



First International Conference on the Management of Erectile Dysfunction

Overview consensus statement

JF Eid, A Nehra, KE Andersson, J Heaton, RW Lewis, A Morales, RB Moreland, JJ Mulcahy, H Porst, JL Pryor, ID Sharlip, G Wagner and M Wyllie

The First International Conference on the Management of Erectile Dysfunction, co-chaired by JF Eid and A Nehra was held in Chicago, Illinois on March 3–4 2000. The First International Conference had three primary goals: to review and critique accumulating and new data from major clinical trials; to stimulate communication among the different disciplines involved in research and clinical care; and to prepare a consensus statement on the current state of knowledge in the field of erectile dysfunction (ED).

An invited group of experts presented, discussed and debated such critical issues as (1) the prevalence and pathology of ED, (2) appropriate diagnostic evaluation, (3) the process of patient care, (4) the mechanisms of action and efficacy for currently approved and development-stage ED therapies, and (5) the relevance of these therapies to patient care. However, the intellectual and scientific range of the conference extended well beyond these topics to cover broader issues in ED treatment. These included: the epidemiology of ED; the role of questionnaires in the evaluation and management of ED; the role of central and peripheral mechanisms in the pathology of ED; clinical trial design; the role of testosterone replacement in ED; pathophysiology and treatment of Peyronie's Disease and priapism; new therapies and delivery mechanisms; and recommendations for future research. Conference participants were invited based upon their acknowledged contributions to either the clinical or basic understanding of ED management and biology. The attendees were internationally prominent experts in the fields of urology, as well as cardiology, epidemiology and drug discovery. The informal format of the conference, which combined brief scientific reports with extended periods of open discussion, offered participants the opportunity to exchange information and develop hypotheses with immediate input and constructive critiques from their multinational colleagues.

An Executive Committee met in special session to distill the essential features and findings of the two-

day meeting. The deliberations of the Executive Committee served two purposes: to formulate what had been learned or established over the course of the Conference, and to state unresolved issues and pose questions to the specialties involved in treatment of ED, questions that will be taken up at the next annual meeting.

The summary

The executive committee felt that the conference had established a baseline of knowledge of epidemiology, basic science and clinical treatment of ED. Individual areas are summarized below.

Epidemiology

ED today has a crudely estimated incidence rate of 25.9 cases per 1000 man-years based on follow-up conducted in the Massachusetts Male Aging Study. The actual incidence rates increase with each decade of age and the risk of ED was greater in men with lower education, diabetes, hypertension, and heart disease. Other risk factors include tobacco use, secondary exposure to smoke and a sedentary lifestyle. Population projections in the US based on this study were 617,715 new cases of ED per year (White males only). The Executive Committee stated the need for peer-reviewed data on prevalence and significance from different regions of the world, reflecting the culture and diversity of different populations in defining the true prevalence of ED and the need for treatment. The committee recommended that a single standard question be used for obtaining epidemiologic data about impotence. However, it was urged that this defining question not be used as a substitute for patient evaluation and that the importance of being stricken with ED from the patient's perspective should somehow be

addressed in order to make the prevalence numbers more relevant to health professionals who are recommending treatment.

Physiology/pathophysiology

Over the last twenty-five years, most of the research into erectile physiology has concentrated on the peripheral mechanism of corpus cavernosal smooth muscle tone. Although central pathways have been evaluated to a degree, the central control of peripheral mechanisms as well as the integration of central and peripheral mechanisms needs further study. The committee stated that there is a need to consider age-dependent defects and risks for the development and progression of ED. It is also important to understand the influence of co-morbidities on accelerating the development of erectile dysfunction. Over the last ten years, the pathophysiology of ED has been shown to involve not only an imbalance in relaxatory and contractile factors, but also to have a structural component. While the link between structure and function has been demonstrated, the role of penile blood oxygen tension or nocturnal penile tumescence in the preservation of penile structure or potency remains to be established. Further research is needed not only in basic mechanisms in physiology but also in animal models of disease to establish the clinical relevance of these concepts.

Therapeutic mechanisms of action

A variety of physiological mechanisms are important in normal erections. The challenge in drug discovery and development is defining these mechanisms and then understanding the potential to harness them therapeutically, with an acceptable, minimal side effect profile. Most current therapies have focused on initiating smooth muscle relaxation of the corpus cavernosum. The committee stated the importance of understanding the role of mediators of constrictor tone. There is a growing need to more effectively access and integrate information from the disciplines of endocrinology, neurology, and cardiology and to enhance our understanding of potential synergies in therapeutic mechanisms for ED.

