Mini Review

Relation of Hyperhomocysteinemia with Osteoporosiss

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ABSTRACT

Osteoporosis is a major health and economic concern worldwide, particularly among postmenopausal women. In determining bone mass and health, environmental, metabolic, and genetic factors all play a role. Evidence of homocysteine's harmful impact on bone health has been increasing for several years. The deleterious effects of homocysteine on bone health appear to be significant when it comes to bone mineral density, fracture risk, and bone markers that have been investigated. Vitamin B insufficiency may play a significant impact in bone metabolism, which has to be researched further. Further research into the effective mechanisms of link between homocysteine and osteoporosis is essential due to variances in genetic predisposition, environmental, sex differences, and nutritional factors.

Keywords: Osteoporosis; Health; Nutritional factors

Introduction

One of the most frequent disorders among the elderly is osteoporosis, which has lately been linked to Hyperhomocysteinemia (HHCY). One of the most common difficulties in osteoporotic patients is frequent bone fracturing, which often results in significant damage, disability, and the need for care (about 2.5 million osteoporotic fractures occur each year in the United States) [1]. Homocysteine is a sulfur-containing amino acid intermediate generated when methionine is broken down. Its high serum level is generally connected to enzyme deficiency or B vitamin shortage (folate, B12, and B6) in normal renal function. Homocysteine (HCY) concentrations in people are largely determined by age and gender. HCY levels in the blood rise with age, and young males (aged 30 years-40 years) often have greater HCY levels than women (around 2 mol/l higher). Because oestrogen plays a role in sex differentiation, the plasma HCY level rises following menopause [2], but the age-related increase in HCY concentration is primarily due to a physiological loss in kidney function [3]. HCY was first identified as a pathogenic agent in the early 1960s. A high circulating HCY level has been proven to be an independent risk factor for a variety of chronic diseases, including cardiovascular and Alzheimer's disease, while moderate HCY levels carry about 10% of the total risk of cardiovascular disease. Furthermore, the frequency of skeletal abnormalities such as osteoporosis has been found to be higher in patients with homocystinuria [4]. Neurodegenerative illnesses, osteoporotic fractures, and pregnancy difficulties have all been linked to HHCY. Indeed, an increased plasma HCY concentration raises the chance of hip fracture, which can result in disability, significant medical costs , and mortality [5]. HCY was identified as a cause of osseous mutations in patients with homocystinuria for the first time in 1957. Accelerated bone growth, skeletal abnormalities, flattened vertebral bodies, and low bone density were all seen in these patients. Furthermore, the frequency of skeletal abnormalities such as osteoporosis has been found to be higher in patients with homocystinuria [4]. Neurodegenerative illnesses, osteoporotic fractures, and pregnancy difficulties have all been linked to HHCY. Indeed, an increased plasma HCY concentration raises the chance of hip fracture, which can result in disability,

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Various Observations

For decades, there had been no link between HHCY and bone illnesses, until two prospective community-based studies discovered a possible link between moderately high plasma HCY and the prevalence of osteoporotic fractures in the senior population. In Amsterdam and Rotterdam, van Meurs et al. studied 2404 senior patients (aged 55 and up) over a period of 11,253 man-years (The Netherlands). They discovered a link between HCY levels and the risk of fracture that was independent of BMD and other possible fracture risk variables. In that study, males with an HCY level in the third quartile (mean value: 13.4 mol/l) had a fracture risk 2.07 times higher than men with an HCY level in the first quartile (average age: 70 years; range: 59 years-91 years). Fracture risk was 3.84 times higher for males in the fourth quartile (mean HCY value: 20.8 mol/l) than for men in the first quartile. In women, the association was less obvious. Périer et al., on the other hand, found contrasting results in 671 postmenopausal women who were followed prospectively for an average of 10 years and concluded that HCY is not an independent risk factor for osteoporotic fractures in healthy postmenopausal women of all ages. The mechanisms underlying the association between HHCY and the risk of fracture are unknown. Some research looked at the relationship between HCY and BMD, however they found no or just a weak link between the two. In fact, given that BMD is just an integral measurement of bone metabolism over a longer period of time, the modest association between HCY and BMD is not surprising. Biochemical indicators of bone metabolism have been examined in investigations that show real-time monitoring of bone metabolism. In patients with HHCY, Dhonukshe-Rutten et al. found an elevated level of bone production and resorption indicators. Herrmann et al. studied post- and pre-menopausal women and found that HCY levels were positively connected with the bone-resorption marker urine deoxypyridinoline crosslinks, but not with the bone-formation marker osteocalcin in serum. HCY has changed bone metabolism towards bone resorption, according to the researchers. Furthermore, higher dosages of HCY promoted osteoclast activity in cultured human osteoclasts, which is consistent with the idea of greater bone resorption in the presence of HHCY. Existing evidence suggests that HHCY can alter osteoclast activity, but the evidence is insufficient to infer that osteoclasts are HCY's primary target in human bone. HCY, on the other hand, was recommended as a risk factor by Gerdhem et al., who conducted the investigation in 996 women from the Osteoporosis Prospective Risk Assessment project. At the outset, they noticed a relationship between high bone-marker levels and low BMD. High HCY concentration was linked to death over a 7-year follow-up period, although no clear relationship to fracture risk was found. The effects of HCY on human bone marrow stromal cells were studied by Kim et al. HCY causes apoptosis in primary human bone marrow stromal cells through the reactive oxygen species-mediated mitochondrial route and NF-B activation in human bone marrow stromal cells, according to the researchers. HCY was discovered to play a role in the development of osteoporosis by inhibiting bone production. Antioxidants may play a role in reducing bone resorption in HHCY patients, according to the findings [7]. In a similar work on osteoclasts, Koh et al. proposed that HCY directly promotes osteoclast development by generating intracellular reactive oxygen species. As a result, an antioxidant appears to reduce bone loss in HHCY patients. Herrmann et al., on the other hand, found that increasing HCY levels by lowering folate, vitamin B12, and B6 levels has no effect on the activity of human osteoblasts. Herrmann et al. and Ozdem et al. further verified the link between HHCY and lower bone quality and disrupted bone metabolism in animal tests, supporting HHCY as a causative osteoporotic factor in rats. While in the old, HHCY is basically brought about by lack of vitamin B, it isn't notable whether these nutrients assume a huge part in bone wellbeing. Considering the instruments, past examinations proposed a decrease in osteoblast movement in relationship with low vitamin B12 focuses [8,9]. Goerss et al. seen that in patients with malicious weakness (brought about by lack of vitamin B12), the dangers of proximal femur, vertebral

