

Bisphosphonate therapy in young people – information sheet

Bisphosphonates are a group of medications that are used to increase bone mineral density. There are both oral and intravenous (infused into a vein) forms of bisphosphonates. In general, children who are treated with this medication have serious bone fragility disorders where the tablet forms of bisphosphonate are not strong enough to be effective, so the intravenous infusions are used. The bisphosphonate that was used previously to treat fragile bones in children and adolescents was called pamidronate, however the main bisphosphonate now used at the Royal Children's Hospital is called Zoledronic acid. We have been using this stronger bisphosphonate for the past several years because it only takes 20 minutes to administer instead of 2 hours and is usually given twice per year instead of every 2 months.

Bisphosphonates act by reducing the function of the osteoclasts (cells that break down bone), therefore leading to more bone formation. This makes the bones more dense, and therefore stronger/less likely to break. There are a wide variety of conditions where bisphosphonates may be used in young people, but predominantly they are used when the patient has been experiencing fractures occurring after minimal trauma (fragility fractures), coupled with low bone mineral density on DXA (bone density) scan.

Zoledronic acid therapy is generally given every 6 months (at 0.05mg/kg). Many patients only need 1-3 years of treatment to make the bones sufficiently stronger. Some may then need ongoing treatment although less frequently, even years apart as they get older.

There are some side effects of bisphosphonates to be aware of prior to use:

- (1) First dose effects – the first time the patient has the treatment, it often causes two side effects:
 - (a) A flu-like reaction which usually doesn't start until 24 hours after the infusion, at which time the child may experience bone pain, fever, lethargy, muscle aches and occasionally vomiting. These problems usually last 2-3 days but sometimes a bit longer, even up to a week. Paracetamol/ibuprofen, fluids and rest are the best treatment.
 - (b) The blood calcium level can drop quickly, and therefore it is recommended to make sure that the young person has a normal Vitamin D level before the first dose. It is important for the young person to take plenty of calcium (either in dairy products such as milk or as a calcium supplement) over the first few days after the infusion.

These two problems are almost always seen after the first dose only.

- (2) Osteonecrosis of the jaw – this is an infection in the mouth, which is well reported in adults taking these agents, but has NEVER been reported in a Paediatric or adolescent aged patient. It seems to be related to the tooth socket not being able to heal as quickly after a tooth pulling/denture rubbing etc. Despite there being no reports in young people, all patients are recommended to have a dental review before their first infusion and if any dental work, especially extractions, are required, then the first dose should be deferred until the tooth socket has healed. If dental work is done during the treatment, then the next dose should be deferred until healing occurs.
- (3) Atypical fractures – in adults using these medications for long periods of time, there have been reports of unusual fractures occurring, particularly in the thigh bone. This type of fracture is due to bones becoming harder. At the same time, standard hip fractures in the elderly are markedly reduced in frequency. While this type of fracture is possible in young people, it is rarely reported and we carefully monitor our patients by regularly checking the bone density, so that we try to avoid a problem of hard, brittle bone
- (4) Uveitis – This is a very rare side effect, where use of the medication can cause inflammation in the eye. If it happened the treatment would need to be ceased.
- (5) Pregnancy – in animal models, there have been concerns that higher doses of bisphosphonates (much more than used in humans) can cause issues in the developing fetus, as the drug crosses the placenta and could prevent normal bone development in a baby. However, there have been no bone effects noted in the offspring of young women who have used bisphosphonates prior to conception. The safe recommendation, however, is to avoid their use if pregnant. Therefore, the young person should have a pregnancy test prior to infusion if there is any chance that they could be pregnant.
- (6) Long term issues – while there is evidence that the medication stays in the skeleton for a long time, bisphosphonates have been used in young people for nearly 3 decades and there have been no significant long-term health issues found to be associated with their use.

For further information, please discuss with your treating clinician.