]. In the most recent reports CKD prevalence is estimated at 15–18%. The number of CKD patients in Poland currently amounts to over 4.2 million, while there are an estimated 600 million of cases worldwide [2].

CKD results from active nephron loss and affects the maintenance of systemic balance. Kidney damage stages are identified using the glomerular filtration rate (eGMR) index. Four stages of kidney failure are distinguished, with stage

* *Correspondence to*: Oddział Neurologii z Pododdziałem Udarowym, Szpital Specjalistyczny – Podkarpacki Ośrodek Onkologiczny w Brzozowie, ul. ks. Bielawskiego 18, 36-200 Brzozów, Poland. Tel.: +48 13 43 09 628.
E-mail address: wojtekr06@gmail.com.

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4 defined as the end-stage renal disease (ESRD). Patients with ESRD require dialysis or kidney transplantation [3, 4].

More and more authors emphasize a specific analogy between kidney diseases (CKD and ESRD) and dementia. Both these conditions may develop slowly, have an insidious onset, and are more prevalent among the elderly [5–7]. In other words, renal function effectiveness and quality of cognitive processes decrease with age [8]. Patients with CKD are at a greater risk for general cognitive decline due to a number of frequent co-morbid factors that contribute to or result from CKD, and include, among other ones, diabetes, vascular diseases, hypertension, atherosclerosis, coronary heart disease, myocardial infarction, atrial fibrillation, anemia, hypercholesterolemia [1, 5, 7–9]. However, cerebral stroke remains the major risk factor for cognitive dysfunction in CKD and ESRD patients [6]. Hypertension and cardiovascular disorders often observed in kidney failure suggest that CKD and ESRD patients are at a higher risk for developing vascular dementia or Alzheimer's dementia, particularly the former [1, 2, 7]. A large proportion of people with kidney diseases are aged over 60 [5], and therefore are at a higher risk of cognitive impairments. Cognitive impairment is construed here as a new deficit in at least two domains of cognitive functioning, e.g. memory, executive functions, attention, processing speed, visuomotor skills or language functions. Sometimes so-called mild cognitive impairments (MCI) may be seen in CKD patients [1]. MCI are an intermediate stage between normal aging processes and mild dementia. Although symptoms of cognitive deterioration (especially as regards memory) are present in MCI, nevertheless they neither meet the diagnostic criteria of dementia nor affect the person's daily living activities. More importantly, cognitive impairment does not have to be reported by the patients themselves, their problems may be noticed by others and are observable in objective cognitive tasks. An accurate diagnosis of mild cognitive impairment is essential since with time a full-blown dementia syndrome develops in 10–50% of MCI patients [10–13]. According to Jodzio, dementia should be considered as a process and not a clear-cut pathological condition. This view is corroborated by the fact that in the course of MCI qualitative and behavioral changes are observed [14].

Cognitive dysfunction in chronic kidney disease (CKD)

Increasingly more reports published recently analyze cognitive impairments in CKD patients. In one of research studies cognitive skills of 825 adults (aged over 55) with chronic kidney disease were investigated. A subgroup of the CKD sample suffered from a co-morbid condition (stroke, hypertension, diabetes, or depression). Cognitive function was assessed using the following methods: the Trail Making Test (TMT), parts A and B, the Controlled Oral Word Association Test (COWAT), the Boston Naming Test, the Buschke Selective Reminding Test (a measure of immediate and delayed verbal recall), and the Modified Mini-Mental State (MMSE-3MS). In contrast to the standard MMSE, additional tasks are included in the 3MS: animal naming, finding similarities, naming body parts, and giving the date and place of birth. This method is more sensitive to MCI. In the reported study a significant decline was found in the patients' general cognitive functioning, with deficits of attention, delayed verbal recall and executive function, but without major impairments of verbal fluency [7].

In another study Slinin et al. investigated cognitive functioning in 5529 CKD men aged over 65, in some cases with a history of co-morbid stroke, hypertension, diabetes, or cardiovascular disease. Cognitive function was assessed using two tools: the 3MS and TMT, part B. Patients with mild-to-moderate CKD were found to score lower on executive function and attention measures, but not on tests assessing global cognitive functioning [6].

Tsai et al. used the Rey Auditory Verbal Learning Test (RAVLT), the Digit Span subtest of WAIS-R, the COWAT and the TMT to investigate the relationship between cognitive function and moderate CKD in Taiwanese women aged 40–54. In the analysis of results a subgroup of CKD female patients with co-morbid diabetes and cardiovascular diseases was also taken into account. Subjects in the sample were found to have difficulty with backward digit span and delayed recall. The authors reported also deficits of attention, working memory and verbal memory, perhaps due to an impairment of executive functions that play an important role in the scanning of stored memories. They compared the profile of these deficits to the pattern of cognitive dysfunction in patients with cerebral vascular changes [15].

In the above-discussed studies no attempt was made to find out to what extent the patients' cognitive deficits were due to CKD, and to what extent might result from comorbid conditions, such as hypertension. Such a differentiation was introduced by Silverwood et al. in their prospective study of verbal memory functioning, mental processing speed, and simple and choice reaction time in CKD patients [16]. Both memory and reaction time were found to deteriorate with the eGFR index lowering. According to the authors, this relationship might result to some degree from diabetes or hypertension [16].

Moreover, detrimental effects of CKD on visual memory and fluid intelligence have been reported in the literature [17]. Madero et al. point out that lower eGFR is associated with poorer performance on tests of cognitive function. Among CKD patients additionally diagnosed with anemia cognitive function tended to improve on treatment implementation [1]. Effectiveness of cognitive processes decreases with increasing levels of serum creatinine, blood uric acid and blood urea, and with decrement in calcium levels [2].

In CKD children, as same as in adults, attention, memory and executive function impairments were observed. Besides, these children showed relatively lower levels of intellectual development, but no evidence of intellectual disability [18].

The presented findings indicate that risk factors for cognitive impairment in CKD include, among other ones, hypertension, diabetes and anemia. Effectiveness of cognitive processes depends also on plasma levels of creatinine, uric acid, urea and calcium. Among the cognitive dysfunctions most frequent in CKD there are deficits of attention, working memory, verbal and visual memory, executive function, and intelligence.