Preoperative bisphosphonate treatment in patients with neuromuscular scoliosis improves bone strength of vertebral body

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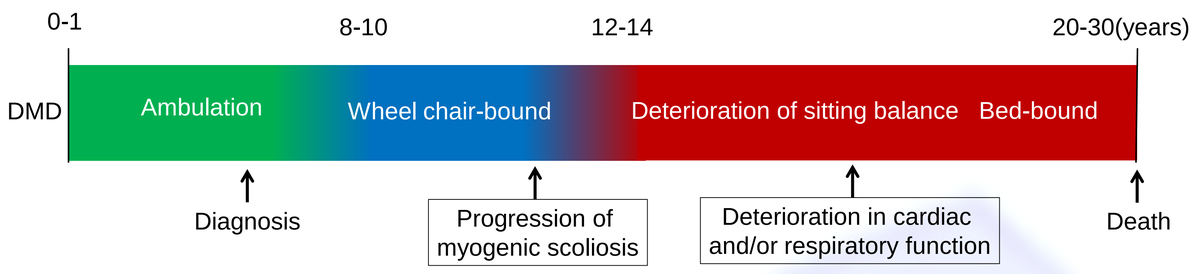
Introduction

- Boys with muscular dystrophy as presented by Duchenne muscular dystrophy (DMD) lose muscle strength and are usually confined to a wheelchair by the age of 12-14.
- Glucocorticoid (Deflazacort) therapy is widely used to extend the ambulatory periods and to prevent scoliosis. If myogenic scoliosis develops after wheelchair-bound life, scoliosis surgery is necessary to acquire the sitting balance.



Osteoporosis is one of the major concerns to perform scoliosis surgery. Patients with DMD or congenital muscular dystrophy (CMD) have fragile bones due to loss of ambulation, glucocorticoid therapy and DMD itself.

Objectives

1) To investigate bone mass and bone metabolism in patients with muscular dystrophy
2) To verify the efficacy and safety of preoperative bisphosphonate (BP) treatment for osteoporosis associated with myogenic scoliosis

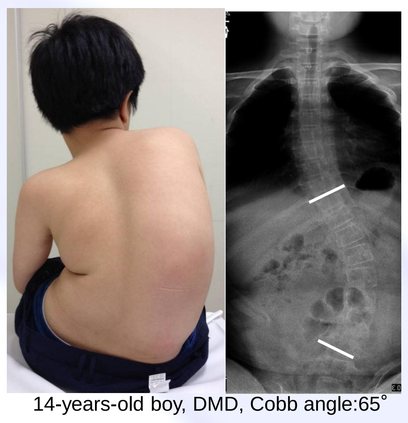
Subjects & Methods

Non-ambulatory boys with muscular dystrophy who had scoliosis surgery were preoperatively administered oral BP (Alendronate 35mg) once a week.
BMD and bone turnover markers were measured before and after BP treatment.

Patients demographics

Number of the patients	12
Age(years)	14.4 ± 1.6
Body weight (kg)	31.1 ± 9.0
Type of muscular dystrophy (cases)	DMD：9, CMD：3
Presence of prevalent fracture	25% (3/12) Femur: 2 cases Humerus: 1 case Vertebrae: 0 case
Previous history of therapy with glucocorticoid	0%(0/9)
Duration of BP treatment (days)	160 ± 53 (85-280)

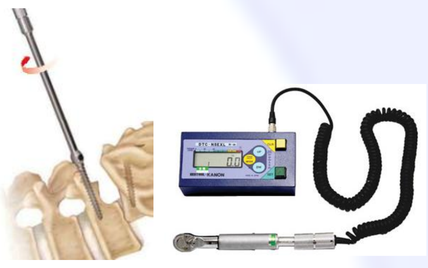
Values are shown as means ± SD.



14-years-old boy, DMD, Cobb angle:65°

Clinical assessments

- ***BMD***
  L2-4, Whole body (T-spine, L-spine, Pelvis)
- ***Bone turnover markers***
  Bony ALP, P1NP, TRACP-5b
- ***Pedicle screw fixation strength***
  Pedicle screw insertional torque during operation



(Digital torque meter DTDK-N5EXL, KANAON)