Drug efficacy and side effects

There is a well-recognized need for a standardized approach to evaluating drug efficacy and side effects as well as a need for a standardized approach and indices to evaluate benefit-risk ratios. The latter

should include drug–drug synergies and interactions. The committee recommended that those involved in patient management take the lead in developing recommendations and suggested that the next annual meeting of this group, supplemented by other clinical and regulatory experts, may be a good forum in which to address these issues.

Diagnostic evaluation

There is clearly a need to define appropriate diagnostic evaluation of ED. The committee stated that a thorough physical exam and psychosexual history are both critical elements of patient evaluation. Existing psychometric tests are currently of limited value in terms of patient evaluation for ED, although they are useful in measuring the efficacy of therapy in ED patients. The committee recommended that primary care physicians and medical students should receive more education on sexual dysfunction evaluation, including how to examine genitalia as part of a physical exam. A good template should be developed for evaluating psychosexual history as part of the exam. Further, there needs to be better definition and standardization of the co-morbidities for ED (ie: diabetes, depression, coronary artery disease). Finally, the relationship between ED and coronary artery disease should be more thoroughly studied.

Therapies in special patient populations

There is a need to look more closely at ED therapies for patients with severe ED and severe coronary artery disease. The committee recommends that the efficacy of ED therapies for special patient groups be further studied. These groups include individuals suffering from depression, diabetes, spinal cord injury, coronary artery disease, those who underwent radical retropubic prostatectomy, individuals who smoke or are exposed to tobacco smoke and men with sedentary behavior. Since the penis is a vascular structure, the committee also recommends further study into possible cardiovascular effects of ED therapies.

Role of primary care physicians and internists

Primary care physicians and internists have taken on an important role in the treatment of ED with the introduction of new oral therapies. While these physicians may have little experience in the complications or alternatives for treating ED, they are often the first to see the patient and recommend

remedies. The committee recommends educating primary care physicians that ED can be an important health concern for patients and their partners and that treatments may have an impact on associated co-morbidities. It is further recommended that physicians take a more holistic approach to management of patients and that physicians recognize that if a specific oral therapy doesn't work, it is important to treat further following a process of care or refer to appropriate specialists in urology and/or psychology.

Emerging and novel therapies

There are at least eight new oral drugs known to be in development, five of which are PDE-5 inhibitors. New delivery systems are imminent: topical via transdermal adsorption enhancers, transnasal, and new injectors that are more 'patient friendly'. Combination therapies are likely to emerge, as synergistic action may improve efficacy and both company-sponsored and investigator-sponsored studies are in progress. The committee recommends postponing decisions on the value of new therapies until adequate published peer-reviewed data is available.

Quality of life

The committee considered and adopted a statement made by WHO First International Consultation on Erectile Dysfunction in 1999, regarding the medical treatment of ED patients. The committee stated that medical treatment is a valid component of the care of ED patients, along with culturally sensitive sexual counseling.

Areas of future research

The areas the committee identified as key for further research include prophylaxis and prevention, gene therapy, combination therapies, diabetes, andropause and couple and partner issues.

Consensus clinical summary

In considering the clinical data available to date, the executive committee concluded that epidemiologic studies predict a large population of men will suffer some form of ED. One of the issues is how to reach this patient population so that those who desire help can be treated. It was concluded that while

questionnaires can be useful in patient screening and clinical trials, they do not replace the office work-up. Further, while oral agents such as sildenafil are efficacious in a population of patients, the demand for new, safe oral agents which provide a spectrum of mechanisms from central nervous system to peripheral smooth muscle relaxation are needed. It is expected that these new medications will arise from basic research of physiologic and pathophysiologic mechanisms. There is also a need to standardize the clinical trial format such that data can be compared and endpoints are relevant and judged on an equal basis. The role of therapy in prophylaxis of potency in middle age and elderly men remains to be established experimentally.

Future directions

Future conferences will continue to address the issues raised in this overview summary and will give more attention to integration of central and peripheral mechanism of erection, prophylaxis and prevention, andropause, issues related to premature ejaculation, recommendations for future clinical trial endpoints and new therapies in development. The discussion repeatedly led to consideration of multiple issues that affect overall health and quality of life for ED patients, including cardiovascular health, the patient's psychological well being, the partner, and the effect of these factors on potency. These topics will be addressed in greater detail in succeeding conferences. Future conferences will also devote increased attention to advanced novel therapies such as tissue engineering and gene therapy. It is anticipated that a yearly meeting of clinicians, researchers, regulatory and governmental authorities, patient advocates and others will continue to improve the understanding and further define the opportunities to enhance the management of ED.

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