A Proposed Study of Hyperbaric Oxygen Therapy Following Radical Prostatectomy: Effects on Erectile Dysfunction

Anthony J. Bella MD, FRCSC
Division of Urology, Department of Surgery and Department of Neuroscience
University of Ottawa

DISCLOSURES

- Consultant/Advisor: Pfizer, Lilly, Bayer and American Medical Systems
- Speaker: Boehringer-Ingelheim, Pfizer, Lilly, Bayer, American Medical Systems
- Research Funding: ACORDA Therapeutics, Prostate Cancer Research Foundation of Canada, NEAUA, CMSHC, Canadian Institute of Health Research, Canadian Foundation for Innovation
INTRODUCTION

- Radical prostatectomy is a primary option for treatment of clinically localized prostate cancers
- Operative morbidity can result in a significant decrease in patient quality of life, even if surgery itself is curative

POST–RADICAL PROSTATECTOMY (RP) SEXUAL DYSFUNCTIONS

- Erectile dysfunction (ED)
- Anejaculation
- Anorgasmia
- Dysorgasmia (painful ejaculation)
- Orgasm-associated urine leak (climacturia)
- Penile shortening
- Penile fibrosis or curvature
POST–RADICAL PROSTATECTOMY (RP)
SEXUAL DYSFUNCTIONS

- Erectile dysfunction
- Penile (cavernous) fibrosis

ETIOLOGY OF ERECTILE DYSFUNCTION

Arterial
- Arterial
- Arteriolar

Cavernosal
- Tunica albuginea
- Cavernous muscle
- Endothelium
- Fibroblastic Trabeculae
- Emissary Vein

Systemic Diseases

Neurological
- Sensory
- Motor
- Autonomic
- Neurotransmitters

Psychological

Drugs

Hormonal
- Testicular
- Pituitary
- Thyroid
ETIOLOGY OF ERECTILE DYSFUNCTION

- Arterial
  - Arterial
  - Arteriolar

- Cavernosal
  - Tunica albuginea
  - Cavernous muscle
  - Endothelium
  - Fibroblastic Trabeculae
  - Emissary Vein

- Systemic Diseases

- Psychological

- Drugs

- Neurological
  - Cavernous Nerve

- Hormonal
  - Testicular
  - Pituitary
  - Thyroid
TREATMENT OF ED

• After fear of death/disability and incontinence, ED is the most common concern for the patient after prostate cancer treatment

• Why?
  Acute nature of the ED
  Last step to normalcy

IS PRESERVATION OF ERECTILE FUNCTION A PATIENT PRIORITY?

• Impotence
• Poor self-esteem
• Depression
• Difficulty with interpersonal relationships
• Decreased quality of life
DEFINING THE POPULATION

• Critical review of contemporary literature would suggest that regardless of surgical approach, the probability of clinically compromised potency is greater than 2 in 3

MULTIPLE HITS = COMPROMISED ERECTILE FUNCTION
MULTIPLE HITS = COMPROMISED ERECTILE FUNCTION

or

A small and atrophic penis does not equal a happy penis

RECOVERY OF ERECTILE FUNCTION AFTER RP

Multivariate Analysis: Clinical and Pathologic Factors

<table>
<thead>
<tr>
<th>Variable</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.0008</td>
</tr>
<tr>
<td>Full potency preoperatively</td>
<td>0.0039</td>
</tr>
<tr>
<td>Neurovascular bundle (NVB) status</td>
<td>0.0204</td>
</tr>
<tr>
<td>Surgical technique (pre- and post-1993)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Pathological stage</td>
<td>0.1279</td>
</tr>
<tr>
<td>Tumor volume</td>
<td>0.1483</td>
</tr>
<tr>
<td>Preoperative prostate-specific antigen</td>
<td>0.3336</td>
</tr>
<tr>
<td>UICC stage</td>
<td>0.5605</td>
</tr>
<tr>
<td>Surgical margins</td>
<td>0.7534</td>
</tr>
</tbody>
</table>
Does early pharmacotherapy improve the recovery of spontaneous erections in clinical practice?
Central to the argument supporting early penile rehabilitation is modulation of:

1. Nerve injury (neuroprotection/regeneration)
2. Nocturnal penile tumescence (oxygenation)

Early therapy may confer:
1. Endothelial benefits
2. Enhanced nerve regeneration
3. Preservation of cavernous smooth muscle

Prophylactic Therapy with ICI

- Bilateral nerve-sparing RP patients: intracavernous alprostadil 3x/week for 12 weeks
- Assessed at 6 months postoperatively
- 15 in treatment group, 15 in control group (unblinded)
- 67% in treatment group had erectile function good enough for sexual intercourse
- 20% in control group had erectile function good enough for sexual intercourse
- Majority of failures had venous leak on duplex ultrasound

ReINVENT
Recovery of Erections: Intervention with Vardenafil Early Nightly Therapy

So, with the current understanding, how are RP patients treated in 2008?
Best (Evidence and Opinion-Based) Practice

- Early assessment of patient
- Define patient EF status and treatment goals

- First line oral PDE-5 inhibitors
- No response - intracavernous injection therapy + PDE-5 inhibitors
Best (Evidence and Opinion-Based) Practice

- Early assessment of patient
- Define patient EF status and treatment goals

- First line oral PDE-5 inhibitors
- No response - intracavernous injection therapy + PDE-5 Inhibitors

- Early treatment = (likely) better long-term potency
- When? 2 weeks after surgery

Is there a potential role for HBO?
Is there a potential role for HBO?

Figure 1: Functional results. Graph showing the mean maximum intracereovascular pressure/mean arterial pressure (ICP/MAP) ratio for each group. The C+H- and C+H+ groups showed a significant reduction in ICP/MAP ratio compared with C- H- ("P < 0.05). But the C+H+ group had a significant recovery of ICP/MAP ratio after hyperbaric oxygen therapy compared with the C+H- group ("P < 0.01).

Is there a potential role for HBO?

Figure 2: Neurotrophic growth factor (NGF) and nitric oxide synthase (NOS) staining. NGF staining: the C+H+ group demonstrated higher density of NGF staining compared with C+H- group ("P < 0.05), whereas staining: the density for aNOS in the C+H+ group was significantly higher compared with C+H- group ("P < 0.001).
Is there a potential role for HBO?

Is there "enough evidence" for HBO?
Is there "enough evidence" for HBO?

- Mechanism of ED - cavernous smooth muscle fibrosis
- Pt population
- Significant morbidity and decreased quality of life
- 'Standard of Care' - intracavernous injection therapy + PDE-5 inhibitors

The Proposal for HBO

- Additive to current management
- Early post-RP, BNS
- 30 sessions
- Two arm trial - PDE-5 vs PDE-5 and HBO
- Introduction of intracavernous injection if non-responsive to PDE-5 or combination
- Initial pilot feasibility study
- Continence benefit?
A Proposed Study of Hyperbaric Oxygen Therapy Following Radical Prostatectomy: Effects on Erectile Dysfunction

Anthony J. Bella MD, FRCSC
Division of Urology, Department of Surgery and Department of Neuroscience
University of Ottawa