

THE ROLE OF PLATELET CGMP AND CAMP VALUES IN PREDICTING RESPONSE TO ORAL PHOSPHODIESTERASE TREATMENT IN MEN WITH ERECTILE DYSFUNCTION

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Introduction & Objectives: We tried to develop a laboratory test by using platelet cyclic guanosine monophosphate (cGMP) and cyclic adenosine monophosphate (cAMP) levels to predict the clinical response of patients with erectile dysfunction (ED) treated with phosphodiesterase (PDE5) inhibitors.

Material & Methods: Between October 2004 - February 2006, 19 patients referring to our clinic because of ED with an average age of 48.3 years (20-66y) and 16 men with a complaint except ED with an average age of 38.7 years (26-62y) were evaluated with a detailed history, physical examination, laboratory tests and IIEF. cGMP & cAMP levels were assessed after adding sodium nitroprusside (SNP), sildenafil (S) and vardenafil (V) to blood samples.

Results: No statistically significant difference was determined for cGMP-SNP, cGMP-S, cGMP-V between the patient and control groups. In the control group, while cAMP-S & cAMP-V are statistically lower than cAMP-SNP ($p < 0.001$), there is no difference between cAMP-S & cAMP-V ($p > 0.05$). In the patient group, cAMP-S is statistically significantly lower than both cAMP-SNP & cAMP-V ($p < 0.001$). While no statistically significant difference is determined for the alteration between cGMP-SNP & cGMP-S, cGMP-SNP & cGMP-V, cGMP-S & cGMP-V and cAMP-SNP & cAMP-S between the patient and control groups, a statistically significant difference is determined for the alteration between cAMP-SNP & cAMP-V and cAMP-S & cAMP-V ($p < 0.001$ for both).

Conclusions: Determining that there is no statistically significant difference for the alteration between cGMP-SNP & cGMP-S, cGMP-SNP & cGMP-V, cGMP-S & cGMP-V and cAMP-SNP & cAMP-S shows that platelet cGMP levels cannot be used as a laboratory test for predicting the clinical response to PDE5 inhibitors. The statistically significant difference between the patient and control groups for the alteration between cAMP-SNP & cAMP-V and cAMP-S & cAMP-V may show that cAMP increase can be inhibited by not fully determined mechanisms in patients with ED. By understanding the interactions between cGMP and cAMP in platelets and cavernosal tissue, and the tissue distributions and functions of PDE enzymes properly, it can be able to predict the clinical response to PDE5 inhibitors.

DO PATIENTS' BASELINE CHARACTERISTICS PREDICT PDE5 INHIBITORS' EFFICACY AND PATIENTS' PREFERENCE? A COMPARATIVE, RANDOMIZED, OPEN-LABEL, CROSSOVER STUDY

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Introduction & Objectives: To investigate the efficacy, the tolerability and the side effects of the three known oral PDE5 inhibitors (Sildenafil, vardenafil HCL, tadalafil) and if these parameters are influenced by specific patients' characteristics.



Material & Methods: 197 patients with ED were participated in the study. All of them completed the IIEF questionnaire following by a detailed medical and psychological history. Baseline variables examined were age, body mass index, alcohol consumption, smoking status, physical activity, ED aetiology/duration, comorbidities in medical history, medication intake, psychological status and baseline scores for the IIEF domains. After a 4 weeks screening period, they received all three PDE5 inhibitors with incidental sequence (fig.1). In every follow up visit, the Sexual encounter Profile (SEP) diary were selected and the IIEF questionnaire was completed. General linear model repeated measures ANOVA controlled were used to determine if any baseline characteristics were associated with the efficacy, tolerability and patients' preference. Post-baseline variables examined were differences in IIEF domains, SEP scores and the presence of side-effects.

