Guidelines for the administration of Intravenous Zoledronic Acid (Zoledronate) in children

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Introduction

Zoledronic Acid belongs to a class of drugs known as Bisphosphonates, which inhibit the action of osteoclasts and therefore bone resorption.

Pamidronate vs Zoledronic Acid, Zoldronic Acid offers the advantage of administering it as a single 30 min infusion every 3-6 months (2-4 days per year); and evidence suggests no difference in the desired treatment effect or side effects.

Indications

Osteoporosis, bone pain secondary to other disorders

Pre treatment

Send blood

> Calcium, phosphate & alkaline phosphatase, urea & electrolytes (U+E) + Mg, Parathyroid hormone (PTH), 25(OH) Vit D levels and fasting C-terminal crosslinks (CTX) levels.

Renal function must be measured before **each** infusion of Zoledronic Acid. Satisfactory renal results must be obtained prior to the commencement of the infusion. Dose modification may be needed. Please contact Dr Kanumakala for further advice

Most recent 25(OH) Vit D level is <25 nmol/L (severe deficiency). Vitamin D deficiency should be treated prior to infusion of zoledronic acid, aiming for levels between 50-120mmol/L Please contact Dr Kanumakala for further advice / see http://www.gp.brightonandhoveccg.nhs.uk/files/paediatric-vitamin-d-guidelines-bsuh-and-brighton-and-hove-ccgpdf

Dental advice, see side effect section.

Patient must be adequately hydrated before infusion. Defined as, the patient is eating and drinking normally. The patient has produced urine on the day of treatment. Try to encourage the patient to have a drink before the infusion.

Dosage

Age	Dosage	Maximum single dose	Frequency
Under 2 years	0.025mg/kg	2mg	3 monthly
2 to 5 years	0.035mg/kg	2mg if under 3 years, 4mg if over 3 years	4 monthly
Over 5 years	0.05mg/kg	4mg	6 monthly

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Administration

Use 4mg/5ml concentrate vials only:

For doses less than 2mg, dilute in 50ml of sodium chloride 0.9% or glucose 5%, and administer via an infusion pump over 30 minutes.

For doses greater than 2mg dilute in 100ml of sodium chloride 0.9% or glucose 5%, and administer via an infusion pump over 30 minutes.

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Post infusion

Calcium supplementation

Adcal-D3 **chewable** tablets or **effervescent** tablets Calcium carbonate 1.5 gram (15mmol of calcium) + Colecalciferol 400 unit.

ONE tablet ONCE a day if under 30KG

ONE tablet TWICE a day if over 30Kg

Paracetamol Use should be advised post infusion and regularly for 2 days. Particularly following first infusion (see side effects)

Bloods repeat U+E and bone profile (Calcium, phosphate & alkaline phosphatase levels) one week after the infusion.

DEXA scans conducted 6-monthly to 1-yearly to monitor bone strength

Audit Please complete the ongoing audit form; please forward the completed form by email or internal post to Dr Kanumakala**. SEE BELOW**

Side Effects

Headache, conjunctivitis, nausea, vomiting, decreased appetite anaemia, hypophosphatemia, hypocalcaemia, hypomagnesemia and renal impairment.

An acute phase reaction within 3 days of infusion (bone pain, fever and flu-like symptoms such as fatigue, rigors, malaise and flushing) can be experienced particularly with the first infusion but usually resolves within a few days. Paracetamol should be prescribed.

Caution should be taken when using in children with a history of seizures due to the risk of hypocalcaemia which can lower the seizure threshold.

In neonates, the acute phase reaction may include respiratory distress if there is pre-existing respiratory difficulty. Management is with appropriate supportive care.

All patients should be encouraged to maintain good oral hygiene, undergo routine dental check-ups, and immediately report any oral symptoms such as dental mobility, pain or swelling on treatment, invasive dental procedures should be performed only after careful consideration and be avoided in close proximity to zoledronic acid administration. The management plan for patients who develop osteonecrosis of the jaw (ONJ) should be set up in close collaboration between the treating physician and a dentist or oral surgeon with expertise in ONJ

Patients with thigh or groin pain with a history of receiving bisphosphonates should be evaluated to rule out a femur fracture

Patients with ear symptoms including: pain, swelling, discharge or chronic ear infections. The possibility of osteonecrosis of the external auditory canal should be considered. Especially in patients who have received bisphosphonates for >2 years.

Drug Interactions

In clinical studies, zoledronic acid has been administered concomitantly with commonly used anticancer agents, diuretics, antibiotics and analgesics without clinically apparent interactions occurring. Zoledronic acid shows no appreciable binding to plasma proteins and does not inhibit human P450 enzymes in vitro, but no formal clinical interaction studies have been performed.

Caution is advised when bisphosphonates are administered with aminoglycosides, calcitonin or loop diuretics, since these agents may have an additive effect, resulting in a lower serum calcium level for longer periods than required.

Caution is indicated when zoledronic acid is used with other potentially nephrotoxic medicinal products. Attention should also be paid to the possibility of hypomagnesaemia developing during treatment.

In multiple myeloma patients, the risk of renal dysfunction may be increased when zoledronic acid is used in combination with thalidomide.

Disposal of waste and Spillage

As per Trust policy for non-cytotoxic waste

References:

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https://www.medicines.org.uk/emc/medicine/29000 accessed 14/11/16

https://www.medicines.org.uk/emc/medicine/28793 accessed 14/11/16

ATTACH PATIENT LABEL

Check list for the administration of Intravenous Zoledronic Acid (Zoledronate) in children

Pre treatment

Send blood

Bone profile, renal function, FBC, calcium, phosphate, alkaline phosphatase, urea & electrolytes (U+E) , Mg, Parathyroid hormone (PTH), 25(OH) Vit D levels fasting C-terminal crosslinks (CTX) levels ☐

Ask about recent Dental procedures ☐

Check patient adequately hydrated. ☐

Dose

Check dose ☐

Post infusion

Calcium supplementation, Prescribed and counselled on need ☐

Paracetamol, Counselled on need ☐

Bloods booked for 1 week. ☐

DEXA scan Booked ☐

Audit, email Dr Kanumakala patient details ☐

Side Effects

Headache, conjunctivitis, nausea, vomiting, decreased appetite anaemia, hypophosphatemia, hypocalcaemia, hypomagnesemia and renal impairment. ☐

Aware of acute phase reactions (In neonates, the acute phase reaction may include respiratory distress.) ☐

Risk in children with history of seizures explained ☐

Patient aware of possible dental issues and to report any dental procedures ☐

Patients to report thigh or groin pain ☐

Patients to report ear symptoms ☐

Please complete this form and send to Dr Kanumakala following each infusion:

Patient details:		
Name of patient:		
Date of birth:		
Hospital or NHS number:		
Bisphosphonate therapy:		
Indication for use		
Bisphosphonate start date		
Last infusion date		
Current Infusion:		
Date of this infusion		
Weight of patient		
Medication used		
Dose used		
Before the infusion:		
U+E results (with date)		
Bone Profile results (with date)		
Vit D levels (with date)		
PTH levels (with date)		
Fasting CTX levels (with date)		
Any problems during infusion:		
After the infusion:		
Is next infusion needed?		
If yes, date booked?		
Repeat U+E results (with date)		
Repeat Bone profile (with date)		
Any comments for Dr Kanumakala:		