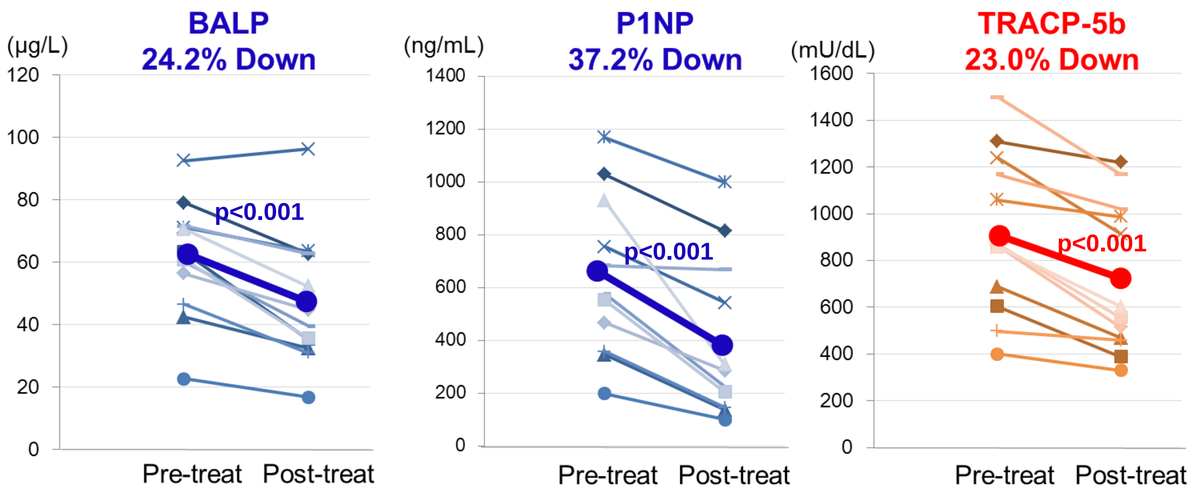
Results

Result 1. ***Non-ambulatory boys with muscular dystrophy had severe bone loss, and BP treatment significantly increased spine BMD.***

	Pre-treatment BMD (g/cm²)	Post- treatment BMD (g/cm²)	Rate of change	*p* value
L2- 4 (Z-score)	**0.50 ± 0.10 (- 4.3 ± 1.9)**	**0.54 ± 0.12 (- 4.1± 1.9)**	**6.5%↑**	**p= 0.02**
T-spine	0.50 ± 0.07	0.54 ± 0.08	**7.5%↑**	**p=0.01**
L-spine	0.58 ± 0.09	0.62 ± 0.10	**6.9%↑**	**p=0.03**
Pelvis	0.47 ± 0.09	0.48 ± 0.09	4.2%↑	p=0.15

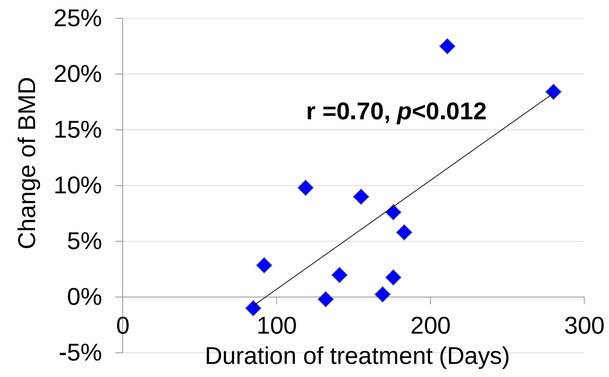
Paired t-test: p<0.05, significant difference

Result 2. ***BP treatment significantly decreased bone turnover.***



Paired t-test: p<0.05, significant difference

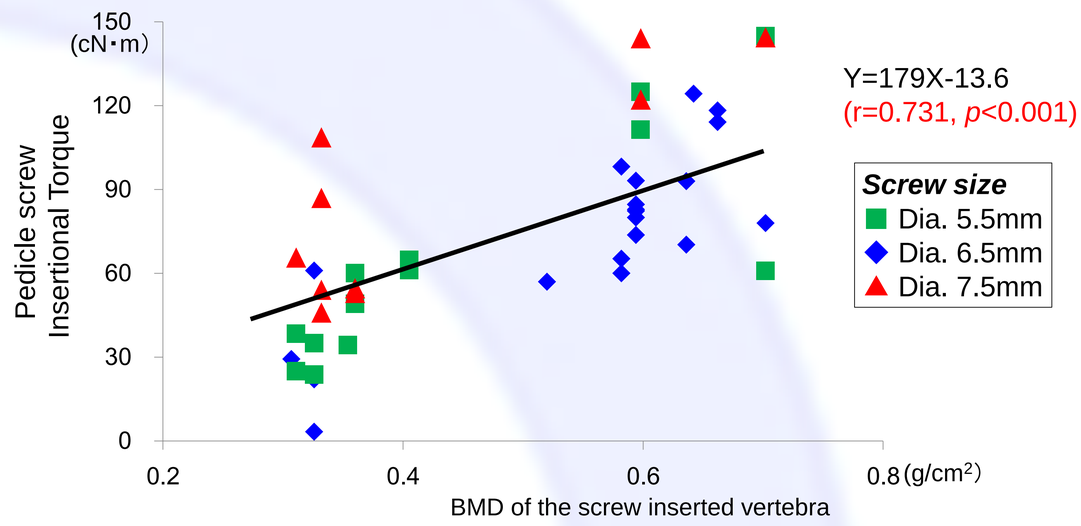
Result 3. ***As the duration of treatment was longer, BMD increased further. There were no incident osteoporotic fractures during BP treatment.***



