

“Deficit erettile e Malformazioni del pene” CORSO TEORICO-PRATICO

Foggia, 24-25 gennaio 2007

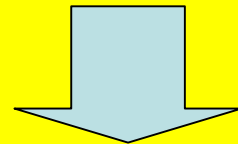
LA TERAPIA MEDICA DELLE MALFORMAZIONI PENIENE

T. Corvasce

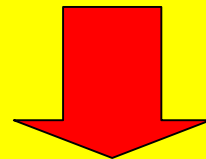
***Clinica Urologica e Centro Trapianti di Rene
Universita' degli Studi di Foggia***

IPOSTESI ETIOPATOGENETICA INCURVAMENTO PENIENO (M. LA PEYRONIE)

- danno microvascolare ripetuto nel tempo**
- soggetti geneticamente predisposti**



**INFILTRATO LINFOCITARIO PERIVASCOLARE
TONACA ALBUGINEA**



**Risposta miofibroblastica locale, perdita di elastina,
deposizione di tessuto collageno-fibrinico (25% casi
tessuto calcifico)**

STORIA NATURALE DELLA M. DI LA PEYRONIE RAZIONALE PER UNA TERAPIA MEDICA

Guarigione

13 %



Stabilizzazione

45 %

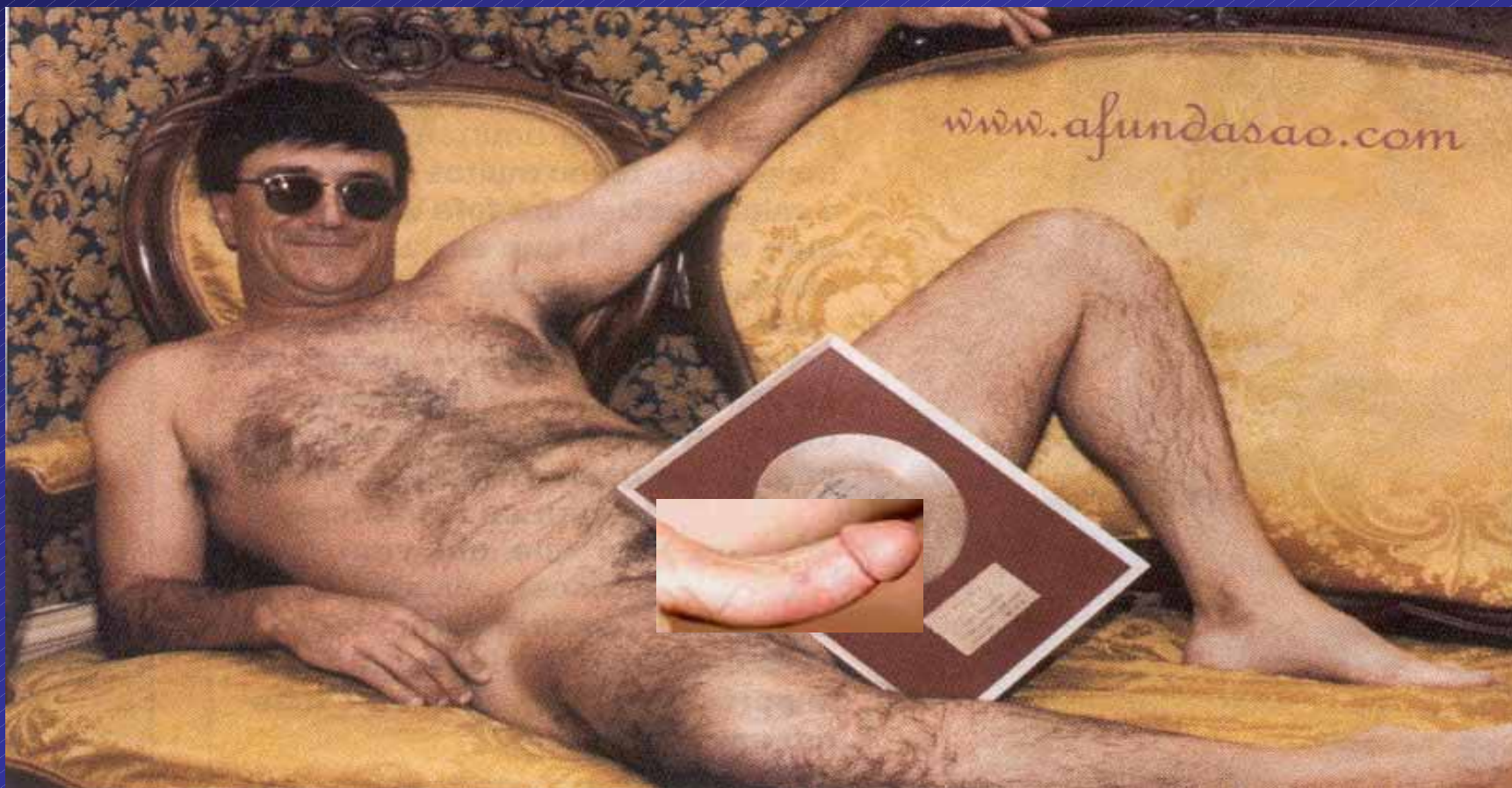
Progressione

42 %

Terapia medica puo' essere indicata

1. erezioni dolorose
2. ridurre rischio ulteriore incurvamento penieno o progressione della placca.

QUALE TERAPIA MEDICA ?



TERAPIA

Trattamento

Potaba

(K paramminobenzoato)



Effetto

1. Inibisce proliferazione fibroblastica
2. Previene progressione incurvamento (30%)
3. GI adverse events
4. Costo elevato

Oral drugs

Results with Potaba therapy for Peyronie's disease

<i>Study</i>	<i>Patients</i>	<i>Improvement in pain</i>	<i>Improved plaque size</i>	<i>Improved angulation</i>
