[연수강좌]

발기부전의 새로운 약물

안 태 영

울산의대 서울아산병원 비뇨기과

발기부전치료의 최신경향

울산의대 서울아산병원 비뇨기과

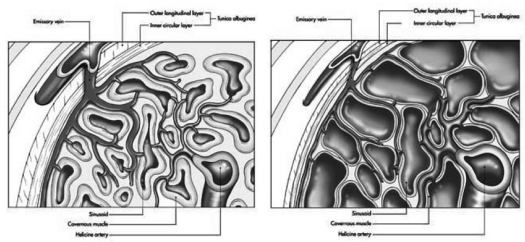
안 태 영

발기부전의 위험인자

✓ 심장 질환	2배
✓ 고혈압	1.5 ~ 2배
✓ 당뇨병	3 ~ 4배
✓ 우울증	2 ~ 3.5배
✓ 하부 요로 증상	1.5 ~ 2배
✓ 고밀도 콜레스테롤 저하	4배
✓ 실직	2배

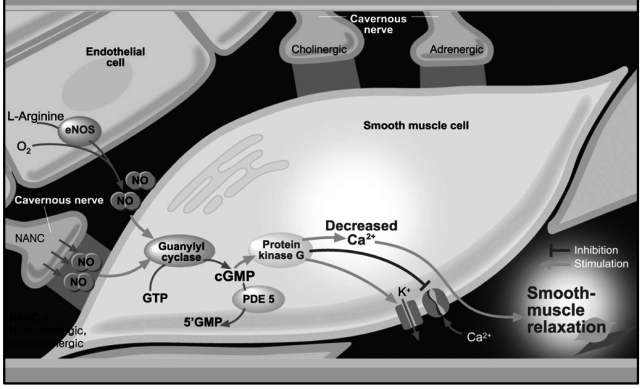
• Ref. Laumann EO *et al. JAMA* 1999; 281: 537-544.
Braun M *et al. Int J Impot Res* 2000; 12: 305-311
Morillo L. Presented at CAU meeting, September 2000, Buenos Aires, Argentina.

발기의 기전



Adapted from Krane et al, 1989

음경발기에서 NO / cGMP의 역할



국제 발기능 설문지

- International Index of Erectile Function

의사관련 요인

❑ 잘못된 복약지도
- 복약지도 사항
  - 지방 함유 음식과 함께 복용을 피함
  - 복용 후 작용시간의 지연 (30 ~ 60 분 후에 작용 시작)
  - 성적 자극이 필요함

❑ 부적절한 용량

❑ 잘못된 진단
- 내분비계 질환
- 폐이로니병
- 사정 장애
- 오르가즘 장애

환자관련 요인

❑ 비현실적인 기대
- "모든 사람에게 효과 있는 것이 아닌가요?"
- "약을 먹으면 항상 단단하게 발기되지 않나요?"
- "나는 분명히 약을 먹었는데, 발기가 되지 않더군요."

❑ 투여의 지속성 결여
- 시험적 복용 횟수가 충분치 못한 경우 (8회 미만)

❑ 부작용에 대한 두려움
- 심혈관계 이상과 같은 심각한 부작용에 대한 두려움

환자관련 요인

❑ 정신 심리적 요인
- 새로운 성생활과 관련된 불안증

❑ 파트너의 요인
- 기타 성기능 장애 동반
  - 성욕저하, 성교통, 질건조증, 불감증 및 오르가즘 장애 등
- 성 건강에 대한 염려
- 일반적인 건강 상태의 이상

❑ 발기력의 개선
- 발기력의 회복 후 약물사용 중지

VIAGRA AND TESTOSTERONE (n=67)

Shabsigh et al

IIEF	T-GEL + VIAGRA	PLACEBO + VIAGRA	P-value
Erectile	5.65	2.97	0.03
Orgasmic	1.53	0.36	0.01
Desire	0.44	0.00	0.21
Satisfaction	1.21	0.70	0.25
Overall	1.62	0.61	0.04
Total	10.44	4.62	0.02

대사증후군의 기준 (NCEP-ATP III, 2001)

Risk Factor Clinical identification (≥3 risk determinants)	Definition Level
Waist circumference	
Men (cm)	> 102 (90)
Women (cm)	> 88 (80)
Triglyceride (mg/dL)	≥ 150
HDL-C	
Men (mg/dL)	< 40
Women (mg/dL)	< 50
Blood pressure	≥ 130 / ≥85
Fasting glucose	≥ 110

