Medication Incident Safety Sharing Program (MISS P)

All hospital Pharmacists are encouraged to submit Medication Incident Cases and Medication Safety Solutions to the SHPHK for sharing. This is not simply an MI reporting program like those being successfully run by the public hospital network or individual private hospitals. We are not focusing on the number or frequency of the MIs. Our aim is to collect educational cases and/or solutions so that members of the SHPHK could benefit by learning from other colleagues' unfortunate mistakes and/or innovative ideas. All submitted materials will be handled in strict confidence. The identity of the institution or the personnel involved will not be revealed. Please support us by sending your cases to Mr Michael Ling, Medication Safety Co-ordinator of SHPHK, at mhmling@yahoo.com.

A 39-year-old lady with good past health was admitted to A&E department on 7/1/2013 for severe back pain. Prior to admission, she had back pain for 4 months and mild neck pain for 2 months. There was no history of injury. She reported left breast mass and slight weight loss over the past few months, and was told to be normal. Examinations suggested that she has carcinoma of left breast.

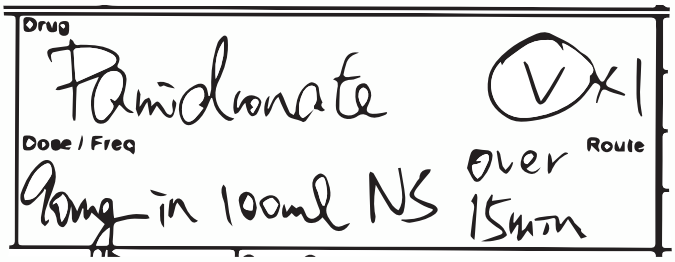
On admission, she was afebrile, BP and pulse stable, sensation intact and reflex normal. X-ray showed collapsed T11. Her serum calcium level on admission was 4.38mmol/L (see Table 1).

Table 1. Revelant Laboratory Investigations on 8 Jan

	2am	10am	5pm	Ref range
Calcium	4.38	4.09	4.26	2.10-2.62 (mmol/L)
Phosphate	2.01	1.93	2.03	0.88-1.45 (mmol/L)
Creatinine	198	-	-	47-82 (μmol/L)
Albumin	42	-	-	35-52 (g/L)

Due to severe hypercalcaemia, urgent rehydration and one dose of pamidronate infusion were prescribed.

Pamidronate for hypercalcaemia of malignancy



The antiresorptive property of bisphosphonates establishes their role as the mainstay in managing hypercalcaemia of malignancy. Dosages are recommended based on corrected serum calcium level; and the British National Formulary (BNF) recommends pamidronate to be given at 15–60 mg as a single infusion or in divided doses over 2–4 days[1]. According to the prescribing information of Aredia®, 60 to 90 mg of pamidonronate could be given as either a single IV infusion over 2 to 24 hours in patients with moderate hypercalcaemia i.e. corrected serum calcium of approximately 3.0-3.375mmol/L; and 90mg for severe hypercalcaemia i.e. corrected serum calcium more than 3.375mmol/L[2]. Local guideline also recommends similar dosages based on the initial albumin-corrected plasma calcium concentrations (see Table 2). In patients with eGFR less than 30 mL/minute/1.73m^2, pamidronate should be avoided except in life-threatening hypercalcaemia if benefit outweighs risk[1].

Table 2. Dosing Recommendation of Disodium Pamidronate (in milligrams)

Corrected plasma Ca^{2+} concentration (mmol/L)	§ Handbook of Internal Medicine 6th Edition[3]	Palliative Care Formulary 4 (PCF4)[4]	Aredia® prescribing information[2]
2.6 – 3.0	30	15 or 30	
3.0 – 3.5	60	30 or 60	60 – 90*
>3.5	90	60 or 90	90*
>4		90	

§ A local guideline
*90mg for patients with corrected serum calcium >3.375mmol/L

What went wrong?