Zarafonitis ⁴¹	21	100%	76%	82%
Hasche-Klunder ²⁹	25	100%	100%	71%
Riley ⁴²	18	100%	11%	75%
Carson ⁴³ 1983	32	44%	56%	58%



Potassium Paraaminobenzoate (POTABA™) in the Treatment of Peyronie's Disease: A Prospective, Placebo-Controlled, Randomized Study

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Available online 13 January 2005

103 Pts PEYRONIE DISEASE
History > 12 months
Non-calcified plaque



51 POTABA



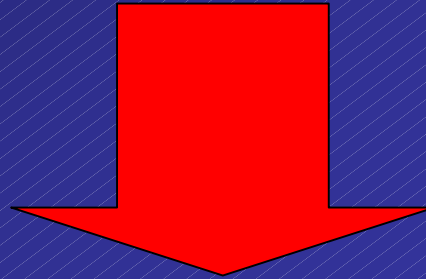
52 placebo

3 g x 4/day x 12 months



END-POINT:

1. REGRESSION IN PLAQUE-SIZE
2. AND/OR REDUCTION IN PC AT LEAST 30%



RESULTS

- No adverse events occurred
- Response rate 74% POTABA vs 50% PLACEBO (p 0,016)
- Mean plaque-size decrease 259 mm² → 142 mm² potaba
- Mean plaque-size 259 mm² → 303 mm² placebo (p 0,042)
- Pre-existing curvature didn't improve under drug (0,066) but under POTABA PC remained stable. Under placebo PC deteriorated significantly 32,5% (p <0,001)
- No significant differences concerning decrease of pain between two groups (82,% vs 77,3%)

CONCLUSIONS

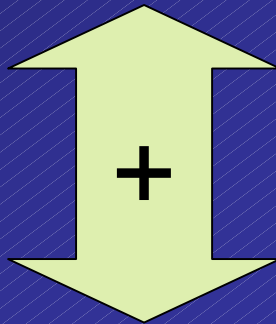
- Potaba has protective effect on deterioration of pre-existing PC
- Stabilize disorder and prevent progression of PC

TERAPIA

Oral drugs

Vitamina E (400 UI b.i.d) per 6 mesi

1. 50% riduz. Dolore
2. No riduz placca o grado incurvamento
3. Scarsi benefici QSI (quality sexual intercourse)