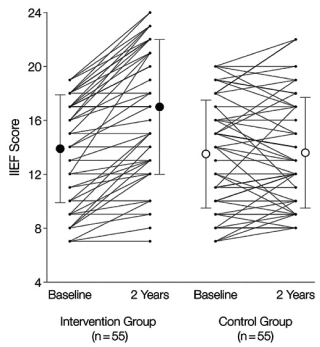
JAMA 285:2486, 2001

Randomized Controlled Trial

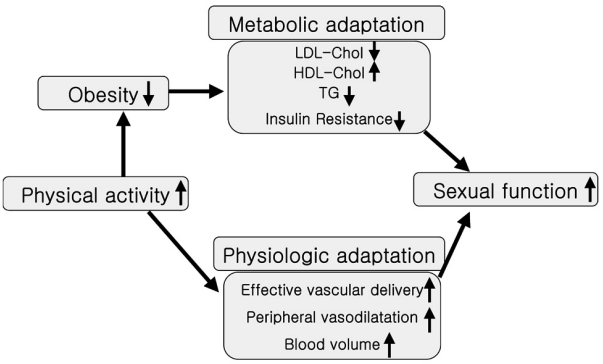
- Italian Study
- Randomized, 2-yrs!!!, n=110 obese (BMI ≥30)
- No diabetes, HTN, or dyslipidemia w/ED
- 21 or less on IIEF
- 55 men reduced calories, increase exercise

Esposito K, et al. JAMA 291:2978-2984, 2004.

Individual Changes in Erectile Function Score of Obese Men



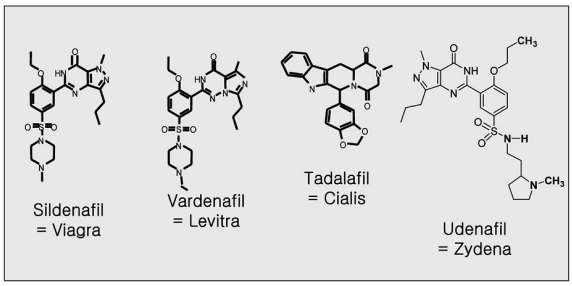
Physical activity- mechanism



Recommendation

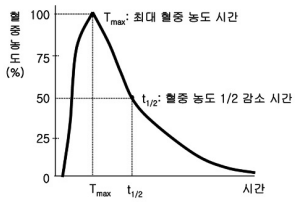
1. Increase daily physical activity.
   Accumulate at least 30 min or more of moderate intensity physical activity on most days of the week.
2. Measure waist circumference in addition to body weight.
3. Diet induced weight loss is good, diet and exercise-induced weight loss is better.

PDE5 억제제의 종류



약물역동학: T_{max} 와 $t_{1/2}$

❑ T_{max} 와 $t_{1/2}$에 따라 약제의 발현 시간과 작용 시간이 결정된다.



	T_{max}	$t_{1/2}$(hr)
• Sildenafil	1.16	3.82
• Vardenafil	0.66	3.94
• Tadalafil	2.0	17.5
• Udenafil	1-1.5	12

❖ 주요 PK 및 약효 특성 비교

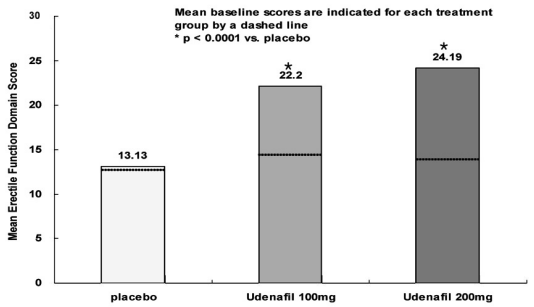
	Udenafil (Zydena)	Sildenafil (Viagra)	Tadalafil (Cialis)	Vardenafil (Levitra)
Half-life	11 - 13 hrs	4 hrs	17.5 hrs	4 hrs
Onset	30- 40 mins (est.)	30-60 mins	45 mins (?)	30-60 mins
Duration	24 hrs (est.)	4 - 8 hrs	36 hrs Could be more longer	6 - 8 hrs
Selectivity to PDE6	X10	X10	X190	X10
Selectivity to PDE11	> X3000	X780	X5	X1160
Major AE's	Headache Facial flushing	Headache Facial flushing Blue-tinged vision	Headache Indigestion Myalgia	Headache Upset stomach

