Scottish Paediatric & Adolescent Rheumatology Network

Protocol for the administration of Pamidronate Infusions in paediatric Rheumatology

Description
Pamidronate is a bisphosphonate drug (2nd generation) used to treat conditions associated with osteoporosis, multiple fractures and bone pain. Bisphosphonates bind strongly to bone mineral and interfere with bone remodelling by slowing the process of osteoclastic bone resorption and bone turnover.

Indications for use in rheumatology

Chronic recurrent multifocal osteomyelitis (CRMO) - symptomatic relief (pain) and anti-inflammatory effect *****

SAPHO (synovitis, acne, pustulosis, hyperostosis, osteitis) - symptomatic relief (pain) and anti-inflammatory effect

Severe osteoporosis associated with active inflammatory disease or steroid use - aim is to reduce long term fracture risk and improve bone health.

*** Hypophosphatasia can mimic CRMO and can be exacerbated by Bisphosphonates. Always ensure Alkaline Phosphatase (ALP) is not below normal limits for age.**

Caution must be used if child has renal impairment. Pamidronate should not be given if creatinine clearance <30mL/min/1.73m2. Patients should be well hydrated pre pamidronate and not receiving aminoglycoside antibiotics.

Pre-treatment

If indication for use is **osteoporosis** the child should have had a baseline DEXA scan.

Calcium supplementation (Calvive or alternative) is essential pre infusion - commence 3 days pre infusion and continue for 7 days.

Calvive effervescent tablets or calcium 20.4mg/ml syrup:

<6yrs – 400mg/day

>6yrs – 1000mg/day

Bloods pre each infusion

Urea and electrolytes, creatinine, calcium, phosphate, alkaline phosphatase, albumin.

A recent Ca result of >2.1mmol/L is required prior to commencing first infusion.

If calcium subsequently falls to < 2.1 mmol/L increase calcium supplements and **withhold or stop infusion until normocalcaemic.**

Bloods pre FIRST infusion - PTH, 25(OH) vitamin D and 1,25 (OH) Vitamin D.

Girls of child bearing potential should have a **pregnancy test** before the administration of pamidronate.

Drug Dose & Preparation

The dose and frequency of pamidronate is influenced by the clinical indication.

Indication	Dose	Frequency
Osteoporosis	1mg/kg	Monthly OR 3 consecutive days every 3 months
CRMO/SAPHO	1mg/kg (Option for 1st dose to be 0.5mg/kg in younger children to reduce severity of flu-like symptoms)	3 consecutive days. Repeat if beneficial and clinically indicated. (No more frequent than 3 monthly)*

The maximum daily dose of pamidronate should not exceed 90mg.

The maximum yearly dose should not exceed 12mg/kg.

Consider using ideal body weight if child obese.

*Patients with CRMO may be treated with different regimens depending on clinical situation. These would include.

- A “watch and wait” approach after initial good response to above treatment plan with a further dose (either a single 1mg/kg dose or 3 consecutive daily 1mg/kg doses) of Pamidronate given in the event of clinical flare.

- Regular treatment with 3 consecutive daily doses every 3 months for a total of 9 or 12 doses.
- A single dose of Pamidronate 1mg/kg given each month until symptoms controlled with a maximum of 12 doses.

Preparation

Pamidronate vials – 15 mg, 30mg and 90mg.

Reconstitute with sterile water as described on vial:

15mg vial – 5 mls sterile water

30mg and 90mg – 10 mls sterile water

Dilute with 250mls of 0.9% sodium chloride (or if renal impairment dilute with 500mls of 0.9% sodium chloride).

The final concentration of pamidronate in the infusion solution should not exceed *36mg/100ml* of diluent or *18mg/100ml* in renal impairment.

Administer infusion over 2-4 hours. (4.5 hours in renal compromise).

Flush cannula with 30ml - 0.9% sodium chloride – **important: run flush at the same rate which the pamidronate infusion ran.**

During infusion:

Monitoring: 4 hourly temperature, heart rate and blood pressure.

For the first cycle, it is advisable for younger children to stay overnight on Day 1 but can go home after Day 2.

Older children (>10yrs) can go home on Day 1 if infusion is in the morning and observed on ward until late afternoon.

Subsequent cycles do not need overnight admission

Expected side effects

Acute phase reaction - 'flu-like' illness with fever, musculoskeletal aches and pains, occasionally vomiting.

Most problems respond to paracetamol and are most likely to occur with the first infusion.

Hypocalcaemia, hypophosphateaemia – rarely symptomatic.

Less commonly – reaction at infusion site, rash, hypertension, anaemia, thrombocytopenia, lymphopenia, altered potassium levels and hypernatraemia.

NB Patients receiving pamidronate infusion should have regular dental check-ups and significant caries or dental abscess should be treated and have resolved before administration of Pamidronate due to the potential risk of osteonecrosis of the jaw.

Benign idiopathic osteonecrosis of the external auditory canal has been reported very rarely in adult patients receiving long term Bisphosphonates

Femoral fractures have been reported however there is no evidence of this in paediatric patients treated with the kind of dosing regimen we use for CRMO.

References

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