

VERAPAMIL FOR PEYRONIE'S DISEASE: NOT VIABLE

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DISCLOSURE

I have the following relevant financial relationships to disclose:

- **Consultant: American Medical Systems, Coloplast**
- **Member, Board of Directors: Sexual Medicine Association of North America**

AGENDA

- Verapamil
 - Mechanism of Action
- Technique of ILV
- Research Data
- Results with Other Agents
- Conclusions

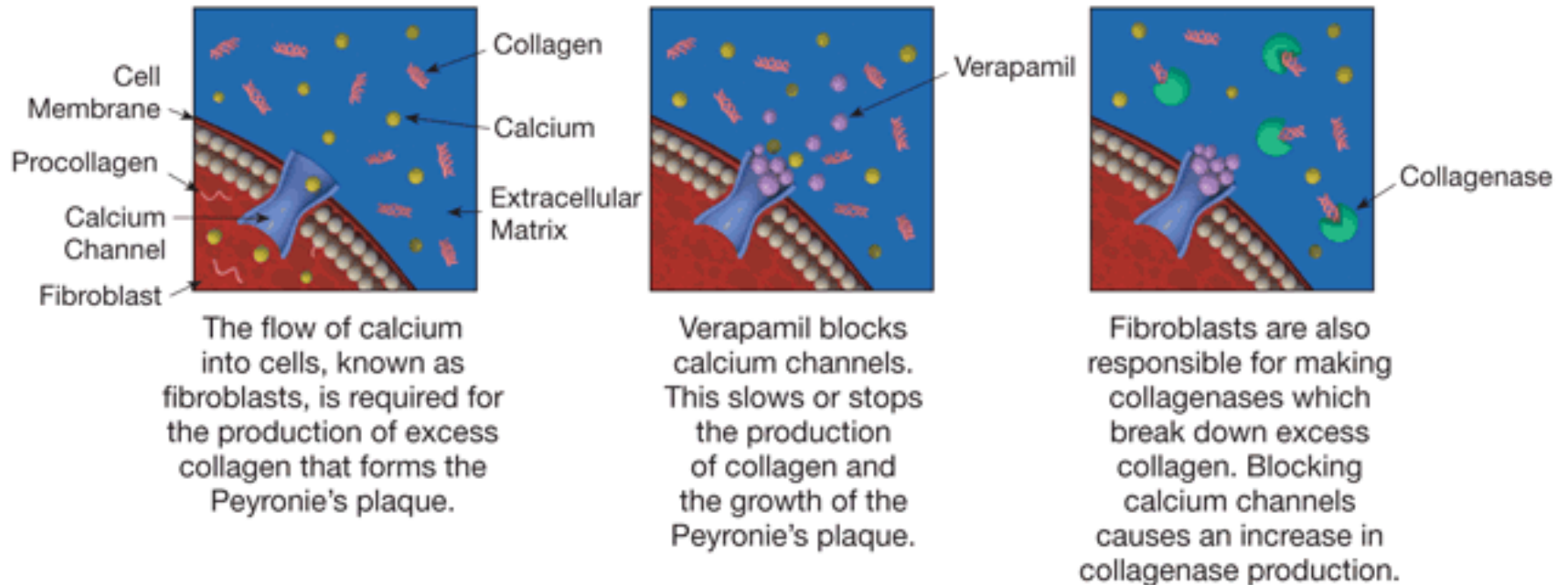


VERAPAMIL

- “L-type” blocker of voltage-dependent calcium channel blocker of the phenylalkylamine class.
- Used commonly for HTN, angina pectoris, cardiac arrhythmia, cluster headaches.
- Useful as vasodilator during cryopreservation of blood vessels.
- Approved by Food & Drug Administration (FDA) - March 1982.

