Old Doc, New Tricks?

Things I am doing differently this year in my FPO practice.

Presenter Disclosure

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Mitigating Potential Bias

- Not Applicable
- Off label: Olanzapine for nausea and vomiting in CINV.

Learning objectives:

By the end of this session it is hoped that participants may:

1. Consider osteoporosis screening in the appropriate patients on androgen deprivation therapy.

2. Appropriate follow up of Gynae-oncology patients.

3. Be able to manage patients that suffer from “hard to treat nausea”.

4. Be able to manage patients with DVT’s due to PICC lines.

Androgen deprivation and Osteoporosis

- Prostate cancer: most common cancer among Canadian men.
- It is the 3rd leading cause of death from cancer in men in Canada.
- Osteoporotic skeletal fractures occur in up to 20% of men with in 5 years of starting androgen deprivation.
- Rapid loss in BMD starts within 6-12 months of starting ADT.

Survival rates by stage

- **Local stage** means that there is no sign that the cancer has spread outside of the prostate. This corresponds to AJCC stages I and II. About 4 out of 5 prostate cancers are found in this early stage. The relative 5-year survival rate for local stage prostate cancer is nearly 100%.
- **Regional stage** means the cancer has spread from the prostate to nearby areas. This includes stage III cancers and the stage IV cancers that haven't spread to distant parts of the body, such as T4 tumors and cancers that have spread to nearby lymph nodes (N1). The relative 5-year survival rate for regional stage prostate cancer is nearly 100%.
- **Distant stage** includes the rest of the stage IV cancers – cancers that have spread to distant lymph nodes, bones, or other organs (M1). The relative 5-year survival rate for distant stage prostate cancer is about 28%.

2010 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada: summary

"Women who are taking aromatase inhibitors and men who are undergoing androgen-deprivation therapy should be assessed for fracture risk, and osteoporosis therapy to prevent fractures should be considered [grade B]"

How quick does bone loss occur?

Average BMD decrease 2.4% during year 1 and 7.6 % in year 2 (2 year loss 2.5%-17%)

worse for men who were: Obese, younger than 75 years old and men who do not exercise.

Thus: Consider BMD testing in men who are on ADT.

When to do CA125?

A Quality Initiative of the

Program in Evidence-Based Care (PEBC), Cancer Care Ontario (CCO)

Follow-up of Patients who are Clinically Disease-free After Primary Treatment for Fallopian Tube, Primary Peritoneal, and Epithelial Ovarian Cancer

T. Le, E.B. Kennedy, J. Dodge, L. Elit, and the Ovarian Follow-up Guideline Expert Panel

Report Date: November 11, 2015

- No evidence that the monitoring of CA125 levels improves survival outcome (in patients who are clinically disease-free after Primary treatment of Fallopian Tube, Primary peritoneal, and Epithelial ovarian cancer). - *actually worsens quality of life!*
- We need to discuss limitations and potential harms of routine measurement of CA125 during follow up after ovarian cancer.
- Counseling is important: 41 to 100% of patients in retrospective studies had symptomatic recurrences.
- 60% of recurrences in endometrial cancers are distant. (Poor prognosis and early detection shows no survival benefit.) At 3 years after potential curative treatment 70-100% of recurrences have occurred.

CancerCare Manitoba :

Health care professionals - Cancer specific Follow up care Resources:

Ovarian, Fallopian Tube, and Peritoneal Cancer

CCMB Follow-up Recommendations

Ovarian, Fallopian Tube, and Peritoneal Cancer Patient Follow-up Treatment Summary and Follow-Up Schedule Form

Patients and/or their health care providers can complete this fill-in-the-blank diagnosis and treatment summary.

