Bisphosphonates therapy in girls with Rett syndrome and bone fragility

Anne-Sophie Lambert[1] Anya Rothenbuhler[1], Perrine Charles[2], Elisabeth Celestin[3], Nadia Bahi-Buisson[3], Agnès Linglart[1].

1. APHP, CMR Calcium-Phosphore, Bicêtre Paris Sud, France
2. APHP, Pitié-Salpetrière, Paris, France
3. Rett Center, Necker-Enfants Malades, Paris, France

BACKGROUND

Rett Syndrome (RS) is a disabling condition due to mutations in *MECP2*.

Girls affected with RS are at risk of developing osteoporosis and fractures at a young age because of their lack of mobility and though a direct effect of MECP2 on bone mineralization.

In these girls, bone fragility inflicts pain and may seriously impair the quality of life.

OBJECTIVE

To retrospectively assess the effect of pamidronate (T) on fractures, bone mineral density (BMD) and bone markers in RS girls with bone fragility.

METHODS

Once diagnosed with bone fragility (Z-score <-2DS + fracture and/or bones pain), RS girls with a mutation in MECP2 received 1.5 mg/kg of pamidronate IV every 3 months for 2 years.
The study lasted from January 1st 2009 to august 31th 2016
Total median (SD) dose received: 9.4 (2.8) mg/kg

RESULTS

Population

16 patients : median age 9.5 years (min 6 – max 42)

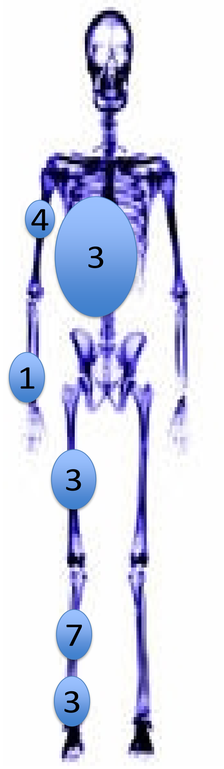
Risk factors for bone fragility:

- *Nutrition*: 9/12 undernourrished: mean BMI:- 4.2 SD (min -5 ; max 0)
  Vit D supplementation: mean 25OHD: 41 ng/ml (18-74)
- Exposition to sodium valproate 10/12 patients
- Pubertal development: 3/12 primary amenorrhea ; 4/12 pubertal delay.
- Ambulatory status: 16/16 not ambulatory

Pain and Fractures

25 fractures in 16 patients
13/16 patients with chronic pain

Patients	Number of Fractures before T	Number of fractures > 6 months before T	Number of fractures < 6 months before T
16	25	9	16

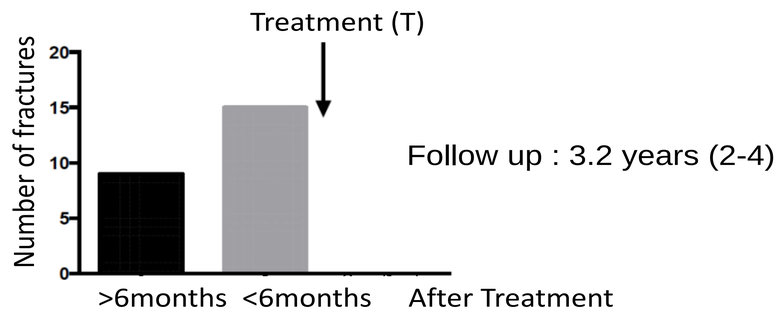


DXA BMD Z-score Spine
Z-score : -3 DS (- 2 ; - 4)

Bone markers
Elevated urinary calcium excretion (calciuria/creatininuria) in 16/16 : median 0.6 (min 0.2 ; max 1.5)(N<0,5)

Treatment

Fractures



Mobility

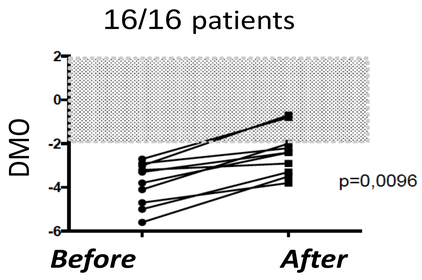
2 patients started to walk around the end of the 2-years therapy.

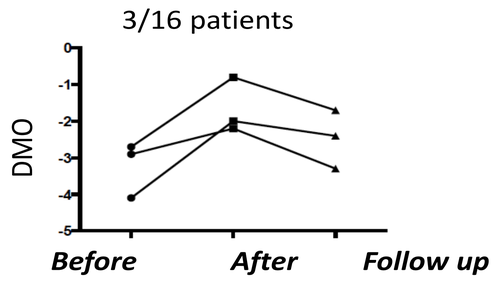
Most parents reported a decrease in chronic pain

Safety

Except for moderate hypocalcemia (4/16) and fever (2/16) pamidronate was well tolerated in all girls.

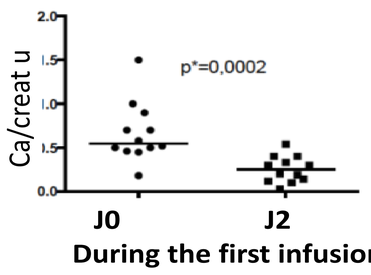
DXA BMD Z-score

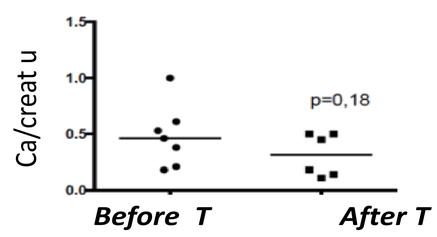




Follow up : M: 3.2 years (2-4)

Urinary calcium excretion





Conclusion:

Our results are in accordance with the beneficial effect of bisphosphonates in children with cerebral palsy and bone fragility. Impaired bone mineralization in RS girls should be screened for and prevented through measures including vitamin D supplements, nutritional support and careful mechanical loading. In girls undergoing fractures, IV bisphosphonates may be an adjuvant treatment to diminish the risk of recurrent fracture, improve bone pain and restore the bone density.

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