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Osteopenia and Osteoporosis in Patients with Hypertension: Age Related Co-morbidity, Causal Relationship or Both?

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ABSTRACT

A reduction in bone mineral density is a common age related disorder. The resultant ostopenia and osteoporosis is associated with considerable disability due to a marked propensity to develop fractures. Hip fractures are common in this population, and besides pain and discomfort, they also accelerate mortality. Since hypertension also is more prevalent in an aging population, it often coexists with these low bone mineral density disorders. Epidemiological and prospective studies indicate that osteoporosis and hypertension often share common risk factors. Newer data also suggests that they may be causally interlinked. Our research indicates a high prevalence of osteropenia and osteroporosis in patients with hypertension. Management options are affected when both conditions co-exist.

Keywords: hypertension, cardiovascular disease, osteoporosis, osteopenia, calcium, vitamin D, salt,

Abbreviations: ASH: American Society of Hypertension; BMD: Bone mineral density; DXA: Dual Energy X-ray Absorptiometry; HRT: Hormone replacement therapy; HTN: Hypertension; JNC-7: The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure.

1. INTRODUCTION

- Osteoporosis is a common disease – it is estimated that 200 million people worldwide suffered from osteoporosis in the year 2006.
- At least 1 in 3 women and 1 in 5 men will suffer from an osteoporotic fracture during their lifetime.
- Osteoporosis is a multi-factorial disease. Its relationship with hypertension is due to both, the aging process and interlinked patho-physiology.
- Lifestyle changes, salt restriction, vitamin D supplementation and thiazide diuretics may help improve both co-existing conditions.

Hypertension and osteoporosis are two common age-related disorders (Perea-Casstrillo et al. 2005). Hypertension is a major risk factor for adverse cardiovascular events, including strokes, ischemic heart disease and heart failure (Williams, 2009). It is also associated with increased cardiovascular mortality. Approximately 20% of the world's adults are estimated to have hypertension (Hajjar et al. 2006). In 2001, almost 54% of all strokes and 47% of all ischemic heart disease related deaths worldwide were attributable to systolic hypertension (Lawes et al. 2004; Williams, 2009). Clinical trials have shown that treating hypertension reduces the risk of these events (SHEP, 1991; MRC, 1985), and decreases cardiovascular mortality (Abegunde et al. 2007). Osteoporosis is also a common disease, with more than 200 million people suffering from it worldwide in the year 2006 (Reginster et al. 2006). Approximately 30% of all postmenopausal women have osteoporosis in the United States and in Europe. Osteoporosis markedly increases the risk of fractures. It is estimated that at least 1 in 3 women and 1 in 5 men will suffer from an osteoporotic fracture during their lifetime (IOF, 2013). The most common fractures occur in vertebrae, hips and distal arms (Melton et al. 2006, Nevitt et al. 1998; Cummings et al. 2002; Cooper et al. 1992; Owen et al. 1982; EPOS, 2002). And an initial fracture becomes a risk factor for a new fracture (Kanis et al. 2004; Melton III et al. 1999). Patients with osteoporosis have a 40 % combined lifetime risk of fractures – this equates with the risk of cardiovascular diseases (Nevitt et al. 1998). It is therefore, like hypertension, not a benign condition. This study looks at the prevalence of osteopenia and osteoporosis in a hypertensive population. Factors influencing this relationship are briefly discussed.

2. METHODS

We reviewed dual-emission X-ray absorptiometry (DXA) scans of 220 consecutive hypertensive patients. Hypertension had been diagnosed by standard blood pressure measurement techniques, using an appropriate-sized cuff at the level of the right atrium, with the patient rested for 5 minutes, and with the back supported. Systolic blood pressure was categorized as follows: Normal: less than 120/80 mmHg; Pre-HTN: 120 to 139/80 to 89 mmHg; HTN: 140/90 mmHg or greater: Stage 1: 140 to 159/90 to 99 mmHg, Stage 2: 160/100 mmHg or greater. All patients had been diagnosed with hypertension with at least 2 consecutive elevated BP measurements (≥140 mm Hg systolic and/or 90 mm Hg diastolic or ≥130/80 mm Hg in the presence of diabetes mellitus or chronic kidney disease). All patients were on lifestyle changes recommendations and conventional anti-hypertensive patients, consistent with JNC 7 (Chobanian et al. 2003) and ASH guidelines (Gradman et al. 2010). Bone mineral density (BMD) was measured at the hip and spine. T scores were considered normal between +1 and -1. T scores were classified as osteopenia between -1 and -2.5 and osteoporosis if lower than -2.5 (NOF, 2013).

