Palliation Of Pain

RADIONUCLIDE THERAPY FOR PALLIATION OF PAIN FROM BONY METASTASES

Overview and Topics to Be Covered

- Reviews the use of radionuclide therapy in nuclear medicine for palliation of pain due to bony metastases.
- Provides a comprehensive overview of Radionuclide Therapy for the purpose of palliating pain caused by bony metastases. This is a very valuable, but very under-utilized procedure that renders pain relief (sometimes complete) in ~80% of all patients treated with the available therapeutic radiopharmaceuticals.
- Lists most important characteristics of therapies used in palliation of bony metastases.
- Covers a historical overview of palliation of pain with therapeutic radiopharmaceuticals
- Describes these radiopharmaceuticals and the physical properties of the associated α–emitting and β- emitting radionuclides as well as typical recommended doses
- Reviews the epidemiology of cancer resulting in pain from metastases, especially breast and prostate cancer
- Lists all the therapeutic approaches utilized for palliating bone pain, with special emphasis on radiopharmaceuticals
- Lists eligibility criteria for undergoing the study
- Gives detailed information about clinical use of each of the three available drugs.
- Discusses typical clinical outcomes
- Outlines the internal radiation dosimetry of each available drug

Epidemiology: Bony Metastases in Breast and Prostate Cancer

- Prostate cancer: 50% of patients have bone disease at time of diagnosis
- Breast cancer: 15% of stage III patients and 50% of Stage IV patients have bone metastases at time of diagnosis

Advances in Cancer Therapy have resulted in more people needing treatment

- Longer survival in many cancers
- Better pain control medication
- More aggressive radiotherapy
- End result: More people living with bone pain.

Some Effects of Bone Pain

- Depression
- Loss of mobility
- Disrupted family patterns
- Decreased quality of life

Therapeutic Approaches to Palliation of Bone Pain

The two most effective therapies are External Beam Radiation Therapy and Radiopharmaceutical Therapy. The others are not very good for treating pain and/or have serious side effects, as noted below.

NSAIDs

- Aspirin, acetaminophen, ibuprofen, naproxen
- Effective when pain is mild
- Effective for a short time early in disease
- May be used with other modalities

Chemotherapy

- Not typically given to control pain; most effective when used before severe pain appears
- Better results in lytic disease
- Not very effective in blastic disease
- Toxic side-effects

Hormonal Therapy

- Most effective when started prior to pain onset
- Only effective in hormonally dependent tumors
- Results in decreased libido & male impotency
- Many patients resist castration
- May have undesirable side-effects
- Second-line therapy is much less effective

External Beam Radiation

- Very effective for localized disease
- Wide-field therapy (hemibody) may be quite effective
- Unmasks new sites of pain
- Limitation on repeat therapy
- May have symptomatic side-effects
- May have additive toxicity to chemotherapy
- High-cost therapy

Narcotic Therapy

- Commonly used modality
- Drug dependency may develop
- Loss of appetite common
- GI symptoms are common
- Patients become depressed and immobile
- Confusion and disorientation common
- Doses escalate with time
- Ultimate decreased quality of life

Radiopharmaceutical Therapy

- Commonly used modality
- Drug dependency does not develop
- Very effective for pain relief- 80% response rate
- May be used in conjunction with other modalities
- Unlike External Beam Therapy, which only treats a painful area, radiopharmaceutical therapy treats pain from bony metastases anywhere in the body. The drugs are considered "Unsealed Sources in the Body" and are preferentially taken up by bone tissue as well as bony metastases, probably due to formation of hydroxyapatite crystals.
- May require multiple doses, e.g., Ra-223 chloride is given in a sequence of 6 injections spaced a month apart
- In some patients, this therapy has a deleterious effect on the bone marrow; therefore WBC and platelet counts need to be done frequently.