Moving Forward After Gynecological Cancer (Ovarian. Fallopian Tube, and Peritoneal)

Includes information for gynecological patients on:

- Cancer recurrence-signs to watch for
- medical tests and cancer screening
- screening recommendations for family members
- what to expect after breast cancer & treatment
- diet, nutrition, exercise and activity recommendations following Ovarian, Fallopian Tube, and Peritoneal Cancer
- Ovarian, Fallopian Tube, and Peritoneal Cancer support and resources in Manitoba

Cancercare Manitoba:

Medical Appointments

- A focused history and physical with abdominal assessment including bimanual pelvic and rectal examination.
- Inquire about new symptoms such as abdominal, back, or pelvic pain or pressure, nausea/indigestion, abdominal bloating, increased abdominal size, anorexia or early satiety, urinary changes such as increased urgency and/or frequency, bowel changes such as constipation, diarrhea, or thin/pencil like stools.

Bloodwork

- Routine CA 125's have not been shown to improve overall survival therefore are routinely not done unless concerning symptoms arise. CA125 *may* be drawn at each visit in Years 1, 2 and 3, if initially elevated, however this is typically only if the patient requests it.
- For a CA125 result above the upper limit of normal, repeat the test in 4-6 weeks.
- Other blood tests, such as liver function tests (LFTs) and blood counts (CBCs) are NOT recommended for follow-up.

CT Imaging

- Follow-up CT imaging of the abdomen and pelvis is performed **only** for patients if symptomatic for recurrence or if indicated by physical exam.

Hard to treat Nausea

CINV= chemo induced nausea and vomiting

Nausea: acute, delayed, and anticipatory.

3 categories of drugs with highest therapeutic index of management of CINV

- 5-HT3 receptor antagonists (Kytril/Zofran)
- Neurokinin-1 receptor antagonists(Emend)
- Glucocorticoids (Dex)

New kid on the block: Olanzapine

- Olanzapine: Blocks serotonin 5-hydroxytryptamine (5-HT2) receptors and dopamine D2 receptors.
- Useful in acute and delayed CINV.
- Standard treatment option in highly emetogenic chemotherapy regimes.
- Dose: unsure 5mg vs 10mg - sedation.

Chemotherapy-associated acute and delayed nausea or vomiting, prevention (off-label use): Oral: 10 mg on the day of chemotherapy (day 1) followed by 10 mg once daily days 2 to 4.

Chemotherapy-associated breakthrough nausea or vomiting (off-label use): Oral: 10 mg once daily for 3 days.

- In studies Olanzapine had a significantly higher rate of nausea control in delayed period.

Olanzapine

- Health Canada alert August 2016: sleep apnea was linked to use of atypical antipsychotics.
- FDA: Olanzapine can cause a rare but serious skin reaction known as drug reaction with eosinophilia and systemic symptoms (DRESS). DRESS may consist of a cutaneous reaction (eg, rash or exfoliative dermatitis) along with eosinophilia, fever, lymphadenopathy and systemic complications such as hepatitis, myocarditis, pericarditis, pancreatitis, nephritis, and pneumonitis and has a mortality rate of up to 10%.

Olanzapine

Side effects:

Prolonged QT interval

Agranulocytosis

Sedation

Orthostatic hypotension (fall risk in elderly)

Anticholinergic effect - constipation, urinary retention dry mouth

EPS: Akathisia. Dystonia. Tardive dyskinesia.

Hyperprolactinemia

Lowers seizure threshold

Weight gain, hyperglycaemia and hyperlipidemia

Body temperature regulation

Esophageal dysmotility/aspiration

Drug interactions: avoid metoclopramide

Catheter related thrombosis

- 70-80% of thrombotic events in superficial and deep veins of the upper extremity are due to catheters.
- pulmonary embolism from upper extremity sources -6%
- embolism may be deep or superficial (more common).
- it may be more common than we think! One study screened patients with cancer with a central catheter for 60% incidence of UEDVT. Another study found 75% of these patients were asymptomatic.

