Bone Mineral Densitometry is Recommended in Pre-liver Transplant Evaluation in Children Suffering from Wilson Disease

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ABSTRACT

Background: Wilson disease (WD) is an autosomal recessive disorder of copper metabolism with an estimated prevalence of 1 in 30,000. Osteoarticular manifestations are common feature of WD and mainly involve osteopenia, osteoporosis, and arthropathy.

Objective: This study aimed to investigate the prevalence of abnormal mineral density in a group of children with WD and evaluate if it is rational to recommend screening in pre-transplantation workups.

Methods: This study included all the children with a confirmed diagnosis of WD, followed at Nemazee Hospital affiliated with Shiraz University of Medical Sciences between 2016 and 2018. The researchers also excluded patients with other underlying diseases, abnormalities of calcium, phosphorus, or vitamin D, or those who used other medications leading to osteoporosis. Bone mineral content (BMC)/Bone mineral density (BMD) of the lumbar spine (LS-BMD) was performed for all included patients with DXA scans.

Results: Evaluation of z-scores showed osteopenia in 40% and osteoporosis in 53.33% of the patients. There was no significant association between the z-score values and cirrhosis in WD patients (P=0.559). There was a significant correlation between the value of z-scores with weight (P=0.007) and BMI (P=0.001) in patients with WD.

Conclusion: The results suggest that WD is intrinsically associated with osteoporosis. Also, patients with WD are at risk of osteopenia and osteoporosis, and screening for evaluation of bone mineral density and prophylactic supplementation may be logical, especially for those who are candidates for liver transplant due to the probability of deterioration of osteopathy in the first few months after liver transplantation.

KEYWORDS: Wilson disease; Osteopenia; Osteoporosis, Liver transplant; Bone mineral densitometry

INTRODUCTION

Wilson disease (WD) is an inherited disorder caused by mutations in the ATP7B gene [1]. The ATP7B gene encodes a plasma membrane copper-transport protein that exports copper from the cells [2]. Defects of this gene prevent the transport protein from functioning properly. As a result, copper accumulates to toxic levels that can damage the tissues and organs [3]. The main symptoms of WD are liver disease, Kayser-Fleischer rings, Central Nervous System (CNS), and psychiatric problems [4]. Osteopenia and osteoporosis are frequently seen in WD patients [5]. Osteopenia can cause a

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in the first 3 months after liver transplantation and an increase in fractures in the first 6 months [13]. On the follow-up of 360 post-transplant patients, 82% had bone loss in the first 4 months after transplantation[25]. On the long-term follow-up of pediatric patients who underwent a liver transplant, Guthery et al. demonstrated that 7.3% of patients had bone loss [26]. There is also 5 times more probability of osteoporosis in post-liver transplant recipients compared to non-transplant ones [27]. Pretransplant osteopenia and osteoporosis are the major risk factors for post-transplant fractures [27]. Sharma et al. demonstrated the association of low BMD with post-transplant mortality and the outcome of patients with hepatocellular carcinoma [28]. Younger age and male sex are associated with more prevalence of osteoporosis in patients with Wilson disease [29]. Guichelaar et al. also demonstrates that younger age is a risk factor for posttransplant bone loss [25].

Immunosuppressive therapy accounts for the aggravation of osteopathy in post-transplant patients [25, 30]. The mechanisms for cyclosporin, an immunosuppressive drug, that are attributed to bone loss are high bone turnover, downregulation of renal calbindin RNA, and impairment of testosterone production [31, 32]. The mechanism of glucocorticoids which induce decreased BMD is the cessation of osteoblastogenesis and induces apoptosis of osteoblasts and osteocytes [33]. The role of glucocorticoids for BMD in post-transplant patients is controversial. Nightingala et al. found no correlation between corticosteroid exposure and BMD in post liver transplant patients [34]. Scolapio et al. reported no effect of corticosteroid use beyond 4 months on BMD in patients who have undergone liver transplantation [35]. Some reports suggest the lower dose and shorter duration of glucocorticoid to decrease low BMD [36, 37]. The increase in BMD was seen by tapering and discontinuing glucocorticoid [35, 38].

Overall, given the risk factors of post-transplant bone loss such as younger age, glucocorticoid medication, immunosuppressive therapy which is inevitable, and pretransplant osteopathy, the importance of low BMD that may be attributed to the outcome and mortality of post-transplant patients, and the high prevalence of osteopathy in WD, we recommend screening of osteoporosis on pre-operation evaluation of pediatric patients with WD, as Guthery et al. also suggest screening for pediatrics [26].

The limitations of our study were the population size; we suggest that further studies should be conducted in the multicenter study and larger population. Patients may benefit from treatment of osteopathies before liver transplant, so it should be considered in further studies as it may affect post-transplant outcome.

In conclusion, osteoporosis and osteopenia are common manifestations in patients with WD. We recommend BMD measurement and proper treatment as soon as WD is diagnosed. Screening for evaluation of bone mineral density and prophylactic supplementation may be logical, especially for those who are candidates for liver transplant.

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