Indications for Therapy with These Drugs:

- Documented malignancy w/ bone metastases from any primary malignancy- must have a bone scan positive for metastatic disease
- Significant use of analgesics, i.e., narcotics
- Life expectancy greater than three months
- Multiple sites of disease or failure of other therapy
- May be used in combination with radiotherapy at first painful metastasis or in combination with multi-modality pain therapy

Eligibility Criteria: Patient may NOT be treated if:

- WBC count is less than 2,400
- Platelet count is less than 60,000
- Patient is pregnant/lactating
- Patient is moribund (life expectancy < 3 months)

Radiopharmaceuticals approved by the Food and Drug Administration:

- P-32 Na phosphate
- Sm-153 EDTMP
- Ra-223 chloride
- Sr-89 chloride

Physical Characteristics of Therapeutic Radionuclides

	Sr-89	**Sm-153**	**P-32**	**Ra-223**
Half-life	50.5 days	46.7 hr	14.3 days	11.4 days
Mode of Decay	β-	β- and γ	β-	α
E (max)	1.463 MeV	0.803 MeV	1.73 MeV	5.78 MeV
Range in Tissue	7 mm	5 mm	8 mm	0.02 mm

Typical Injected Doses:

- 4 mCi of Sr-89 chloride
- 1 mCi/kg of Sm-153-EDTMP (maximum 100 mCi)
- 4 mCi of P-32 Na phosphate
- 1.35 μCi/kg of Ra-223 chloride (maximum 0.16 mCi)

General information

- Divalent Ra-223 and Sr-89 chlorides are bone localizing calcium analogs with distribution very similar to Tc-MDP
- P-32 Na Phosphate and Sm-153 EDTMP are bone localizing phosphate analogs with a distribution very similar to that of Tc-99m MDP
- Ratio of metastatic lesions to normal bone = 5:1
- Ratio of metastatic lesions to marrow = 10:1
- Retention of these drugs in metastases is significantly longer than in normal bone tissue
- No reported adverse reactions
- 30-50% of patients have measurable decrease in WBC and platelets
- Recovery begins at about 6 weeks; by 12 weeks, typically back to normal
- Flare phenomenon (increased pain for a few days early in the course of treatment) is often prognostic indicator of successful treatment

- 80% Response rate overall for all four drugs. Onset of effect at 10 to 20 days for Sm-153 and 15-25 days for Sr-89 due to half lives (46.7 hr and 50.5 d, respectively)
- Sm-153 has a gamma ray usable for imaging
- 20% of prostate Ca patients become pain free
- Average duration of effect is up to 6 mo
- Range of relief was between 4 and 12 mo
- Greater success with prostate cancer than breast cancer
- Retreatment no sooner than 90 days (if a minimal effect has been obtained, retreatment at 30-45 days may be indicated)
- Osteosarcoma outcome questionable- usually not beneficial

Radionuclide Therapy: Clinical Outcomes

80% response divided into 3 groups, based on pain and medication diaries

Moderate response: morphine moving down to codeine

Marked response: morphine moving down to Advil, Aleve, other non-steroidal drug

Dramatic response: morphine moving down to no drugs

Patient Evaluation

- Most effective way to evaluate drug efficacy is to ask patient to keep both a medication diary and a pain diary.
- While we typically do draw bloods periodically to check the CBC, that sheds no light on whether patient's treatment has been effective; it only indicates if there has been a deleterious effect on bone marrow.

Internal Radiation Dosimetry of Ra-223 chloride, Sr-89 chloride, and Sm-153 EDTMP

Radiation Absorbed Dose For Ra-233 Chloride (70 kg Adult)		
Target Organ	**Rad/mCi**	**Rad/mCi mGy/MBq**
Bone Surfaces	4262	1151
Liver	11.01	2.98
Spleen	0.33	0.09
Gonads	1.80	0.49
Whole Body	85.5	23.11

Radiation Absorbed Dose For Sr-89 Chloride (70 kg Adult)		
Target Organ	**Rad/mCi**	**Rad/mCi mGy/MBq**
Bone Surfaces	60.0	16.2
Liver	6.0	1.62
Spleen	7.25	1.96
Gonads	1.0	0.27
Whole Body	10	2.70

Radiation Absorbed Dose For Sm-153 EDTMP (70 kg Adult)		
Target Organ	**Rad/mCi**	**Rad/mCi mGy/MBq**
Bone Surfaces	25.0	6.76
Liver	0.019	0.0051
Ovaries	0.032	0.0086
Testes	0.020	0.0054
Whole Body	0.040	0.011

Consultants In Nuclear Medicine
Nucmedconsultants@comcast.net
Stephen Karesh, PhD
Phone: 773-802-7617
Fax: 773-304-2545
2910 W. Estes Ave. Chicago, IL 60645-2394