Clinical Study - *Phase 3*

- Objectives
  - To evaluate the efficacy, safety and tolerability of oral Udenafil in patients with ED
  - To examine the therapeutic effects of Udenafil on ED at 12 hours after dosing
- Design
  - double-blind, placebo-controlled, randomized, parallel group, fixed dose
  - Part 1 : 4 week treatment-free run-in period, 12 week treatment period (instructed to attempt the intercourse at 30min ~ 8hrs after dosing) dose levels - Udenafil 100mg, 200mg
  - Part 2 : 4 week treatment-free run-in period, 4 week treatment period (instructed to attempt the intercourse at 12hrs after dosing) dose levels - Udenafil 100mg

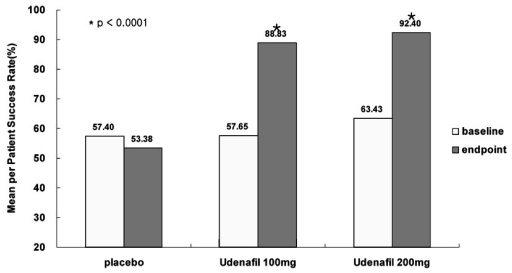
Clinical Study - *Phase 3 ; part 1*

- IIEF EFdomain



Clinical Study – *Phase 3 ; part 1*

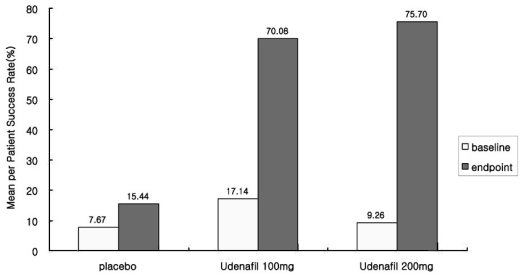
- SEP Q2



SEP Question 2 : Were you able to insert your penis into your partner's vagina?

Clinical Study – *Phase 3 ; part 1*

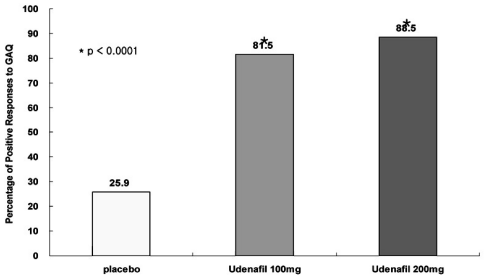
- SEP Q3



SEP Question 3 : Did your erection last long enough for you to complete intercourse with ejaculation?

Clinical Study – *Phase 3 ; part 1*

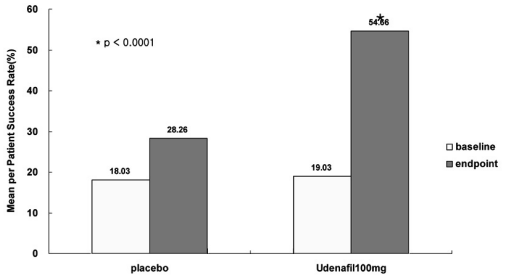
- GAQ



GAQ : Has the treatment you have been taking over the past 4 weeks improved your erection?

Clinical Study – *Phase 3 ; part 2*

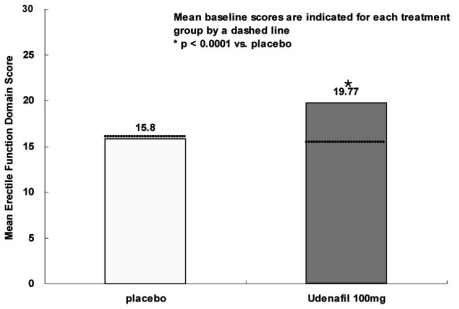
- SEP Q3

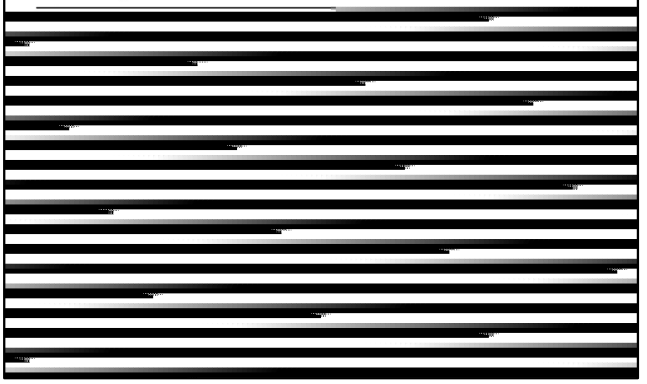


SEP Question 3 : Did your erection last long enough for you to complete intercourse with ejaculation

Clinical Study – *Phase 3 ; part 2*

- IIEF EF domain



Clinical Study – *Phase 2 + Phase 3*

- Safety – Adverse Events