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Chronic pain in hemodialysis patients: Role of bone mineral metabolism

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Abstract *Background:* Pain is one of the most common complaints in clinical practice because it is a symptom for a myriad of physical and mental problems. The high prevalence of pain in the chronic kidney disease (CKD) population is particularly concerning because pain has been shown to adversely affect quality of life. The aim of this study was to evaluate the prevalence and possible causes of chronic pain in patients with end stage renal disease on long-term hemodialysis (HD).

Methods: We prospectively enrolled 100 patients who were undergoing maintenance HD for at least 6 months or more. Pain was evaluated using the Brief Pain Inventory (BPI). Data collected on each participant included age, gender, body mass index (BMI), time on dialysis and biochemical findings.

Results: The average age was 42.06 years ranged from 22 to 58 years; the average duration on dialysis was 4.97 years. 52 patients were males and 48 were females. Although 52% of patients experienced chronic pain, only 25% described the pain as severe, 28% described pain as moderate while 52% of patients described as mild. Musculoskeletal pain was the most frequent form of chronic pain reported by patients who were on HD (54%). Malnutrition and high CRP were highly statistically associated with chronic pain ($p < 0.001$). High statistical significant correlation was found between lower calcium, lower 25(OH) D3 levels, higher parathyroid hormone (PTH) levels and experienced chronic pain ($p < 0.001$).

Conclusion: Chronic pain is highly experienced in long-term hemodialysis patients. Malnutrition, high CRP and disturbed bone mineral metabolism are highly correlated with the incident of this pain.

1. Introduction

Pain is a frequent complaint of hemodialysis (HD) patients.[1,2] The information regarding its origins, frequency, and management is relatively scarce. Most published data come indirectly

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from studies focusing on health-related quality of life.[1,2] The reported frequency of pain varies widely in these patients. Murtagh et al.,[3] in a review of symptoms in ESRD, reported that the mean prevalence of pain is of 47%, with a range of 8–82%. The International Association for the Study of Pain (IASP) has defined pain as "an unpleasant sensory and emotional experience associated with an actual or potential harm to the body".[4] In most patients, severity of pain ranges from moderate to severe.[5] Important sources of pain are musculoskeletal disorders, peripheral neuropathy and critical limb ischemia. Moreover renal replacement therapy with hemodialysis or peritoneal dialysis is associated with additional pain manifestations.[6,7] Three quarters of ESRD patients suffer unnecessarily from inadequately or untreated pain.[1,5] In the Dialysis Outcomes and Practice Patterns Study (DOPPS), 74% of subjects reported a moderate to severe pain without analgesic prescription.[8] These hurdles are due to several factors: The caregivers are frequently unaware of this problem and have concerns about adverse effects of the analgesic therapy, and the patients fear the side effects of medication, the extra burden of daily tablets and the potential risk of addiction in the case of opiate medication.[9] Although well-accepted guidelines are available for the management of cancer-related pain, no such recommendations exist for pain associated with HD.[10] One review[11] suggested using the same step-wise approach declared by the World Health Organization to treat cancer pain; however, the treatment of HD patients is complicated by the need to adjust frequently the dosage of analgesic drugs and by increased risk for adverse effects.[12,13] because of the high prevalence and adverse effects of this complaint, and we designed this study aiming to evaluate its incidence and characters of distribution in our hemodialysis community and trying to find out the major determinants of this very common complaint.

2. Patients and methods

This prospective cross-sectional study was carried out in the internal medicine department and renal unit, Zagazig university hospital, Egypt. One hundred eligible patients who had been undergoing maintenance HD for at least 6 months were recruited for this study. They were followed for one year (from December 2013 to December 2014). Informed written consent was taken from all participants and then they were randomly selected and interviewed during dialysis sessions. They were divided according to the presence or absence of chronic pain into two groups: **Group 1**: it included 48 patients. They were 25 males and 23 females, with age range from 22 to 50 years (mean ± SD: 42.12 ± 10.32 years). They were treated with a regular HD for ⩾6 months and they did not experience chronic pain. **Group 2:** it included 52 patients. They were 28 males and 24 females, with an age range from 21 to 58 years, (mean ± SD: 42.06 ± 10.26 years). They were treated with a regular HD for ⩾6 months and they were complaining from different types of chronic pain.

