Hip Fracture Acute Treatment Pathway (fragility fractures in patients >65 years)

TARGET AUDIENCE	Secondary care.
PATIENT GROUP	All patients admitted to NHS Lanarkshire with a hip fracture due to fragility and aged 65 years and over

Clinical Guidelines Summary

Day 0 – Day 2 post op:

Referral to Pathway if patients meet the following criteria:

- Hip fracture due to low trauma (ie. fall from standing height or less)
- Post hip operation
- 4 doses of 50,000 IU vitamin D administered/prescribed on HEPMA
- Bloods obtained : U&E, Ca, Vit D

≥48hours Post op (Part of Geriatric Comprehensive Assessment)

Medicine for Older Adult doctor will complete eligibility checklist for IV Zoledronic post hip fracture:

- Theical D3 1 tab daily or equivalent started
- Calcium level >2.2 mmol/l
- Vit D level >50 nmol/lor at least 50,000IU Vit D administered
- Good Dentition / Good gum health (if dentures)
- CrCl (using actual bodyweight) >35 mL/min
- Not on bisphosphonates/ denosumab/ teriparatide/ romosozumab

IV Zoledronic acid to be prescribed by Medicine for Older Adult doctor if eligible

Referral to Fracture Liaison Service (FLS) if Outcome 1 and 4 (Keep status as "In progress")

-Outcome 1: First IV Zoledronic Acid administered, onward referral to FLS for completion of 2 further doses

-Outcome 4: Referral to FLS for consideration of other therapy

Hip Fracture Acute Treatment Pathway (fragility fractures in patients >65 years)

Introduction

Patients with hip fracture due to low trauma (i.e. fragility fracture) are at high risk of future fracture and have a high mortality.

A second hip fracture is observed in 1 in 3 patients with an index hip fracture, within 1.5 years on average[Error! Reference source not found.].

Vitamin D loading

Four doses of 50,000 IU colecalciferol given orally over 4 days should commence on admission if serum calcium is <2.6 mmol/l. A consensus statement recommends a loading regime of 150,000–250,000 IU given in 'split' doses over 1–7 days, as vitamin D deficiency is common in this population. Adequate vitamin D levels will reduce the risk of symptomatic hypocalcaemia after administration of IV Zoledronic acid.

Daily oral calcium and vitamin D supplementation should be commenced thereafter with either TheiCal D3 1 tablet daily or other formulary product.

Zoledronic acid Treatment Pathway

Patients 65 years and older will be reviewed by a member of the Medicine for the Older Adult Medical Team ≥ 48 hours post operatively.

As per Clinical Guidelines Summary, patients will be assessed for eligibility for IV Zoledronic acid including ensuring

- serum calcium is > 2.2mmol/l
- vitamin D level is >50nmol/l or that at least 50,000IU of colecalciferol has been administered
- The patients estimated creatinine clearance is >35ml/min based on actual body weight
- That the patient has good dentition or gum health if they have dentures
- The patient is not already receiving a bisphosphonate/ denosumab/ teriparatide/ romosozumab

The Medicine for the Older Adult doctor will prescribe a single dose of 5mg IV Zoledronic Acid on HEPMA

The patient will be referred to the Fracture Liaison Service via the Trakcare referral process for ongoing follow up and further doses of IV Zoledronic Acid if appropriate.

(The patient will receive a patient information leaflet for Zoledronic Acid available to print from the Royal Osteoporosis Society)[7].

Zoledronic acid

Zoledronic acid is a nitrogen-containing Bisphosphonate with potent inhibitory effects on osteoclastic bone resorption and a high binding affinity for bone mineral. It has a long duration of action and is the most potent Bisphosphonate available for the management of osteoporotic fracture risk. 5mg intravenous Zoledronic acid is licensed for use in postmenopausal women and men with a recent low-trauma hip fracture. Its use in the management of hip fracture prevention in men and postmenopausal women is advocated in the updated SIGN Guideline[1].

In those with a hip fracture, DXA proven osteoporosis is not required prior to Zoledronic acid therapy. Zoledronic acid is preferred in this group of patients as it has clinical benefit within 1 month. In contrast, oral bisphosphonate therapies only exhibit clinical benefit after 6 months.

The Health Outcomes and Reduced Incidence with Zoledronic Acid Once Yearly (HORIZON) Pivotal Fracture Trial: In this large randomised control trial (RCT) of more than 7000 postmenopausal women with osteoporosis[3], the treatment arm (3889 patients) was randomised to receiving 3 doses of an annual infusion of 5 mg zoledronic acid intravenously. Zoledronic acid reduces risk of hip fracture by 41% and vertebral fracture by 70% compared to placebo.

The Health Outcomes and Reduced Incidence with Zoledronic Acid Once Yearly (HORIZON) Recurrent Fracture Trial: This RCT recruited more than 2000 patients following a hip fracture[4]. The treatment arm received an annual infusion of 5 mg zoledronic acid, with first dose given within 90 days after repair of a low-trauma hip fracture. Treatment led to a relative risk reduction of 46% in vertebral fractures, and a non-significant relative risk reduction in hip fracture by 30%.

Potential harms

Most common adverse effects are acute phase response; 42.4% patients treated with IV Zoledronic acid in HORIZON-PFT compared to 11.7% in placebo[3].