Results: 102 patients completed the three treatments period and included in the analysis. Participants' IIEF scores were significantly lower at the baseline compared to the other 3 visits irrespective of the drug taken. Only for the ED-subscale there was a significant difference ($p < 0.01$) between sildenafil use and tadalafil use, as the study sample had slightly lower IIEF score using sildelafil compared to the

treatment period using tadalafil. All the baseline variables influenced the behaviour of PDE5 inhibitors at least at one of the subscales of the IIEF questionnaire. In addition, there were differences between two PDE5 inhibitors in the same patient depending on special conditions, such as alcohol consumption or ED duration. SEP scores confirmed the IIEF answers by each patient showing preference to the substance which improved more the hardness, the duration and the number of sexual attempts.

Conclusions: We identified that baseline characteristics can influence the efficacy, tolerability and patient's satisfaction. Despite their similarity in way of acting, the three PDE5 inhibitors have differences and patient can distinguish these and prefer one or the other depending on his 'profit'.

CAN ANDROGEN STATUS, DURATION OF ED OR PARTNERSHIP-STATUS PREDICT PDE5- INHIBITOR SUCCESS IN THE FIRST-LINE TREATMENT OF MEN WITH ED?

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Introduction & Objectives: PDE-5-inhibitors represent a highly successful first-line treatment in men with erectile dysfunction (ED). However, about 35% of men do not report an adequate response to oral medication. Aim of our study was to reveal predictors for PDE-5-inhibitor first-line therapy failure, particularly focused on androgen-status.

Material & Methods: All men between 50-65yrs of age presenting without any prior ED-therapy at the andrological outpatient-clinic of the Paracelsus Medical University Salzburg due to ED were offered to enter this prospective evaluation. Patients completed a baseline questionnaire and a standardised hormonal status. ED was quantified according to the IIEF. In addition, various aspects of partnership-status were asked for. After 4-6 weeks of oral sildenafil 50-100mg 1-3 times weekly a reevaluation took place.

Results: In total, 32 men with a mean age of 58yrs (50-65) entered our analysis. Mean total testosterone was 5.4ng/ml (2.7-9.7), mean free testosterone 12.2pg/ml (7.3-18.1) and mean DHEAS 4.9umol/l. Mean IIEF was 12.3 at baseline and 17.9 after 4-6 weeks of treatment. Partnership-status did not predict sildenafil-response. 80% had an ED-duration >1a and had a smaller mean IIEF-score improvement compared to men with ED-duration of less than one year: 4.3 versus 8.1 points. Total testosterone- and free testosterone-levels did not correspond to the IIEF-response; yet men with DHEAS below 5umol/l had a mean IIEF-increase of 4.1 versus 6.1 points in men with DHEAS >5umol/l. When defining treatment success as an IIEF-increase >4 points, men with DHEAS above average had 70% versus 40%-success rate and men with ED-duration <1yrs had 75% versus 50% success rate (n.s.).

Conclusions: According to this pilot study, serum testosterone and partnership status do not predict sildenafil response. The potential role of DHEAS with this respect warrants further studies.

SEXUAL SELF-CONFIDENCE FOLLOWING TADALAFIL ONCE-A-DAY VERSUS SILDENAFIL CITRATE AS NEEDED IN THE TREATMENT OF MEN WITH ERECTILE DYSFUNCTION

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Introduction & Objectives: Phosphodiesterase 5 (PDE5) inhibitors, such as tadalafil and sildenafil, are the first-line treatment choice for men with erectile dysfunction (ED). Safe and effective use of tadalafil once-a-day (OaD) has been demonstrated. However, this is the first direct comparison of tadalafil OaD vs sildenafil citrate as needed (pro re nata [PRN]) on psychosocial outcomes in men with ED.

Material & Methods: This was a global, multicenter, randomised, open-label, active-comparator controlled, clinical trial in men with chronic ED and a history of successful PRN use of any PDE5 inhibitor. Patients were randomised to one of six treatment sequences in a 3x3 crossover design: tadalafil OaD, tadalafil PRN, and sildenafil citrate PRN (n=378; the mean age was 56 years; the majority were Caucasian [67.5%] or Hispanic [27.8%]; 25.9% had severe ED; 69.0% reported prior tadalafil PRN use and 60.6% reported prior sildenafil citrate use). Each sequence involved an 8-week treatment phase separated by a 7- to 10-day wash-