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Mini-Review

Osteoporosis in chronic kidney disease; a mini-review on current knowledge

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Abstract

In patients with end-stage kidney failure (creatinine clearance <10 mL/minute, including patients receiving dialysis) because of higher risk for hypercalcemia after calcium and vitamin D administration and for hypocalcemia after denosumab administration, serum calcium, phosphorus, 25-hydroxyvitamin D, and parathyroid hormone levels should be measured after four months of calcium prescriptions and approximately 10 days after denosumab administration. In patients with estimated glomerular filtration rate <30 mL/minute and fragility fracture, if there is no evidence of metabolic bone disease, after initiation of osteoporosis therapy, measurement of bone mineral density at beginning and two years after later may be helpful for monitoring of response to therapy.

Keywords: Osteoporosis, Kidney, Vitamin D

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Introduction

Osteoporosis is a common disease that is characterized by low bone mass with micro architectural disruption and skeletal fragility, resulting in an increased risk of fracture (1,2). In chronic kidney disease, changes in calcium and phosphorus and vitamin D metabolism lead to derangement of bone structure and architecture and progress with worsening of kidney function and lead to osteoporosis and fractures (1-4). In fact, end-stage kidney failure increases risk of fragility fractures. Measurement of bone mineral density (BMD) by dual energy x-ray absorptiometry (DXA) is the standard method of diagnosing osteoporosis but it is uncertain whether, BMD by DXA can be useful for prediction of fracture risk in end-stage kidney failure patients. In end-stage kidney failure patients with fracture, BMD at the lumbar spine and radial reigns (one-third of distal radius), were significantly lower than end-stage kidney failure patients without fracture but not at the femoral neck (1-5). Although DXA is the preferred technique to assess BMD in patients with and without chronic kidney disease, DXA estimates areal BMD and not volumetric BMD (2-7). It also cannot distinguish between cortical and trabecular bone, and do not assess bone microarchitecture or bone turnover. Therefore high resolution micro-CT and micro-MRI, allow noninvasive three-dimensional evaluation of bone microarchitecture. Therefore, BMD (DXA) testing is not routinely performed to assess fracture risk in patients with chronic kidney disease and estimated glomerular filtration rate <30 ml/minute except, who have fragility fracture and no evidence of metabolic bone disease, including renal osteodystrophy (2-9). In patients with chronic kidney disease and estimated glomerular filtration rate ≥30 mL/minute, the WHO criteria for BMD (T-score -2.5) or the presence of a fragility fracture can be used for the diagnosis of osteoporosis. In patients with advance chronic kidney disease (estimated glomerular filtration rate <30 ml/minute), the bone metabolism disorder are more profound and prevalent, therefor WHO-BMD criteria for the diagnosis of osteoporosis usually cannot be applicable (4-10).

According to this findings, diagnosis of osteoporosis in stages 4-5 chronic kidney disease who have low T-scores or history of a fragility fracture suggested by excluding chronic kidney disease-metabolic bone disease, especially renal osteodystrophy (1-8). In these patients measurement of bone specific alkaline phosphatase and serum calcium, phosphorous, parathyroid hormone,

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Implication for health policy/practice/research/ medical education

In chronic kidney disease, changes in calcium and phosphorus and vitamin D metabolism lead to derangement of bone structure and architecture and progress with worsening of kidney function and lead to osteoporosis and fractures.

and 25-hydroxyvitamin D should be considered to prevent or manage renal osteodystrophy and controlling secondary hyperparathyroidism and also preventing of parathormone over-suppression and adynamic bone disease , in addition to treating acidosis and calcium and vitamin D deficiency (5-12). When parathormone levels has received to six times or more above its normal limit, it is frequently associated with features of severe parathyroid bone disease (osteitis fibrosa cystic), however, in oppose to this data, if the parathyroid hormone is <150 pg/ml, there is a strong prediction of about 85% for suggestion of renal adynamic bone disease, and if this level received to <100 pg/ml especially whit low serum alkaline phosphates, the possibility increases to over 90% and should be managed prior to initiating osteoporosis therapy (3-12). In patients with chronic kidney disease, calcium and phosphorus usually remain normal until GFR received to 25 to 40 ml/minute in which hypocalcaemia is predictable until adynamic bone disease has accrued and makes patients hypercalcemic, also 25-hydroxyvitamin D deficiency is a common finding due to lack of its synthesize in the kidney tissue especially in the estimated glomerular filtration rate less than 40 ml/minute. Biochemical markers of bone turnover usually cannot be used because these markers in advanced chronic kidney disease (estimated glomerular filtration rate <30 mL/minute), are not cleared by the kidneys (2-12).

Various evidences, prefer measurement of bone specific alkaline phosphatase (BSAP), tartrate resistant acid phosphatase (TRAP5b, an osteoclast cellular marker), and the trimeric propeptide type I collagen (PINP) which are not cleared by kidney, in them bone specific alkaline phosphatase is the most valuable as mentioned previously (4-10).

Treatment

Lifestyle changes, including exercise, avoidance of smoking, avoidance of alcohol intake, and fall prevention particularly in estimated glomerular filtration rate <15 mL/minute are necessary in all of patients at high risk for fracture because patients with advance chronic kidney disease often have sarcopenia, a condition of muscle mass deficiency and weakness and recurrent falling (5-14). An appropriate diet for the prevention of fracture includes an adequate intake of calories (to avoid malnutrition), calcium, and vitamin D which include a total calcium intake (diet plus supplement) of 1200 mg/day, with 500 mg/day of which provided by calcium supplements and about 800 international units of vitamin D (cholecalciferol or ergocalciferol) daily (5-15).

