Subcutaneous Testosterone-Anastrozole Therapy in Breast Cancer Survivors

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Abstract 221
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Learning Objectives

After reading and reviewing this material, the participant should be better able to:

• Identify symptoms of androgen deficiency in pre and post menopausal breast cancer survivors
• Recognize the potential role of subcutaneous testosterone-anastrozole implant therapy in safely treating those symptoms
Outline

• Background
• Methods
• Results
• Conclusion
• Future
Background

• Both pre and post menopausal breast cancer survivors commonly experience symptoms of hormone deficiency that can adversely affect their health and quality of life.
Efficacy of Testosterone Therapy

- Continuous testosterone therapy, delivered by subcutaneous (SC) implant, effectively treats hormone/androgen deficiency symptoms as measured by the HRQOL, Menopause Rating Scale (MRS) in both pre and post menopausal patients.
Symptoms improved with SC continuous testosterone therapy

- Hot flashes, sweating
- Heart discomfort
- Insomnia, sleep problems
- Depressive mood, Irritability, Anxiety
- Physical fatigue, Memory loss
- Sexual dysfunction
- Incontinence, bladder problems
- Vaginal dryness
- Joint and muscular pain
Additional potential benefits in breast cancer survivors

• Testosterone protects against bone loss
• Testosterone stimulates bone marrow and enhances immune function
Background

- Evidence supports that testosterone is breast protective\textsuperscript{2,3}
- Testosterone can be aromatized to estradiol which may have adverse effects on breast cancer proliferation
- Third generation aromatase inhibitors effectively inhibit the aromatization of testosterone to estradiol
Preliminary data: 35 male patients

- 12 mg of anastrozole, a third generation aromatase inhibitor (AI), delivered *subcutaneously* by pellet implant, with up to 1200 mg of testosterone, effectively prevented the conversion of testosterone to estradiol in male patients with previously elevated estradiol levels.
Subcutaneous delivery (implants)

- Consistent delivery and consistent absorption
- Effective therapy
- Avoids entero-hepatic circulation
  - Bypasses liver
  - Does not affect clotting factors
  - Absence of GI side effects
- Circadian release
- No compliance issues
- Well tolerated
- Simple procedure to insert
Testosterone-Anastrozole Implant

• 3.1 x 6.1 mm implant
  – 60 mg testosterone
  – 4 mg anastrozole

  Powdered is compressed and sterilized

• Dose females: 2 implants
  – 120 mg testosterone
  – 8 mg of anastrozole
Simple 2 minute Procedure
Methods

• Breast cancer survivors were referred from their oncologists or self-referred (with permission from oncologist) for symptoms of androgen deficiency including bone loss

• Prior to July 2009, oral AI therapy was prescribed in conjunctions with SC testosterone in ER positive patients
Methods

• Data was available on 75 testosterone-anastrozole inserts performed in 43 of 55 breast cancer survivors treated between July 2009 and May 2010
Patient Demographics

• 38/43 patients were > 5 years from diagnosis
• 40/43 tumors were ER pos / non-invasive Ca

Tumor Stage
– 8 DCIS, 1 LCIS
– 19 Stage I
– 10 Stage II
– 1 Stage III
– 4 Stage IV
Methods: procedure, testing

- Two anastrozole-testosterone (A-T) implants (120 mg testosterone, 8 mg anastrozole) were inserted subcutaneously (SC) using local anesthesia in the upper gluteal area.
- Serum testosterone and estradiol levels were measured two weeks following implantation.
Results (Clinical)

- Subcutaneous testosterone-anastrozole therapy was effective in treating symptoms of hormone/androgen deficiency in breast cancer survivors
- All patients achieved relief of symptoms with therapeutic testosterone levels
  - Mean: 281 ng/dl, range: 120-518 ng/dl
Results

• In 70 of 75 (93.3%) testosterone-anastrozole pellet insertions (43 patients), serum estradiol measured ≤30 pg/ml
• A single post-menopausal patient on A-T had an estradiol level >40 pg/ml
  – Subsequent level measured <30 pg/ml
Results: E2 levels T alone vs. A-T

• Control group (n=119)
  – Post menopausal females treated with Testosterone implants alone (T)

• Estradiol levels: T vs. A-T
  – 42% (50/119) of patients treated with Testosterone alone had an E2>30 pg/ml
  – 6.7% (5/75) of patients treated with Anastrozole in combination with Testosterone (A-T) had an E2>30 pg/ml
The levels of Estradiol (E2) in the group with the aromatase inhibitor is significantly less than in the group without it (2-sample Wilcoxon rank sum test, P<0.0001). The separation of E2 in both groups is almost disjoint as illustrated by the kernel density plot.
Clinical follow up

- There have been no adverse drug events in over 170 insertions in 67 breast cancer survivors (Through September 2010)
- No breast cancer survivor treated with subcutaneous testosterone therapy has been diagnosed with recurrent disease in up to 4 years of therapy
Results

- There has been no progression of disease in 2 ER pos patients and 1 ER neg patient with metastatic disease treated for up to 30 months
  - The 4th patient presented with active disease and has responded to chemotherapy with minimal side effects from the chemotherapy. She continues on therapy and disease is stable.
Conclusion

• The combination of testosterone with anastrozole, delivered subcutaneously as a pellet implant, provides therapeutic levels of testosterone without elevating estradiol levels
Current & Future Studies

• Testosterone Implant-Breast Cancer Incidence Trial (Current) Glaser, Dimitrakakis
  – IRB approved, 10 year prospective study looking at the incidence of breast cancer in pre and post menopausal women treated with subcutaneous testosterone therapy

• ATTICA Breast* Trial (Future) Glaser, Dimitrakakis
  – Randomized, placebo controlled trial treating BrCa survivors on no current therapy, with SC A-T implants

*Anastrozole-Testosterone Therapy in CA Breast
Pending IRB approval and Funding
References


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