MP665

DENOSUMAB FOR FEMALE HEMODIALYSIS PATIENTS WITH LOW BONE MINERAL DENSITY, A CASE CONTROL STUDY FOR TWO YEARS

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INTRODUCTION AND AIMS: Low bone mass is a world public health concern that results in increased risk of fractures. Denosumab is a monoclonal antibody against the receptor activator of nuclear factor-κβ ligand (RANKL), a cytokine that is essential for the formation, function, and survival of osteoclasts. By binding RANKL, denosumab prevents the interaction of RANKL with RANK on osteoclasts and reversibly inhibits osteoclast-mediated bone resorption. Renal function impairment does not significantly affect the pharmacokinetics and pharmacodynamics of denosumab. (JBMR 27 2012 1471-1479) However, there have been few reports on denosumab use in dialysis patients. This was an observational retrospective case control study.
We treated female hemodialysis patients with low bone mineral density (BMD) in Saiyuu Kawaguchi Clinic with Denosumab for two years, and evaluated the effects on radius BMD.

Table 1. Baseline characteristics.

	Densumab	Control	P
N	17	15	
Age (years)	74.6 ± 10.9	69.4 ± 8.0	NS
Duration of HD (years)	8.5 ± 5.9	10.6 ± 6.1	NS
BMD (% of young adult mean)	49.6 ± 10.2	52.2 ± 12.1	NS

Table 2. Baseline parameters of patients

	Denosumab	Control	P
Corrected Ca mg/dl	9.3 ± 0.3	8.9 ± 0.5	NS
Phosphate mg/dl	5.5 ± 1.0	4.6 ± 1.0	NS
Whole PTH pg/dl	138 (64.5 to 255)	127 (55 to 232)	NS
ALP U/l	323 ± 183	152 ± 104	NS

Median and interquartile range were shown for whole PTH.
Reference range of ALP is 115 to 359 U/l.

Table 3. Ca and whole PTH in the course of the treatment

	Corrected Ca mg/dl	whole-PTH pg/dl
Before the 1st dose	9.3 ± 0.3	138 (64.5 to 255)
Before the 3rd dose	9.7 ± 0.8	192 (119 to 281)
Before the 5th dose	10.3 ± 0.7	89 (42.5 to 150.5)

Median and interquartile range were shown for whole PTH.

Table 4. BMD change from the baseline

	1 year (%)	2 year (%)
Denosumab	5.2 ± 6.6	3.9 ± 6.0
Control	-5.4 ± 5.7	-7.4 ± 7.0
P	P<0.001	P<0.001

METHODS: Thirty one female hemodialysis patients with low BMD (less than 70% of young adult mean) were enrolled. Patients were excluded if they had taken condition that influence bone metabolism or taken bisphosphonates, parathyroid hormone, corticosteroids, or selective estrogen-receptor modulators. Patients were excluded if they had active peptic ulcer, abnormal hepatic function, malignant disease, past history of severe brain stroke or past history of parathyroidectomy.
Seventeen patients (mean age 74.6 ± 10.9 year old, BMD 49.6 ± 10.2 % of young adult mean) were treated with denosumab 60 mg every six months, and fourteen patients (mean age 69.4 ± 8.0 year old, BMD 52.2 ± 12.1 % of young adult mean) were not treated with denosumab (control group) (Table1. 2).
BMD at distal third of radius was measured by X-ray absorptiometry on a DTX-200 densitometer. Dialysates with a calcium content of 2.5 mEq/l were used. A combination of calcium-based phosphate binder, sevelamer, lanthanum carbonate hydrate, calcitriol, alfacalcidol and cinacalcet were titrated according to the serum calcium or phosphate levels.

RESULTS: All results were expressed as mean (± standard error) or median (interquartile range) value. The administration of the drug was clinically well tolerated. Corrected serum calcium before treatment was 9.3 ± 0.3 mg/dl, 9.7 ± 0.8 mg/dl at 12 months, and 10.3 ± 0.7 mg/dl at 24 months. Whole PTH before treatment was 138 (64.5 to 255) pg/ml, 192 (55 to 232) at 12 months, and 89 (42.5 to 150.5) pg/dl at 24 months (Table 3). Episodes of hypocalcemia associated with PTH increase were seen, but easily overcome by increase carbonate calcium, calcitriol or alfacalcidol.
At one year, BMD at the distal third of radius increased 5.2 ± 6.6% in donosumab group and decreased 5.4 ± 5.7 % in control group (P<0.001). At two year, BMD increased 3.9 ± 6.0% in denosumab group and decreased 7.4 ± 7.0% in control group (P<0.001)(Table 4).

CONCLUSIONS: In this observational study, denosumab that was administered subcutaneously every 6 months resulted in an increase in distal third of the radius bone mineral density in female hemodialysis patients.
Further studies are needed in order to establish denosumab use in the treatment and prevention of hemodialysis patients with low BMD.

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