Reviewer's report

Title: Indirect comparison of interventions using published randomised trials: systematic review of PDE-5 inhibitors for erectile dysfunction

Version: 1  Date: 31 August 2005

Reviewer: Petros Perimenis

Reviewer's report:

General
Due to the availability of three PDE5 inhibitors for the treatment of erectile dysfunction (ED) of diverse etiology, the main issue for physicians and patients is the decision regarding to which drug to use. Because of the lack of trust-worthy head-to-head comparison of efficacy of these agents, such a therapeutic decision is not easy. However, a direct comparison is objectively difficult because of the particularity of ED as chronic disease (i.e. several risk factors, possible comorbidities, grade of severity) and the specific issues involved, such as psychological and cultural status, behavioral dimensions, expectations and partner's contribution. Only a well designed blind parallel study of a strictly homogenous group of men, or a blind randomized crossover trial would provide such evidence. On the other hand, it is remarkable that the investigators characteristically hesitate or avoid searching these ‘deep waters’.

Under these circumstances the above systematic review is of utmost importance not only for those closely related with this field but also for a wider spectrum of physicians and especially for the primary care givers. Firstly because, after researching of the relevant literature, the authors made an exceptional and clear indirect comparison of efficacy and safety of PDE5 inhibitors; secondly, because the physicians who manage ED need evidence in order to make the best choice, taking into consideration patient age and needs, and couple habits, behavior and expectations. Although the systematic review was well designed and the authors obviously made a great effort to extract and analyze data, still many questions need to be answered. However, the main results of this review are of great value. It was shown that,

1. In order to accurately compare indirectly PDE5 inhibitors and apply the results in clinical practice, we need to ‘speak the same language’, namely to use standard inclusion and exclusion criteria, to report on common and well defined outcomes, and to record in detail side effects, withdrawals and dropouts.

2. Sildenafil has been extensively studied in every inhabited continent and in several clinical conditions. Thus, its efficacy and safety outcomes have a broad value for the general population of men suffering from ED. This is the main reason why even nowadays the majority of the physicians firstly prescribe sildenafil when manage ED.

3. Although the review demonstrated consistency between the three agents, overall sildenafil showed a trend towards better efficacy and less adverse events. In my opinion sildenafil is more efficacious than the other PDE5 inhibitors whenever is administered to treat ED in a couple with a more or less standardized sexual life when intercourse is engaged approximately 1h after drug administration. On the other hand, the administration of tadalafil is considered to offer a wider ‘window to chance’ and thus, may be the choice in cases with more spontaneous sexual behavior. Vardenafil seems to have some of the pharmacodynamic and clinical characteristics of sildenafil and may be used accordingly.

When I assess a study on PDE5 inhibitors, I underline the need for adequate patient and partner education, and the consequent effort for treatment compliance. As practically there is not much difference between 60% or 70% successful attempts rate with one or another drug, what makes the difference is a comprehensive ED management, dosing instructions, regular follow up focused on treatment success, and couple’s realistic expectations. Given the nature of sexual disorders and the
effectiveness of PDE5 inhibitors, ED treatment discloses physician’s rather than drug’s efficacy.

Petros Perimenis
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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Page 4, paragraph of Efficacy, 8th dot change to: function IIEF domain score
Page 5, 1st paragraph of Side Effects add: Myalgia and/or back pain (As they occurred in a high percentage of patients, especially those under tadalafil)
Page 7, 2nd paragraph for vardenafil: The authors mention the quality scores of 8 trials, while 7 were included in this review.
Page 24, Table 2: It must be noted that the numbers represent patients studied and not trials.

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Discretionary Revisions (which the author can choose to ignore)

What next?: Accept after minor essential revisions

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:

'I declare that I have no competing interests'