

## HEMODIALYSIS INDUCED HEADACHE; A GLIMPSE THROUGH THE PAST DECADE

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### ABSTRACT

Dialysis may induce severe headache as a result of a large amount of water and electrolyte shifts. It is important to recognize it because it can be a great problem to the patient and changing dialysis parameters or methods can prevent it. There is a paucity of data on how to treat dialysis-related headaches. Prevention can be achieved through using Bicarbonate dialysate, Slow dialysis with reduced blood flow rate, Sodium profile & Ultrafiltration profile, to prevent sudden alterations in serum sodium and blood pressure levels, Caffeine ingestion during hemodialysis, in habitual caffeine consumers, Despite the high prevalence of headache in the dialysis population, there is a paucity of research surrounding its pathophysiology and treatment. The factors leading to hemodialysis headache and its management need to be evaluated further to improve the quality of life of patients with ESRD on dialysis.

### INTRODUCTION

Dialysis is a type of treatment that helps the body to remove extra fluid and waste products from blood when the kidneys are not able to do so. Dialysis was first used successfully in the 1940's and later became a standard treatment for kidney failure starting in the 1970s. Since then, millions of patients have been helped by these treatments.<sup>[1]</sup> Dialysis can be done at various set up's like a hospital, a dialysis center, or at home itself. The nephrologist will decide which type of dialysis and which place is best, based on the medical condition and patient's own preference. Dialysis is helpful for two different situations. Acute kidney injury (AKI) which is a sudden episode of renal failure or damage that happens within a few hours or days. AKI is usually treated in a hospital setting with intravenous fluids (given through the vein). In severe cases, dialysis may also be needed for a short time until the kidneys get better. The second one is Chronic Renal Failure (CRF), when 10-15% of the kidney function only remains properly, measured by an estimated glomerular filtration rate (eGFR) of less than 15 mL/min. At this stage, kidneys are no longer able to keep the patient alive without some extra help. This is also known as End-Stage Renal Disease (ESRD). With Renal failure, dialysis is only able to do some of the work of healthy kidneys, but it is not a cure for the disease. With ESRD, the person will need dialysis for the

rest of the life or until they are able to get a renal transplant.

Headaches are estimated to affect over 90% of the general population at some time in their lives and may be encountered by physicians in a wide variety of clinical settings. The overwhelming majority of recurrent headaches occur in the context of what are known as primary headache disorders, in which no identifiable underlying cause can be found. Some headaches, however, classified as secondary headache disorders, are symptomatic of an underlying abnormality that may include anything from transient viral illness, to intracranial tumor, aneurysm, or drug withdrawal. Prevalence studies indicate that a benign process, such as a mild febrile illness or alcohol withdrawal, usually causes secondary headaches and that the lifetime prevalence of headache resulting from more ominous intracranial structural lesions is less than 2%.<sup>[2]</sup> Headache occurs when nociceptive neurons within the trigeminal, vagus, or glossopharyngeal cranial nerves or within the upper cervical roots become depolarized. Information from procedures involving intracerebral electrode implantation suggests that direct electrical or mechanical activation of areas within the brain involved in pain processing may also cause headache.

Dialysis may induce severe headache as a result of a large amount of water and electrolyte shifts. It is important to recognize it because it can be a great problem to the patient and changing dialysis parameters or methods can prevent it. Nearly one-third of patients undergoing dialysis have hemodialysis headache (HDH), and it is associated with mild to moderate depression. HDH has been recognized for many years, but the pathophysiology of this condition is not known. High arterial blood pressure, decreased serum osmolality, sodium washout, and high blood urea nitrogen level are reported risk factors for HDH.<sup>[3]</sup> The factors leading to hemodialysis headache and its management need to be evaluated further to improve the quality of life of patients with ESRD on dialysis.<sup>[4]</sup>

### METHODOLOGY

Based on a literature search in the major medical and epidemiological databases. The keywords “hemodialysis induced headache”, “hemodialysis and headache” and “renal dialysis and headache in ESRD patients” were used. In this review we have included articles published between 2013 and 2023. Articles that addressed the discussion of dialysis headache and written only in English were included. Editorials, comments, letter to the editor, articles that were not fully available or those who lacked accurate information were excluded. To ensure the validity of these articles, the selected studies were analyzed in detail regarding demographic and clinical characteristics and risk factors associated with dialysis headache in patients with chronic kidney disease undergoing hemodialysis. Of the 606 articles found, only 12 met the inclusion criteria and were analyzed. The study was conducted in compliance with PRISMA guidelines 2020 update.