3. RESULTS

Of the 220 patients with hypertension, there were 123 (55.9%) males and 97 (44.1%) females. Their ages ranged from 20 years to 87 years. Of these patients, 102 (46.4%) [67 (65.7%) males; 35 (34.3%) females] had normal T scores. 118 (53.6%) [56 (47.5%) males; 62 (52.5%) females] had abnormal T scores. Of the 118 with abnormal T scores, 75 (63.6%) [35 (46.7%) males; 40 (53.3%) females] had T scores consistent with osteopenia (-1 to -25) and 43 (36.4%) [20 (46.5%) males; 23 (53.5%) females] had T scores consistent with osteoporosis (less than -25), (Figure 1).

4. DISCUSSION

Several dietary, hormonal, environmental, lifestyle and genetic factors play a role in the patho-physiology of osteoporosis and its relationship to hypertension.

4.1. The role of calcium

Over 64 observational studies have found a positive association between an elevated calcium intake and increased bone mass, reduced age related bone loss and a decrease in osteoporotic fractures (Robert et al. 2000). Although evidence strongly connects high dietary calcium intake with healthier bones (Cumming et al. 1990; Welton et al. 1995) calcium supplementation may not help if osteoporosis is already established. Associated supplementation with vitamin D and targeted osteoporosis treatment is often needed in these patients. Calcium supplements, with or without vitamin D tend to increase the risk of myocardial infarction and stroke, (Bolland et al. 2010). and this danger should play a role in the therapeutic decision.

4.2. The role of Vitamin D

Vitamin D helps in the absorption of calcium (IOM, 2010). Higher intakes and adequate levels of vitamin D are associated with protection from osteoporosis, (Nieves et al. 2008) and hip fractures (Feskanich et al. 2003). Vitamin D supplementation has a beneficial effect on BMD, and reduces the risk of falls and fractures. Supplementation also appears to be extremely safe (Cranney et al. 2007).

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4.3. The role of Vitamin K

The protective role of Vitamin K in preserving bone mineral density and preventing fractures has been shown by several epidemiologic and intervention studies. Vitamin K dependent proteins are also involved in bone metabolism, besides the major role they play in blood coagulation. Vitamin K supplementation improves the bone turnover profile and decreases the level of circulating under carboxylated osteocalcin. Vitamin K drugs like phytonadione and menaquinone may play a beneficial role in the prevention and treatment of osteoporosis (Adams et al. 2005). Coumarin based anticoagulants may deleteriously affect vertebral BMD and fracture risk in the long term. Anticoagulated patients should therefore be assessed for osteoporosis risk, and advised proper diet and supplements for a healthy bone health (Pearson et al. 2007).

4.4. The role of salt

Epidemiological studies have established the role of salt intake in the pathogenesis of osteoporosis (Jones et al. 1997; Caudarella et al. 2009). A high salt intake is associated with increased calcium excretion in the urine. The resultant calcium loss induces a negative calcium balance predisposing to osteoporosis (Itoh et al. 1999; Burger et al. 2000). Dietary salt reduction in hypertensive patients helps reduce urinary sodium and calcium excretion and thereby prevents bone loss (Woo et al. 2009; Devine et al. 1995).

4.5. The role of hormonal factors

Estrogen regulates bone mineral density by their pro-osteoblastic and anti-osteoclastic effects (Krum et al. 2008). The Womens Health Initiative demonstrated in 2002 a reduction in osteoporotic fractures with hormone replacement therapy (Rossouw et al. 2002). However, HRT has been associated with an increased risk of breast cancer, venous thromboembolism and cardiovascular events. HRT is therefore usually prescribed to younger women with early menopause and osteoporosis.