VERAPAMIL

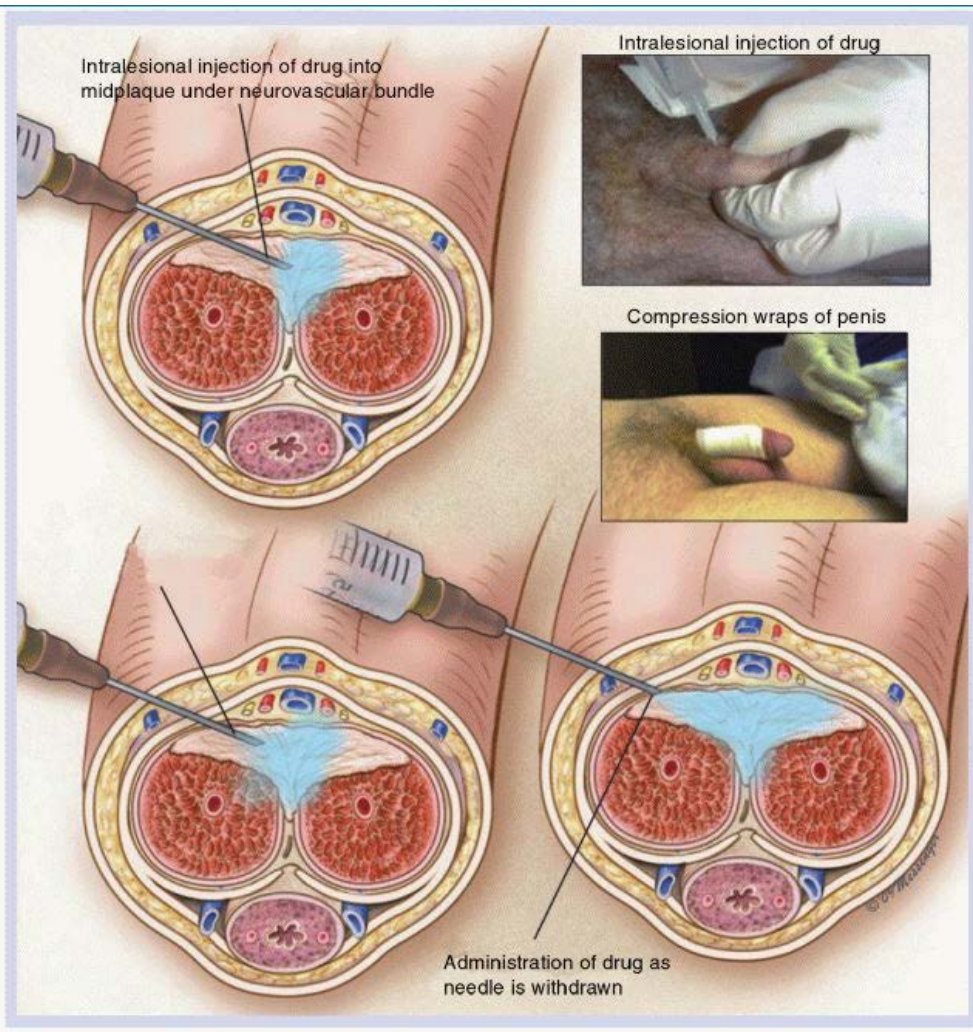
Proposed Mechanism of Action for Peyronie's Disease



Roth M, Eickelberg O, Kohler E, Erne P, Block LH. Ca²⁺ channel blockers modulate metabolism of collagens within the extracellular matrix. Proc Natl Acad Sci U S A. 1996;93:5478-5482.

Mulhall JP, Anderson MS, Lubrano T, Shankey TV. Peyronie's disease cell culture models: phenotypic, genotypic and functional analyses. Int J Impot Res. 2002;14:397-405.