Atrial fibrillation (AF): In one trial, AF was more common overall in the zoledronic acid group (2.5% v 1.9%, not significant (NS)) but the difference was significant for patients with AF requiring hospital admission (50 patients (1.3%) versus 20 patients (0.5%)). Most events occurred more than 30 days after infusion, by which time zoledronic acid is undetectable in the circulation.

Long term exposure to potent bisphosphonates is rarely associated with Medication-related osteonecrosis of the jaw or atypical femoral fracture.

Does IV Zoledronic acid affect Fracture healing?

Small studies[5, 6] have not noted any adverse effects on hip fracture healing when Zoledronic acid was given within 2 weeks of hip fracture. The limitations are that these studies are relatively small in number.

As there is insufficient evidence to assess outcomes if initiated within 1 week, ongoing audits have been set up to verify this. The national hip fracture audit has adopted the administration of Zoledronic acid ≥48hours post-op as a national standard.

Conclusion

Administering Zoledronic acid at the time of the hospital admission for hip fracture represents a unique opportunity to prevent further fractures in a cohort at high risk of re-fracturing. In a health climate with budget limitations and inpatient-capacity restrictions, this will reduce number of patient contacts with the health service. Within this guideline, any eligible patient will be prescribed IV Zoledronic acid ≥48hours post-op by the Medicine for Older Adult doctor as part of the comprehensive geriatric assessment. Completion of the electronic Trakcare form will also generate a referral to the Fracture Liaison Service (FLS) for outcomes 1 and 4 (see Appendix and summary).

References/Evidence

1. Schemitsch, E et al. Hip fracture predicts subsequent hip fracture: a retrospective observational study to support a call to early hip fracture prevention efforts in post-fracture patients. Osteoporos Int 33, 113–122 (2022). https://doi.org/10.1007/s00198-021-06080-5
2. SIGN Guidelines 142 Management of osteoporosis and the prevention of fragility fractures, Revised January 2021.
3. Black, Dennis M et al. “Once-yearly zoledronic acid for treatment of postmenopausal osteoporosis.” The New England journal of medicine vol. 356,18 (2007): 1809-22. doi:10.1056/NEJMoa067312
4. Lyles, Kenneth W et al. “Zoledronic acid and clinical fractures and mortality after hip fracture.” The New England journal of medicine vol. 357,18 (2007): 1799-809. doi:10.1056/NEJMoa074941
5. Colon-Emeric C et al. “Association between timing of Zoledronic acid infusion and hip fracture healing.” Osteoporos Int. 2011;22(8):2329-2336
6. Sargin, S et al. “Effects of Zoledronic Acid Treatment on Fracture Healing, Morbidity and Mortality in Elderly Patients with Osteoporotic Hip Fractures.” Strategies in trauma and limb reconstruction vol. 14,3 (2019): 126-131. doi:10.5005/jp-journals-10080-1439
7. Zoledronate (zoledronic acid). https://strwebprdmedia.blob.core.windows.net/media/2cmhexi4/ros-zoledronate.pdf. Accessed 11/1/24.

Appendices

1. Governance information for Guidance document

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Distribution	

CHANGE RECORD

Date	Lead Author	Change	Version No.
			1
			2
			3
		.	4
			5

2.You can include additional appendices with complimentary information that doesn't fit into the main text of your guideline, but is crucial and supports its understanding.

Appendix 1 – Trakcare (electronic) workbench

Hip Fracture Acute Treatment Pathway - (for fragility fractures in patients >65 y/o)

Orthopaedic team to initiate referral:

1	**Hip fracture due to low trauma (ie. fall from standing height or less** *Please do not refer traumatic fractures here*	Mandatory drop-down list • Yes • No
2	**Date of hip operation**	Mandatory Calendar Box
3	**4 doses of 50,000 IU vitamin D administered/prescribed on HEPMA**	Mandatory drop-down list • Yes • No
4	**Bloods obtained : U&E, Ca, Vit D**	Mandatory drop-down list • Yes • No
	It is mandatory to have questions 1,3,4 answered "YES" before request will be accepted	

Processing notes to be completed during geriatric assessment:

Cut and paste one option as below :

Outcome 1: First IV Zoledronic Acid (IV Zol) administered, onward referral to FLS for completion of 2 further doses

Date of IV Zol prescription:

All IV Zol criteria met (Calcium level >2.2; Vit D replete; Dentition adequate; CrCl mL/min >35; not on osteoporosis treatment previously)

Outcome 2: First IV Zoledronic Acid (IV Zol) administered, not appropriate for further does (frailty/poor prognosis)

Date of IV Zol prescription:

All IV Zol criteria met (Calcium level >2.2; Vit D replete; Dentition adequate; CrCl mL/min >35; not on osteoporosis treatment previously)

Outcome 3: Not appropriate for IV Zoledronic Acid (due to poor CrCl or dentition)

Outcome 4: Referral to FLS for consideration of other therapy

FLS service involvement

Pathway following:

Outcome 1: Patient will enter FLS pathway, Dual-energy X-ray absorptiometry (DXA) and dental assessment (if appropriate) organised. If DXA confirms osteoporosis and continues to meet eligibility criteria, 2 further doses of IV Zoledronic Acid administered on an outpatient basis.

Outcome 2: No further follow up.

Outcome 3: No further follow up.

Outcome 4: Urgent Dual-energy X-ray absorptiometry (DXA) and urgent osteoporosis clinic appointment.

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