Result 4. ***All patients could continue to use BP without any adverse effects.***

Adherence: 100%, no adverse effects such as gastrointestinal tract disturbance

Result 5. ***As spine BMD increased, higher fixation strength of pedicle screw was obtained.***



<Preliminary calculation>

	Pre- treat	Post- treat	Rate of change
BMD (X)	0.50 g/cm²	0.54 g/cm²	**6.5%↑**
Torque (Y)	75.9 cN·m	83.1 cN·m	***9.5%↑***

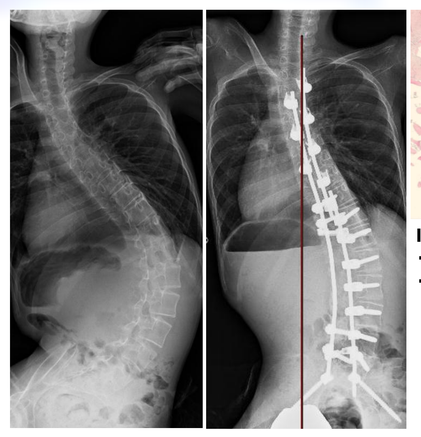
Case Presentation

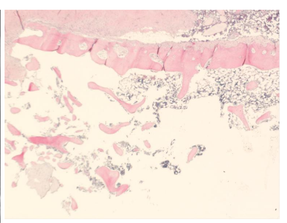
15-years-old DMD boy

- Height: 156cm, weight: 25kg
- Non-steroid user
- Non-ambulatory at the age of eight
- Difficult to keep sitting at the age of fourteen
- Duration of treatment: 183 days

BMD	Pre-treat BMD (g/cm²)	Post- treat BMD (g/cm²)	Rate of change
L2-4	0.311	0.330	5.8%↑
T- spine	0.370	0.405	7.3%↑
L-spine	0.443	0.453	6.9%↑
Pelvis	0.322	0.344	5.5%↑

Bone turnover markers；
BALP: 21%↓, P1NP: 39%↓, TRACP-5b: 40%↓





Iliac bone biopsy (HE stain)
- Severe cortical porosity
- Less connectivity of trabecula

Discussion

- Several studies showed the efficacy and safety of BP for osteoporosis associated with DMD.

	Subjects (N)	Age (years)	GCs	BP	Route	Duration	Pre-treat BMD (Z score)	Change of BMD (Δ Z score)	AE
Gillianet et al (2005)	DMD16	10.8	User	Alendronate 2.5~5mg/day	p.o.	2 years	-1.9	-.0.04SD	Sever AE: None
Sborocchi et al (2012)	DMD7	11.6	User (6/7)	Pamidronate Zoledronate	i.v.	2 years	-2.1	+0.5SD	Acute reaction after 1st injection
This study	DMD9 CMD3	14.4	Non - user	Alendronate 35mg/week	p.o.	160 days	-4.4	+0.2SD	None

GCs: glucocorticoids, SD: standard deviation, AE: adverse effect.

- BP treatment improves the survival rate in DMD patients with glucocorticoids.

Gordon KE et al., Pediatrics (2011) e353-358.

- BP should be considered as a treatment option with due caution for severe osteoporosis associated with DMD.

Bianchi ML et al., Neuromuscular Disorders (2011) 298-303.

Conclusions

- **Twelve patients with muscular dystrophy had severe osteoporosis with high bone turnover, and BP treatment significantly increased spine BMD and decreased bone turnover without any adverse effects.**
- **Improvement of bone fragility by preoperative BP treatment will secure success in surgical treatments for myogenic scoliosis.**

Disclosure

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- None of the authors has any financial interest with any of the commercial entities.
- All authors state that they have no conflicts of interest.