VERAPAMIL INJECTION TECHNIQUE



Treatment Technique

- Penile block with 10 mL 0.5% bupivacaine/2% lidocaine
- **MULTIPLE** puncture technique w/25 g needle
- Verapamil 5 mg in 3 cc NaCl (total volume 5 mL)
- 1 injection q 2 weeks x 3 months (6 total)
- Wrap with compression dressing
- Monitor blood pressure
- Give 6 additional injections if no improvement

ISSUES WITH VERAPAMIL STUDIES

- Study Design
 - Few Randomized
 - Few Placebo-controlled
 - Adequately powered ?
- Definition of successful treatment
 - Absolute change in curvature
 - Resolution of pain
 - Change in plaque size
 - Improvement in EF
- Best way to measure outcomes
 - Objective – office-based assessment
 - Subjective – patient report

OVERVIEW OF STUDIES

	n	Dose/Duration	Method	F/U (mos)	Results	↓ Curvature (Degree)
Levine (2007)	156	10 mg Biweekly x 6 mo	No Control group Non-randomized	30.4	↑ Plaque size ↓ Curvature 62% ↓ Pain 84% ↑ Sexual function 71%	31.0
Bennett (2007)	94	10 mg Biweekly x 3 mo	No Control group Non-randomized	5	↓ Curvature 18% ~ Curvature 60% ↑ Curvature 22% ↓ Pain 100%	12.0
Rehman (1998)	14	10-27 mg weekly x 6 mo	Randomized, Placebo-controlled	3	↓ Plaque size 57% ↓ Deviation 29% ↓ Pain 100% ↑ Sexual function 43%	8.1
Nicolai (1998)	40	10 mg Biweekly x 6 mo	Randomized, Placebo-controlled	3	No Effect	5.2
Steiger (1999)	52	1 umol biweekly x 6 months	Randomized, Placebo-controlled	48	No Effect	9

Evaluation of Verapamil Efficacy in Peyronie'S Disease Comparing With Pentoxifylline

M. Alizadeh¹, F. Karimi² & M. R. Fallah¹

- Prospective, randomized study of 190 patients with PD
- 3 Groups
 - Oral pentoxifylline 400 mg TID x 6 months
 - Verapamil 10 mg biweekly x 6 months
 - Pentoxifylline + ILV x 6 months



	Pentox (%)	ILV (%)	Pentox+ILV (%)
↓ Curve	26.7	36.7	36.7
↓ ED	46.7*	66.7	86.7*
↓ Pain	73.3**	76.7	80**

* p=0.001 ** p=0.001

- No significant difference in curvature reduction

OTHER INJECTABLES

Agent	Dose	Mechanism of Action	Clinical Effect
Interferons	1–10 000 U per week	Decrease fibroblast proliferation <i>in vitro</i> , reduce ECM, and increase collagenase activity	↓ Curvature of 27% Resolution of pain in 67% ↓ Plaque size by 54.6%
Orgotein	4 mg biweekly	Anti-inflammatory with pronounced superoxide dismutase activity	Improvement in “sexual function”
Corticosteroids	25-50 mg every 1-6 weeks	Anti inflammatory	100% resolution of pain No significant difference in curvature, or plaque size
Collagenase	0.58 mg	Lysis of collagen	↓ Curvature of 17.0° [34.0%]

Gelbard M, et al. Clinical efficacy, safety and tolerability of collagenase clostridium histolyticum for the treatment of Peyronie disease in 2 large double-blind, randomized, placebo controlled phase 3 studies. *J Urol* 2013;190:199–207

Dickstein R, Uberoi J, Munarriz R. Severe, disabling, and/or chronic penile pain associated with Peyronie's Disease: management with subcutaneous steroid injection. *J Androl* 2010; 31: 445–449.

Gustafson H, Johannsson B, Edsmyr F. Peyronie's Disease: experience of local treatment with orgotein. *Eur Urol* 1981; 7: 346–348

Hellstrom WJ, et al. Single-blind, multicenter placebo-controlled parallel study to assess the safety and efficacy of intralesional interferon alpha-2B for minimally invasive treatment for Peyronie's disease. *J Urol* 2006; 176: 394–398.

VERAPAMIL

- Requires multiple sessions
- Requires multiple penile injections in each session
- Not FDA approved for PD
- Limited curvature correction

VERAPAMIL FOR PD?



Time to show verapamil the door.

THANK YOU



Green Power (1975)
David Hammons (American b. 1943)