Risk for thrombosis:

» Port< PICC (particularly those who are ill or have malignancy),

previous thrombosis, chemical irritation

» subclavian insertion site,

» improper positioning of catheter tip: Innominate vein or junction of the innominate vein with SVC - 46% risk vs 6% if tip in right atrium or SVC,

» size of catheter/lumen diameter,

» 5-15% risk for hospitalized patients vs 2-5% for ambulatory patients

» recently surgery and cancer,

» incidence higher in left sided catheters

» Catheter infection

» Prothrombotic states - Factor V Leiden 3x higher risk, patients with antibody -positive heparin induced thrombocytopenia (HIT) with a central catheter vs none had 9% risk vs 0%. Underlying malignancy gave you a 32% higher risk.

» Hormonal therapy: OCP

» Chemical irritation (phlebitis) - potassium chloride, diazepam, antibiotics (Vanco) chemotherapy, hypotonic or hypertonic electrolyte solutions. Chemo causes

Clinical presentation

- No symptoms
- Inability to draw blood from catheter (40% mechanical reason 60% thrombosis/fibrin sheath
- symptomatic: phlebitis, extremity oedema, embolization (suspect with pulmonary emboli or acute neurological insult)

EJvR1

Slide 19

EJvR1 reported incidence of asymptomatic catheter-induced UEDVT in prospective series of patients with subclavian catheters has ranged from 5 to 13 percent. However, thrombi are detected over 50 % of patients with malignancy and those undergoing bone marrow transplantation

Erika Janse van Rensburg, 9/25/2016

Treatment phlebitis (superficial):

- Limited data but pulmonary embolism is rare.
- Anticoagulation is suggested in patients who are at risk for DVT. (e.g. thrombophillia, superficial thrombosis in proximity of deep vein)
- Generally symptomatic treatment: NSAIDS, warm or cool compress, extremity elevation.
- Removal of peripheral catheter and stop infusion.

Catheter induced UEDVT:

- Anticoagulation (Grade 2B) - uncomplicated cases 3 months. Longer if catheter stays in place (especially patients with cancer). Deep vein thrombolysis is not suggested as first line therapy (Grade 2C) - no better outcomes vs anticoagulation.
- Catheter stays in place if functional, not infected, and in correct position. Monitor and remove line if worsening symptoms on anticoagulation.
- Prophylactic anticoagulation for patients (with cancer) with catheters are not recommended. Grade 2A. UNLESS patient is high risk and risk of thrombosis outweighs risk of bleeding e.g. bulky disease, hereditary thrombophillia, suboptimal catheter tip location.

UEDVT: what anticoagulation?

- LMWH for at least 5 days followed by LMWH (preferred) or Vitamin K antagonists (over lap of 5 days minimum and INR >2) for minimum of 3 months or as long as catheter remains.
- UFH: 1)patients with severe renal insufficiency (CrCl <30ml/min). 2) patients with increased risk of bleeding where rapid reversal is needed. 3) Pt who received thrombolytic therapy.
- When to remove catheter if blocked? 3-5 days after anticoagulant therapy was initiated.
- DOACs : Generally NOT recommended due to unpredictable GI absorption (nausea, vomiting, diarrhoea) frequent hepatic and renal impairment, =and potential drug interactions with chemo.

LMW dosing:

- Dalteparin 200 U/kg daily for the first month then continue at ~150 U/kg daily.
- Tinzaparin 175 IU/kg daily.
- Enoxaparin 1 mg/kg twice daily.

The dose of LMWH in obese patients should not be capped but based on actual body weight. For patients weighing more than the upper limit accommodated by a single pre-filled syringe (i.e., 90 kg for dalteparin, 100 kg for enoxaparin and 103 kg for tinzaparin), twice daily dosing or use of multi-dose vials (available for all 3 LMWHs) is recommended.

Thrombosis Canada: Clinical guideline.

Questions:

Photo's by Desmond Snyman 4 May 1980- 4 September 2016