**Intralesional Interferon alpha 2b
(5 Milioni UI weekly x 12 wks)**

1. 83 % riduz. Dolore (associato a Vit E)
2. No riduz placca o grado incurvamento
3. Scarsi benefici QSI (quality sexual interc)
4. Effetti collaterali (febbre, mialgia, artralgia)
5. Costo della terapia



TERAPIA

Trattamento

Oral drugs

Tamoxifene
(anti-estrogeno NS
20 mg bid x 3/6 mesi)

Results with tamoxifen therapy for Peyronie's disease

Study	Patients	Improvement in pain	Improved plaque size	Improved angulation
Ralph ³⁹	36	80%	34%	35%
Teloken ¹⁸	25	67% ^a	<u>31%^a</u>	<u>46%^a</u>

^aNon-significant versus placebo-controlled patients.

Effetto

Tumori desmoidi

Modula secrez TGFβ1

No differenze vs placebo per effetti su

1. Dolore
2. Placca (size)
3. Grado di Incurvamento

- *Risposta* > *in fase acuta*

Effetti Collaterali

Vampate, riduzione libido e volume
eiaculato

Teloken C et al J Urol 1999



TERAPIA

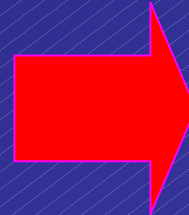
Oral drugs

Trattamento

Effetto

Colchicina

(0,5 mg daily to → 1 mg bid x 3-6 m)



1. Inibisce microtubuli
2. Attivita' antiinfiammatoria ed antifibroblastica
3. Utile nella fase acuta del dolore con lieve incurvamento penieno (30°)

Effetti Collaterali

GI (33%), Febbre, Rash, Anemia aplastica, miopatia, edema angioneurotico

Results with colchicine therapy for Peyronie's disease

<i>Study</i>	<i>Patients</i>	<i>Improvement in pain</i>	<i>Improved plaque size</i>	<i>Improved angulation</i>
Akkus ³³	1994 24	78%	50%	37%
Kadioglu ³⁴	2000 60	95%	NR	30%
Flores ³⁵	2001 59	<u>71%</u>	<u>47%</u>	<u>55%</u>

LOCALIZED DRUG ADMINISTRATION

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A PROSPECTIVE, RANDOMIZED STUDY USING TRANSDERMAL ELECTROMOTIVE ADMINISTRATION OF VERAPAMIL AND DEXAMETHASONE FOR PEYRONIE'S DISEASE

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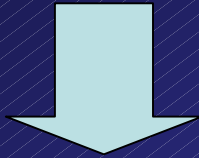
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Laboratories, Medolla, Department of Science and Society, University of Cassino, Cassino, Department of Experimental Medicine,
University of L'Aquila, L'Aquila, and Operative Unit of Urology, "Antonio Ferrino" Hospital, Brindisi, Italy*

96 Pts PEYRONIE DISEASE

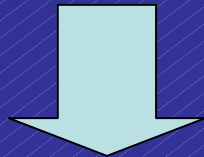
Inclusion Criteria: clinical evidence PD,
Deformity and/or pain

Exclusion Criteria: recent tx with calcium blockers
or corticosteroids, therapies interfering with
verapamil or dexamethasone, DE due
neurological, hormonal, vascular or psychological
causes

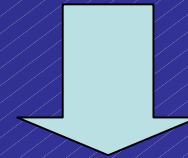
- **Randomisation** (2 factors): plaque $\leq 1 \text{ mm}^3$ vs
plaque $> 1 \text{ mm}^3$ and PC $\leq 35^\circ$ vs PC $> 35^\circ$
- **Clinical assessment**: before and 4 wks after
conclusion of tx.
- **Treatment plane**: 4 session/wk for 6 consecutive
wks



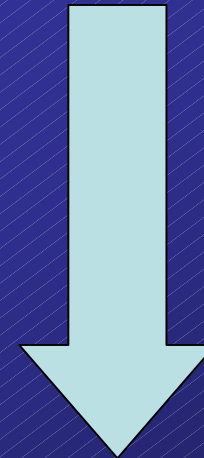
47 pts received transdermal Electromotive. A skin electrode sited over the plaque and filled with 5 mg verapamil and 8 mg dexamethasone into 5 ml of volume with anode over plaque and catode at lower abdome. A current generator provided direct current of 2,4 mA at 2500 Hz for 20 minutes. Monitoring BP and heart rate