### RESULTS

Among 362 patients, 198[52.69%] men and 164[45.30%] women were found to have HDH. No statistically significant difference was found in the electrolyte levels between patients having HDH and without HDH. The headache was moderate in most but needed a paracetamol tablet to relieve the headache. Vertex location, bilateral headache, dull nature, and moderate severity were the most prevalent features of HDH. There were no statistically significant differences between the HDH and control groups with respect to causes of end-stage renal disease. Most articles suggest that low blood Mg level and high blood sodium level may be risk factors for HDH. Magnesium supplementation may help patients with HDH whose serum Mg levels are found to be low. It is also found that regulating the frequency and timing of dialysis may provide better management in patients with high BUN levels and high pre-dialysis blood pressure.

### DISCUSSION

According to the 2013 diagnostic criteria presented in the International Classification of Headache Disorders-3

beta, dialysis-related headache presents the following characteristics:

- A. At least three episodes of acute headache fulfilling the criteria C & D
- B. The patient is undergoing hemodialysis
- C. Evidence of causation is shown through at least two of the following:

Each headache episode starts during hemodialysis

One or both of the following:

Each headache episode worsens during hemodialysis

Each headache attack resolves within 72 hours after completion of hemodialysis

The headache episodes disappear after a successful kidney transplant and the end of hemodialysis

- D. The headache cannot be better classified by other ICHD-3 criteria.<sup>[4]</sup>

The pathophysiology of dialysis-related headache has not been completely elucidated. However certain factors seem to be associated with it, like sudden alterations of blood pressure, low levels of blood of magnesium, high calcium or magnesium in dialysate fluid. etc. The causes includes Caffeine withdrawal (removed by dialysis), Acetate dialysate, Intradialytic hypertension / hypotension, Hard water syndrome [high levels of calcium/ magnesium in dialysate: The maximum allowable levels and are as follows: calcium  $\leq 2$  mg/L, magnesium  $\leq 4$  mg/L(according to AAMI standards)]Fluoride/chloramine intoxication (in dialysate), Hypomagnesemia, In addition, acute yet transient alteration in serotonin levels, cerebral vasoconstriction, hypoxemia, or renin-angiotensin-aldosterone disturbances that contribute to headache. For example, patients on dialysis with hypertension who have sudden drop in blood pressure can activate their renin-angiotensin system causing vasoconstriction in order to increase their blood pressure.<sup>[5]</sup>

There is a paucity of data on how to treat dialysis-related headaches. The following medications can be tried in the treatment. Patients, who consume more than 200 mg of caffeine per day for more than 2 weeks, may experience bilateral and/or pulsatile headache within 24 hours after last caffeine intake. In these patients, on administration of 100 mg caffeine, the headache disappears within 1 hour. Amitriptyline /chlorpromazine, Angiotensin-converting enzyme inhibitors (isolated case report), Magnesium replacement (in patients who have hypomagnesemia), Onabotulinum toxin (only FDA approved drug in treatment for prevention of chronic migraine, though not tested in dialysis patients with chronic daily headache).<sup>[6-10]</sup>

Prevention can be achieved through using Bicarbonate dialysate, Slow dialysis with reduced blood flow rate, Sodium profile & Ultrafiltration profile, to prevent sudden alterations in serum sodium and blood pressure levels, Caffeine ingestion during hemodialysis, in habitual caffeine consumers, Despite the high prevalence of headache in the dialysis population, there is a paucity

of research surrounding its pathophysiology and treatment.<sup>[12]</sup>

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