In view of the high serum calcium level (4.38mmol/L) on admission, a single dose of 90mg pamidronate was prescribed. The concentration and infusion time of pamidronate, however, are inappropriate. The concentration of the infusion solution should not exceed 90mg/250ml[1]. Meanwhile, the infusion rate should not exceed 60mg/hour[1,2]. In patients with mild to moderate renal impairment, the maximum recommended infusion rate is 90mg over 4 hours[2] or 20mg/hour[1]. Longer infusions (i.e. >2 hours) may reduce the risk for nephrotoxicity, particularly in patients with preexisting renal insufficiency[2].

Eight hours later...

After the dose of 90mg pamidronate, her serum calcium remained high (4.09mmol/L). Another dose of pamidronate was prescribed and administered.

It should be appreciated that the onset of pamidronate is not immediate. After a dose of pamidronate, the plasma-calcium concentrations generally start declining 24 to 48 hours with normalisation within 3 to 7 days5. Thus it is not surprising that the calcium level remained high only 8 hours after a dose of pamidronate. Retreatment with pamidronate should only be initiated after a minimum of 7 days of the previous course of pamidronate2. If rapid serum calcium level reduction is required, calcitonin therapy may be necessary[6]. Subcutaneous or intramuscular calcitonin has an onset of action of about 2 hours, and duration of action 6-8 hours[7].

Another 7 hours later...

After the second dose of 90mg pamidronate, serum calcium level remained high (4.26mmol/L). Salcatonin 240mcg Q12H SC and hydrocortisone 200mg Q8H IV were prescribed to treat her hypercalcaemia. Serum calcium level started to drop gradually one day later, and was normalized after 3 days. However, serum phosphate level dropped from high to low (0.74mmol/L) 6 days after pamidronate (see Table 3).

Proposed Safety Solutions

1) **Check past dispensing records** to ensure pamidronate was not prescribed within the last 7 days for hypercalcemia of malignancy.

2) **Check patient's creatinine clearance**, since pamidronate should not be used in patients with CrCl<30ml/min, unless for life-threatening hypercalcaemia of maglinancy.

3) **Check patient's corrected serum calcium** to make sure dosing is appropriate with regard to calcium level [corrected calcium (mmol/L) = 0.02 * (40 g/L – patient's albumin (g/L)) + measured Ca]

4) **Add a warning prompt** at the point of data entry to remind colleagues about the special caution of pamidonate.

5) **Prepare a standardised dilution table** to avoid incorrect dilution and administration time.

Table 3. Revlevant Serial Laboratory Investigations

	9/1 3am	9/1 11am	11/1 11am	12/1 11am	14/1 11am	Reference range
Calcium	3.94	3.72	2.97	2.62	2.16	2.10-2.62 (mmol/L)
Phosphate	1.4	1.7	0.89	0.79	0.74	0.88-1.45 (mmol/L)
Creatinine	-	-	160	152	140	47-82 (μmol/L)

References

1. British Medical Association and The Royal Pharmaceutical Society. British National Formulary 64 (Sep 2012).

2. Novartis. Aredia® prescribing information. URL: http://www.pharma.us.novartis.com/product/pi/pdf/aredia.pdf Accessed online 18 Feb 2013.

3.Hospital Authority, HKSAR. Handbook of Internal Medicine, 6th Edition (2011).

4. Twycross R, Wilcock A (Editors-in-Chief). Palliative Care Formulary, 4th Edition (2011).

5. Sweetman S (Editor). Matindale: The Complete Drug Reference.

6. DiPiro J (Executive editor). Pharmacotherapy: A Pathophysiologic Approach, 8th Edition (2011).

7. American Pharmacists Association. Drug Information Handbook, 21st Edition (2012).

Grace CHENG is a resident pharmacist working at the Queen Elizabeth Hospital

Fanny KWOK is a resident pharmacist working at the Kowloon Hospital