Hormone replacement therapy

Estrogen is used for prevention of osteoporosis in premenopausal women with chronic kidney disease and amenorrhea without need to dose adjustment. If resumption of menses is unlikely, estrogen therapy is usually the preferred treatment, but in postmenopausal women increases in the incidence of breast cancer, coronary heart disease, stroke, and venous thromboembolism make this strategies undesirable (7-16).

Pharmacologic therapy

Treatment of osteoporosis in patients with estimated glomerular filtration rate ≥30 mL/minute is not different from those in postmenopausal women and older men without chronic kidney disease and can be measured by use of bisphosphonates, which can reduce the risk of fracture in this patients (with estimated glomerular filtration rate ≥30 ml/minute or ≥35 for zoledronic acid) if there is any biochemical evidence for chronic kidney disease-metabolic bone disease (CKD-MBD), with any reduction in dose of prescribed bisphosphonates (1-9). In patient with stages of 4-5 of chronic kidney disease (estimated glomerular filtration rate <30 ml/ minute) or on dialysis, efficacy and short-term safety of oral bisphosphonates, and denosumab examined. Some experts advised that in the patient with estimated glomerular filtration rate <15 ml/minute (stages of 4-5 of chronic kidney disease) and osteoporotic fracture, in whom the risk of recurrent fracture and mortality are high, if biochemical tests or bone biopsy roll out metabolic bone disease, a bisphosphonate, preferably risedronate 35 mg every other week, for not more than three consecutive years, recommended and reasonable. However, all of these drugs typically contraindicated in estimated glomerular filtration rate <30 ml/minute in usual situations, but if we have no other options, and the patient was at the high risk of recurrent fracture we can use denosumab (4-18). Denosumab is a good choice in patients with stages of 4-5 of chronic kidney disease (estimated glomerular filtration rate <30 ml/minute) or on dialysis with estimated glomerular filtration rate between 15 and 30 ml/minute because it is not cleared by the kidney and has a reasonable efficacy, but it is not known whether denosumab can prevent metastatic vascular calcification. Raloxifene and calcitonin, are not advocated to use in stage 4 of chronic kidney disease because it is not showing that they have a benefit for reducing non-vertebral fracture. In addition, raloxifene increases the risk of thromboembolism. If an

oral bisphosphonate or denosumab is contraindicated or not tolerated, an intravenous bisphosphonate (usually contraindicated with estimated glomerular filtration rate <35 ml/minute) could be considered especially in patients whit higher risk for recurrent fracture and mortality (11-19). In this group of patients, use of a slower infusion rate (60 minutes) can lower the risk of kidney injury and should not be prescribe more than three years. In patients with evidence of CKD-MBD, there is no effectiveness for any osteoporosis treatment to reduce risk of fracture. There are no differences in the side effects occurrence between patients with normal or impaired renal function in the risedronate group and there are no increase in serum creatinine in them. Thus, oral bisphosphonates appear to be effective in individuals with moderately reduced renal function (10-22). There are few patients in the zoledronic acid postmenopausal group with an estimated glomerular filtration rate below 30 ml/minute to provide strong data on use of this bisphosphonate in severely compromised chronic kidney disease patients and occurrence of acute kidney injury is a rare but serious side effect after use of zoledronic acid, especially in patients with moderate to severe renal failure. Intravenous zoledronic acid (5 mg) increased their serum creatinine concentration as twice 9 to 11 days after the 15-minute infusion, but the serum creatinine came back to previous level before the next annual infusion (3-15). Ibandronate is another members of this group given as 3 mg infusion during 15 minutes or as an injection every three months and was compered whit oral alendronate (70 mg weekly) in postmenopausal women whit moderate renal disease (<30 ml/minute estimated glomerular filtration rate <60 ml/minute), the efficacy of both drugs are similar and there was no differences between their side effects especially on the glomerular filtration rate of the patients (8-16).

Denosumab

While, it is not exerted by the kidneys, there for no contraindication and restriction of its use in creatinine clearances below 35 ml/minute is considered. Denosumab is an effective drug in reduction of fracture risk and any major adverse effects was reported whit its use especially any prominent changes in glomerular filtration rate of patients but it is not clear that in patients whit estimated glomerular filtration rate <15 ml/min it has a prominent effect in reduction of fracture risk but this drug is effective and safe in glomerular filtration rate >15 ml/min (6-18).

Teriparatide

Although parathyroid hormone 1-34 (teriparatide) is effective in increasing bone mineral density and reduction of fracture risk, there are no data about efficacy of teriparatide in patients with end-stage kidney failure and glomerular filtration rate <10 ml/min (10-19).

Raloxifene

Raloxifene is an effective but a little weaker than antiresorptive drugs in prevention and treatment of osteoporosis especially in patients whit breast cancer. In the women with glomerular filtration rate <45 ml/minute, and even glomerular filtration rate <30 ml/minute, in comparison with placebo, raloxifene improved BMD and reduced vertebral fractures and incidence of adverse events were similar between raloxifene and placebo, there for it may be a reasonable choice in patients whit end-stage kidney failure (11-20).

Monitoring of therapy

In patients with end-stage kidney failure (creatinine clearance <10 ml/minute, including patients receiving dialysis) because of higher risk for hypercalcemia after calcium and vitamin D administration and for hypocalcemia after denosumab administration, serum calcium, phosphorus, 25-hydroxyvitamin D, and parathyroid hormone levels should be measured after four months of calcium prescriptions and approximately 10 days after denosumab administration. In patients with glomerular filtration rate <30 ml/minute and fragility fracture, if there is no evidence of metabolic bone disease, after initiation of osteoporosis therapy, measurement of BMD at beginning and two years after later may be helpful for monitoring of response to therapy (12-25).

Author's contribution

HM is the single author of the paper.

Conflict of interests

The author declared no competing interests.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the author.

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