37 pts completed study



49 pts received transdermal Electromotive lidocaine 2%



36 pts completed study



RESULTS

Treatment efficacy

	Verapamil + Dexamethasone			Lidocaine			p Value Among Groups (Mann-Whitney-Wilcoxon rank sum test)
	Before	After	p Value	Before	After	p Value (Wilcoxon signed rank test)	
Median mm ³ plaque vol (IQR)	824.4 (986.7)	347.7 (421.7)	<0.0001	771.4 (630.0)	766.6 (692.5)	0.167	<0.0001
Median degrees penile deviation (IQR)	43.0 (21.5)	21.0 (21.0)	<0.0001	41.0 (22.5)	41.0 (23.0)	0.433	<0.0001
Range penile deviation (degrees)	28-73	2-60		25-70	17-71		
No. pain on erection:							
None	0	28		0	4		
Mild	9	7	<0.0001	12	8	0.046	
Moderate	28	2		24	24		

CONCLUSIONS

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PENILE RADIOTHERAPY



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CLINICAL INVESTIGATION

Benign Disease

RESULTS OF RADIOTHERAPY FOR PEYRONIE'S DISEASE

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**FROM 1983-2000 154 pts were irradiated
101 complete follow up**

Mean age 54 yrs

Mean duration symptoms before tx 18 months

Mean duration f-u: 5 yrs

Before radiotx: 57/94 pts had had no pretreatment

24 (oral medication POTABA)

10 (injection into the foci)

2 (had been operated)

1 (local radiotherapy)



- **48/92 pts (52%) reported painful erections**

- **1 pts DE**

- **Mean penile deviation 45°**

- **88 pts suffered also of Dupuytren's disease**

- **All pts received 2 Gy/day (total dose 30 Gy 72 pts, 36 Gy 25 pts, 34 Gy 1 pt, 40 Gy 1 pt). 1 pt discontinued tx after 32 Gy; in 3 others dose was elevated → short interruption of radiotx**

Extent of the disease before radiotherapy

Classification	Patients	%
Maximum diameter of foci (84/101 patients)		
<5 mm	7	8
5–10 mm	36	43
>10 mm	41	49
Number of foci (83/101 patients)		
1	54	65
2	25	30
3 and more	4	5
Quality of foci (89/101 patients)		
Fibrous	28	31
Cartilaginous	27	30
Calcified	34	39

Figures are restricted to the 101 patients for whom follow-up data are available (69% of all patients treated for the disease).

Results during follow-up

	No. of follow-up datasets			
	1	2	3	4
Mean time interval from the end of radiotherapy (days)	80	460	1100	1400
<u>Deviation</u>				
Data available (patients)	101/101	89/101	68/101	47/101
Improved	23 (23%)	23 (26%)	17 (25%)	15 (32%)
Stable	71 (70%)	55 (62%)	46 (68%)	29 (62%)
Worse	7 (7%)	11 (12%)	5 (7%)	3 (6%)
<u>No. of foci</u>				
Data available (patients)	101/101	87/101	62/101	36/101
Improved	16 (16%)	16 (18%)	9 (15%)	5 (14%)
Stable	79 (78%)	66 (76%)	52 (84%)	30 (83%)
Worse	6 (6%)	5 (6%)	1 (1%)	1 (3%)
<u>Quality of foci</u>				
Data available (patients)	101/101	84/101	63/101	36/101
Softened	32 (32%)	22 (26%)	18 (29%)	8 (22%)
Stable	65 (64%)	54 (64%)	42 (67%)	26 (72%)
Hardened	4 (4%)	8 (10%)	3 (4%)	2 (6%)
<u>Size of foci</u>				
Data available (patients)	101/101	93/101	69/101	48/101
Improved	23 (23%)	28 (30%)	16 (23%)	13 (27%)
Stable	71 (70%)	57 (61%)	47 (68%)	32 (67%)
Worse	7 (7%)	8 (9%)	6 (9%)	3 (6%)
<u>Pain</u>				
Data available (patients)	87/101	92/101	69/101	56/101
Patients with pain (before RT: 48/92 patients, 52%)	26 (30%)	25 (27%)	14 (20%)	5 (10%)
<u>Erectile dysfunction</u>				
Data available (patients)	85/101	84/101	71/101	47/101
Patients with ED (before RT: 1/72 patients, 1%)	6 (7%)	4 (5%)	6 (8%)	3 (6%)

Abbreviations: ED = erectile dysfunction; RT = radiotherapy.