Androgens in men are also bone protective, stimulating bone formation and inhibiting bone resorption (Vanderschuren et al. 2008). They help in the maintenance of cancellous bone mass and expansion of cortical bone (Vanderschueren et al. 2004). Androgens also increase muscle mass and strength, (Notelovitz et al. 2002) preventing falls and related fractures. Older hypogonadal males may therefore benefit with androgen replacement therapy in cases of osteoporosis, reduced muscle strength and increased risk of falling (Mosekilde et al. 2013).

4.6. The role of race

Racial differences have been noted with osteoporosis. In general, Asians have more vertebral osteoporosis than Caucasians (Ross et al. 1991). Caucasians have more hip fractures than Asians, due to structural differences in the femurs, and more than African Americans, who have a greater bone mass (Aloia et al. 1998; Faulkner et al. 1993). Aboriginal Canadians also suffer from higher fracture risks (Leslie et al. 2005).

4.7. The role of environmental factors

Lack of access to dairy foods and associated low calcium intake has been associated with lower bone mass and higher hip fracture rates seen between two rural districts of Croatia (Matkovic et al. 1979). Lack of exposure to sunlight has also been suggested as a reason behind the strong association between vitamin D insufficiency and hip fractures (Leif et al. 2005; Glerup et al. 2000). Poor nutrition resulting in a low BMI is also a risk factor for fractures (De et al. 2005) and osteoporosis (Morin et al. 2009; Meyer et al. 1998; Ricci et al. 1998). Several studies have linked osteoporosis to low income people (Leslie et al. 2005; Brennan et al. 2009).

4.8. The role of lifestyle factors

Besides an improper diet and inadequate intake of various nutritional factors, (Nieves, 2005) smoking and lack of exercise also play an important role in the etiology of osteoporosis. Physical activity helps regulate bone maintenance and stimulate bone formation. There is an added benefit of strengthening muscles, improving balance, and a reduced overall risk of falls and fractures (Borer, 2005). Weight bearing exercise helps mechanical loading on the skeleton. This further helps increase and preserve bone mass (Hata et al. 2003). Tobacco consumption has been associated with a reduction in BMD in both sexes (5-8%), irrespective of calcium intake or body weight (Nguyen et al. 1994).

4.9. The role of genetics

Genetic factors appear to be the most important factor in the pathogenesis of osteoporosis and may control up to 80% of its variance. They influence both the peak bone mass and the rate of change in bone density. Osteoporosis is a polygenic disorder, determined by the effects of several genes, each with relatively modest effects on bone mass and other determinants of fracture risk. The vitamin D receptor gene - VDR, (Ozbas et al. 2012) the collagen type I alpha I

gene - COLIA1 (Grant et al. 1996) and the estrogen receptor gene (ER) alpha have been widely investigated and found to play a role in regulating BMD (Williams et al. 2007). Polymorphisms in and around the genes encoding interleukin-6, tumor necrosis factor beta and the estrogen receptor have also been associated with bone mass variations in some populations. Detection of a genetic predisposition to osteoporosis should allow for early intervention in order to delay or prevent the negative ramifications of this disease.

4.10. The role of hypertension

Research data suggests that osteoporosis and hypertension share common abnormalities in calcium metabolism. Hypertensive patients often have lower calcium intake and reduced vitamin D levels. Hypertensive patients also have higher salt intakes and tend to excrete higher amounts of calcium in their urine for a given sodium intake. This results in secondary hyperthyroidism. Angiotensin II also stimulates the formation of osteoclasts, thereby decreasing bone density.