Inclusion criteria: All patients who were free from diabetes mellitus (DM), connective tissue diseases, heart failure, liver diseases or evident acute infection and were not receiving medications that may modify pain or the immune response like non-steroidal anti-inflammatory medications or corticosteroids were included in the study.

Exclusion criteria: Patients with central venous catheters and Arteriovenous fistula (AVF) that were prone to limb ischemic pain were excluded from the study. Also, patients with recurrent pain due to needling, headaches and muscle cramps during the HD procedure were excluded as these conditions may be perceived as a chronic pain and so can affect the results of our study. Our patients were free of cancer for the last 2 years prior to the study.

They were treated thrice weekly HD sessions for 4 h duration using volumetric machines and high-flux polysulphone membrane (Haidylena Medical SAE, Cairo, Egypt). The dialysate flow was 500 mL/min and the blood flow rate ranged from 270 to 350 mL/min. We used standard bicarbonate dialysate (38 mEq/l) with normal calcium bath of 1.25 mmo/l.

Demographic and clinical data were collected for all patients. Demographic data included complete history taking, age, gender, body mass index (BMI), nutritional status, time on dialysis and the type of blood access. Clinical data included the following: complete blood count (CBC), serum calcium, phosphorus, uric acid, intact parathyroid hormone (iPTH by immunoradiometric assay (N-TACT PTH SP IRMA; DiaSorin), 25-hydroxyvitamin D3 [25(OH)D3] by Elisa, serum albumin, alanine transaminase (ALT), aspartate transaminase (AST), and C-reactive protein (CRP). Also, we determined serum low-density lipoprotein (LDL), serum high-density lipoprotein (HDL) and triglyceride (TG), and single pool Kt/V using Daugirdas formula.[14]

A Hitachi747 Clinical Analyzer was used to determine the serum levels of albumin, glucose, iron, calcium, and phosphorus. A Hitachi 917 was used for C-reactive protein, and Advia 120 (Bayer, Leverkusen, Germany) was used to determine hemoglobin levels. Serum total cholesterol (TC), triglycerides (TGs), HDL cholesterol (HDL-C), and LDL cholesterol (LDL-C), were measured calorimetrically using commercially available kits on the fully auto analyzer of Clinical Biochemistry Laboratory

2.1. Pain assessment (brief pain inventory score)

All patients were interviewed during their HD session evaluated for the presence of pain by using the Brief Pain Inventory (BPI)[15] which is an instrument for evaluating pain that assesses the intensity and characteristics of pain and determines the impact of pain on important aspects of a patient's life. The BPI uses a 10-point scale to evaluate the intensity of pain whereby 0 = "no pain" and 10 = severe pain.[15] On the basis of the BPI scale, pain was classified as mild (1–4 points), moderate (5–6 points), or severe (7–10 points).[17] Chronic pain was defined as pain of >3 months duration.[17]

2.2. Dialysis malnutrition score

Assessment of the nutritional status uses Modified Subjective Global Assessment – Dialysis Malnutrition Score which consists of seven features: weight change, dietary intake, GI symptoms, functional capacity, comorbidity, subcutaneous fat and signs of muscle wasting. Each component has a score from 1 (normal) to 5 (very severe). Thus the malnutrition score (sum of all seven components) is a number between 7 (normal) and 35 (severely malnourished). Lower score denotes tendency toward a normal nutritional status. A higher score is considered to be an indicator of the presence of malnutrition elements i.e. protein energy malnutrition.[16]

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