Results of radiotherapy in literature

Reference	Number of patients	General improvement	Relief of pain	Improvement of deviation	Reduction of induration
Rodrigues <i>et al.</i> , 1995 (2)	38	60%	76%	48%	—
Wagenknecht, 1996 (3)	1420	60%	—	—	—
Koren <i>et al.</i> , 1996 (4)	265	66.4%	61.5%	—	—
Alth <i>et al.</i> , 1985 (6)	2210	69%	—	—	—
Alth <i>et al.</i> , 1975 (7)	1524	69%	61.4%	11.2%	—
Ludvik <i>et al.</i> , 1968 (9)	259	—	96.9%	78%	85.7%
Landthaler <i>et al.</i> , 1983 (10)	92	30.43%	73%	20%	20%
Martin <i>et al.</i> , 1972 (11)	142	—	84.3%	62.7%	76.4%
Schreiber <i>et al.</i> , 1978 (12)	49	75%	78%	57%	63%
Culibrk <i>et al.</i> , 2001 (14)	35	29%	—	—	—
Incrocci <i>et al.</i> , 2000 (17)	106	—	69%	29%	—
Incrocci <i>et al.</i> , 2000 (18)	179	—	83%	23%	—
Bruns <i>et al.</i> , 1999 (19)	24	66%	—	—	—
Viljoen <i>et al.</i> , 1993 (20)	47	—	84%	38.6%	—
Kammerer, 1988 (21)	49	57.1%	—	—	—
Weisser <i>et al.</i> , 1987 (22)	54	—	79%	69%	59%
Wagenknecht <i>et al.</i> , 1982 (23)	113	44%	—	—	—
Mira <i>et al.</i> , 1980 (24)	56	41%	—	—	—
Schmitt <i>et al.</i> , 1997 (25)	49	75%	—	—	—
Furlow <i>et al.</i> , 1975 (26)	90	—	100%	52%	58%
Helvie <i>et al.</i> , 1972 (27)	40	72%	72%	29%	35%
Dunlap <i>et al.</i> , 1969 (28)	23	—	91.3%	65.2%	65.2%
Feder, 1971 (29)	37	—	56%	14%	—
Meineke <i>et al.</i> , 2003 (30)	67	—	84%	38%	56%

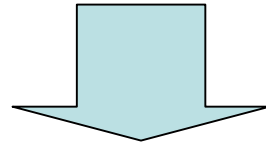
CONCLUSIONS

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Recenti studi

The Effect of Pentoxifylline on Cultured Human Tunical Fibroblasts from Patients with Peyronie's Disease

PTX effectively inhibited the TGF- β induced production of collagen I in Peyronie Plaque cells



The results of this study *support and may elucidate the beneficial effect of PTX* in Peyronie's disease seen in our clinical practice.



Thomas X. Minor et al.
American Urological Association Annual Meeting
May 21 - 26, 2005 San Antonio, Texas, USA

RUOLO DELLA TERAPIA MEDICA NELL'INCURVAMENTO PENIENO

- Limitato alla fase acuta della flogosi fino a stabilizzazione della placca
- Alcuni farmaci sembra che evitino la progressione della CP
- ***Necessari studi long-term di tipo randomizzato/doppio-cieco con controllo placebo, valutazione standardizzata QSI, Pain scale, controllo obiettivo placca e curve~value pre-post terapia dai quali si evidenzi una significativa' statistica (Dohle G. Eur Urol 2006)***

Difronte ad una Peyronie acuta o subacuta la nostra Lei rimane sempre insoddisfatta, con lo sguardo di chi spera nel prossimo futuro si possa curare piu' efficacemente tale patologia e non perdere piu' i tanti treni del piacere di coppia !



**FISCHIETTO
PERFETTO !**