INTRODUCTION

The Place of PDE5 Inhibitors in the Treatment of Erectile Dysfunction

There can be little doubt that the introduction into clinical practice of oral phosphodiesterase type 5 (PDE5) inhibitors has had a major and positive impact on the quality of life in men with erectile dysfunction (ED) of various causes. PDE5 inhibitors have largely supplanted less subjectively appealing local treatments for ED, such as vacuum constriction devices, penile self-injection therapy, transurethral alprostadil, and inflatable penile prostheses, as first-line therapy in the majority of men seeking treatment for ED. The first of these PDE5 inhibitors was sildenafil (Viagra™). In spite of the benefits of sildenafil, its ocular effect, which manifests as dose-related changes in blue-tinted vision in some patients, reflects its weak inhibition of PDE6 and lack of selectivity.

Furthermore, the Men’s Attitude Towards Life Events and Sexuality (MALES) study (1,2) has indicated that many patients remain dissatisfied or apprehensive about treatment, indicating the need for a continuing search for viable alternative approaches to the treatment of ED by PDE5 inhibition.
The MALES Study

To evaluate the prevalence of self-reported sexual dysfunction, a representative sample of 27,838 adult males (aged 20–75 yr) in eight countries across Europe and North and South America* were interviewed between February and April of 2001 using a standard questionnaire (1). As such, it is the largest survey about ED yet conducted. Overall, the prevalence of self-reported ED in this population was 16%. In European and South American countries, the prevalence of ED was similar and ranged between 10 and 14%, but the prevalence was higher in the United States (22%). This may be related to the higher prevalence of diabetes and depression in the US, both of which are risk factors for ED.

Of the total cohort, 4422 men self-reported ED (16%); approximately half of these indicated that they had never sought treatment for ED. Of the population of 3291 men with self-reported ED who participated in phase II of the study, 28% of respondents had tried a PDE5 inhibitor† at least once, and about a quarter (23% of 749) respondents expressed dissatisfaction with it. Commonly cited reasons for such dissatisfaction and abandonment of use of a PDE5 inhibitor were suboptimal hardness of erection (34% of 255 respondents), complete failure of therapy (34%), and lack of reliability of therapy (22%). When asked what they were seeking in ED therapy, reliability was the most important concern, cited by 47% of respondents. Of those subjects with ED who had never used a PDE5 inhibitor, or had used it only once, 42% of 2542 respondents cited safety concerns as the reason for avoiding its use.

Thus, the MALES study has shown the following:

• ED is an undertreated condition.
• Men with ED were not wholly satisfied with treatment with a PDE5 inhibitor at the time of the study.
• Patients with ED need to be counseled to overcome safety concerns about PDE5 inhibitors.
• Those with ED represent a population of subjects with unmet need.
• There is an ongoing need for effective and reliable PDE5 inhibitor treatment.
• Rapid onset and reliability are important treatment attributes.

Furthermore, in a sample of 2912 men with ED (2), the perceived severity of self-reported ED strongly correlated with both the perception that the condition is permanent and a reduction in sexual activity ($p < 0.0001$). The perceived severity, however, did not correlate with the temporal duration of ED. Analysis of these data also indicates that men who self-report mild ED

---

*United States, $n = 6162$; United Kingdom, $n = 3024$; Germany, $n = 3163$; France, $n = 3018$; Italy, $n = 3249$; Spain, $n = 3121$; Mexico, $n = 3046$; Brazil, $n = 3055$.

†At the time of the survey, only one PDE5 inhibitor (sildenafil) was available.