and lower arm cracks were 1.9, 1.8 and 2.8 times more than controls, individually. In one planned preliminary on 600 patients with osteopenia and osteoporosis, the significant job of B nutrients in bone wellbeing was examined. Sato et al. treated the patients with 5 mg of folic corrosive and 1500 μg of vitamin B12 or fake treatment for quite some time. They noticed an around 75% abatement in the frequency of cracks in the treatment bunch, which was practically identical with that of alendronate. Considering the different folate fixations in various compartments of the body, Golbahar et al. recommended RBC folate as a preferred indicator of BMD over plasma folate, for which lack might be related with the pathogenesis of osteoporosis in postmenopausal ladies . Roughly 1 year after the fact, Gjesdal et al. played out one more review on 5338 older patients to look at the relationship between hip BMD and plasma levels of HCY, folate, vitamin B12 and the Methylenetetrahydrofolate Reductase (MTHFR) polymorphism. They presumed that raised HCY and low folate levels were related with decreased BMD in ladies yet not in ment. In another new review, Green et al. researched 276 solid more seasoned subjects who were haphazardly appointed to get either day by day supplement of folate, vitamin B12 and vitamin B6 or fake treatment for a long time. By estimating bonespecific soluble phosphatase and bone-inferred collagen parts at gauge and the finish of study, they presumed that supplementation with folate and vitamin B6 and B12 can bring down plasma HCY however has no impact on bone turnover. Concerning the meaning of folic corrosive, many gatherings concentrated on the impact of the C677T MTHFR polymorphism on bone. An increment of break occurrence was recognized with each Tallele, particularly in patients with low folate levels. There are a few problematic outcomes in this issue. Li et al. revealed no relationship between MTHFR (C677T) and the BMD of Chinese men or ladies. They played out the future science bunch study on postmenopausal ladies, old ladies and older men. High folate and vitamin B admission in the review populace, added to the low number of patients and low pervasiveness of the TT genotype, ought to be considered. Abrahamsen et al. affirmed that in the most minimal quartile of riboflavin, B12, B6 and folate admission, BMD in MTHFR TT genotype is just altogether diminished, basically at the hour of menopause, and vitamin B supplementation would simply be expected to influence BMD in around 2% of the populace, for example, those with the TT genotype and low vitamin B consumption. They likewise noticed critical skeletal impacts of this normal polymorphism at lumbar spine in men at 25 years old years. Hong et al., they included 1899 Chinese postmenopausal ladies to confirm the relationship of the MTHFR polymorphism with BMD and cracks. They showed that the MTHFR C677T polymorphism is an autonomous indicator of break hazard, despite the fact that it just weakly affected BMD. Other than higher break hazard, low flowing degrees of vitamin B12 and folic corrosive are additionally connected with low BMD, which is in concurrence with the connection among HCY and BMD [10]. Baines et al. concentrated on the connection between plasma HCY, its determinant folate, vitamin B12, vitamin B6, MTHFR genotype and BMD in 328 postmenopausal ladies. As indicated by the standard BMD, the subjects were doled out to three gatherings of control, osteopenic and osteoporotic. The osteoporotic patients showed an altogether lower serum folate and a higher frequency of late crack. All in all, they observed that low serum folate is a significant gamble factor for osteoporosis, with HCY level having a lesser significance. The two nutrients B12 and B6, by influencing HCY, may likewise affect the skeleton, albeit a more fragile one than folate.

Conclusion

The identification of the link between brittle bone and cardiovascular disease will be aided by future advancements in healthcare and medicine. Given the limits of current research, designing the most trustworthy clinical trials would allow us to draw more accurate conclusions. When considering the many modes of action of HCY and the determinants of folate levels in serum or RBCs on bone, it is evident that more research is needed. Further research is needed to determine the relationship between oxidative stress, HCY, and osteoporosis. In future clinical trials, simultaneous assessment of osteoblast and osteclast indicators as well as BMD should be considered.

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