4.11. The role of anti-hypertensive medications

Given the association of increased salt intake and the associated excessive urinary loss of calcium (Caudarella et al. 2009; Wasnich et al. 1983) thiazide diuretics appear to be helpful as they decrease the obligatory urinary calcium loss (Ray et al. 1989; LaCroix et al. 1990). Studies also show that activation of RAS induces accelerated bone resorption. There is also some suggestion that ACE inhibitors may improve bone metabolism (Shimizu et al. 2009; Hideo et al. 2008). Beta blockers may also play a role in the prevention of osteoporosis, (Schlienger et al. 2004) although conclusive human studies are lacking.

5. CONCLUSION

Our data suggests that osteopenia and osteoporosis is extremely common in hypertensive patients. With prolongation of the average life span this co-morbidity is becoming a major public health problem. T scores consistent with osteopenia were found in approximately 34% and those consistent with osteoporosis were found in approximately 20% of our hypertensive population. The presence of low bone mineral density in more than one half our hypertensive patients prognosticates a worse clinical course. Anti-hypertensive treatment, preferably including a thiazide diuretic, combined with strategies to prevent and treat osteopenia and osteoporosis may further help improve the quality of life and prognosis in these patients.

SUMMARY OF RESEARCH

The frequent co-existence of osteoporosis and hypertension is not surprising as they both increase in prevalence as people get older. However scientific studies indicate that there may also be a causal association between the two. Since both increase the risk of major deleterious events, their combined presence demands a much more aggressive and a much more specific approach in management.

FUTURE ISSUES

1.Can new pharmaceutical agents target both osteoporosis and hypertension?
2.Do pre-hypertension and osteopenia co-exist? What are the clinical implications?

DISCLOSURE STATEMENT

The author has no conflicts of interest to disclose.

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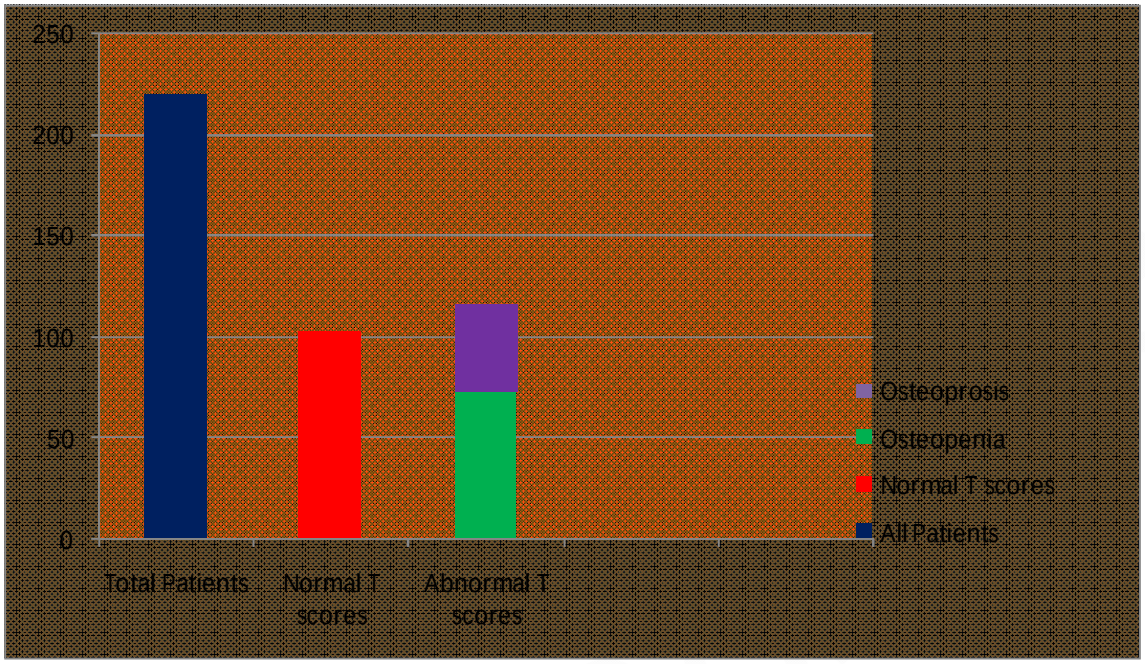

Figure 1

Distribution of T scores in patients with hypertension

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