Osteoporosis-osteopenia therapy

Bisphosphonate therapy

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Background

Patients with cystic fibrosis are at high risk for early bone loss, which may cause fractures. Prevalence of CF-related bone disease (CFBD) is described in 24% of the adult population and has also been reported in the pediatric population (Braun C, 2016). Lung transplant recipients with CF remain at risk of skeletal fragility despite prompt initiation of post-transplant anti-osteoporosis therapy (Durette G, 2021). CFBD is probably directly related to the CFTR defect itself, but is also worsened by vitamin D, vitamin K and calcium deficiency, poor nutritional status, inactivity resulting in decreased weight bearing, diabetes mellitus, sex hormone deficiency and frequent use of glucocorticoid therapy. Moreover, chronic pulmonary inflammation leads to elevated levels of circulating cytokines, which promote bone resorption and suppress bone formation. New radiological tools, such as high-resolution peripheral quantitative computed tomography, allow an accurate evaluation of cortical and trabecular bone micro-architecture in addition to compartmental density (Braun C,2016).

Bone disease treatment (Putman MS, 2019) (Ullal J, 2021) and etiology (Gur M, 2020) have been discussed about current knowledge and future directions. Particularly (Vallellano JM, 2021) it has been investigated CFDB relation to clinical and bone metabolism markers in children, who demonstrated a normal bone mineral density along with altered remodelling.

Thanks of their inhibitory effect on osteoclasts, bisphosphonates reduce bone turnover and increase bone mineral density (BMD). They can have an important role in patients with a significantly low BMD, mainly if they are listed for solid organ transplantation and/or are taking a prolonged course of oral glucocorticoids.

Bisphosphonate therapy includes different drug administration protocols. Thanks to their selective action, usually bisphosphonates are not associated with severe adverse events, even if upper gastrointestinal side effects are often associated with oral agents and flu-like symptoms with the i.v. ones. Recently (Karahasanovic A, 2016) it has been reported that it is important to be aware of symptomatic leukopenia in immunosuppressive patients after treatment with zoledronic acid. Bisphosphonate therapy in adults and children has been included in European Guidelines (Sermet-Gaudelus I, 2011),(Paccou J, 2013), (Marquette M, 2016) targeted towards assessment, prevention and treatment of low BMD in CF.

Issues

Bisphosphonate efficacy in improving BMD, decreasing fracture rates, increasing quality of life and survival.

Short- and long-term adverse effects of bisphosphonate therapy.

Concomitant corticosteroid therapy efficacy in reducing i.v. administration adverse events.

What is known

One Cochrane review (Conwell LS, 2014), is available. It includes 7 RCT with 237 enrolled adult CF patients treated for 12 to 24 months. In 6 RCT, bisphosphonates were administered to non-transplanted patients, while in the other one only post-trasplant patients were included. Data showed that there was no significant reduction in fracture rates at 12 months. In patients taking bisphosphonates, after six months the percentage of bone mineral density increased.Severe bone pain and flu-like symptoms were associated with i.v. administration except in post-transplant patients receiving corticosteroid treatment.

In 2023 another Cochrane review (Jeffery TC, 2023), included nine studies, with a total of 385 partecipants (113 aged 5 to 18 years). Biphosphonates were compared to either placebo or calcium with or without vitamin D. Oral and intravenous bisphosphonates showed to be effective in increasing bone mineral density, but insufficient data are available to determine whether treatment reduces fractures.

One RCT (Bianchi ML, 2013) showed that a correct calcium plus vitamin D intake alone may be able to improve bone mineral density in some young patients.

Unresolved questions

Bisphosphonate efficacy in improving BMD, decreasing fracture rates, increasing quality of life and survival.

Short- and long-term adverse effects of bisphosphonate therapy.

Concomitant corticosteroid therapy efficacy in reducing i.v. administration adverse events.

Up to now, no RCTs are ongoing about this issue.

Keywords

Bone Diseases; Osteoporosis; Bisphosphonates; Bone Density Conservation Agents;