

Review

# Erectile dysfunction and diabetes: A review of the current evidence-based medicine and a synthesis of the main available therapies

V. Phé, M. Rouprêt\*

*Urology and Andrology Academic Department of Pitié-Salpêtrière Hospital, Assistance publique–Hôpitaux de Paris,  
faculté de médecine Pierre-et-Marie-Curie, University Paris-VI, Paris, France*

Received 7 August 2011; accepted 25 September 2011  
Available online 4 November 2011

## Abstract

**Aim.** – This review aimed to provide an update of the epidemiology, pathophysiology and management of erectile dysfunction (ED) in diabetes patients.

**Methods.** – Data on the management of ED in diabetes patients in the literature were analyzed using Medline, and by matching the following keywords: diabetes; erectile dysfunction; endothelial dysfunction; cardiovascular disease; phosphodiesterase inhibitors; intracavernous injection; and penile prosthesis.

**Results.** – ED has a higher incidence in diabetic patients. The pathophysiology is multifactorial, involving endothelial dysfunction, specific complications of diabetes and psychological factors. Recent studies have shown that ED is able to predict future cardiovascular events not only in non-diabetics, but also in patients with diabetes. ED could also be a potential marker to screen for silent coronary artery disease. The management of ED has been revolutionized by the discovery of phosphodiesterase type-5 (PDE5) inhibitors, the first-line therapeutic options for diabetic men with ED that are efficient and safe. As a second line, intracavernous injections remain a gold-standard treatment, although a vacuum device can be used as well. In cases of failure, penile prosthesis may be considered. Hypogonadism, commonly found in diabetics, may require identification and treatment. Optimized glycaemic control, management of associated co-morbidities and lifestyle modifications are essential in all patients. As ED and diabetes negatively impact male self-esteem, and generate depression and anxiety, the psychological treatment of patients is also likely to be beneficial.

**Conclusion.** – The aetiology of diabetic ED is multifactorial. Endothelial dysfunction is the link between diabetes-induced ED and coronary artery disease. A global approach is needed for the successful management of diabetic ED.

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**Keywords:** Diabetes; Erectile dysfunction; Endothelial dysfunction; Cardiovascular disease; Phosphodiesterase inhibitors; Intracavernous injection; Penile prosthesis; Review

## Résumé

Dysfonction érectile et diabète : revue de la littérature scientifique et synthèse des traitements disponibles.

**Objectif.** – Réaliser une revue de la physiopathologie et de la prise en charge de la dysfonction érectile (DE) chez le patient diabétique.

**Méthodes.** – Une revue de la littérature a été réalisée dans Pubmed avec les mots-clés: diabète; dysfonction érectile; dysfonction endothéliale; maladie cardio-vasculaire; IPDE5; injection intra-caverneuse et implant pénien.

**Résultats.** – La DE a une prévalence plus élevée chez les patients diabétiques que dans la population générale. La physiopathologie est multifactorielle, impliquant une dysfonction de l'endothélium vasculaire, les complications spécifiques du diabète et les facteurs psychologiques. La DE est un facteur prédictif de survenue d'événements cardiovasculaires chez les diabétiques. De plus, la DE est un marqueur potentiel pour le dépistage d'une maladie coronarienne silencieuse. La prise en charge de la DE a été révolutionnée par la découverte des inhibiteurs de la phosphodiésterase de type 5, qui ont une efficacité et une sécurité prouvées. Ils représentent la première ligne de traitement de la DE chez le patient diabétique. En deuxième intention, les injections intracaverneuses sont proposées. L'implant pénien est une solution de dernier recours. L'équilibre glycémique, la prise en charge des comorbidités et le changement de mode de vie sont essentiels chez ces patients. Enfin, parce que la DE est responsable de dépression, l'accompagnement psychologique ne doit pas être négligé.

\* Corresponding author. Hôpital Pitié-Salpêtrière, 47-83, boulevard de l'Hôpital, 75013 Paris, France.  
E-mail address: [morgan.roupret@psl.aphp.fr](mailto:morgan.roupret@psl.aphp.fr) (M. Rouprêt).

**Conclusion.** – L'étiologie de la DE chez les patients diabétique est multifactorielle. La dysfonction endothéliale est le lien avec la maladie coronarienne. La prise en charge de la DE chez le patient diabétique doit être globale.

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**Mots clés :** Diabète ; Dysfonction érectile ; Dysfonction endothéliale ; Maladie cardiovasculaire ; Inhibiteur de la phosphodiesterase ; Injection intracaverneuse ; Implant pénien ; Revue

## 1. Introduction

The US National Institutes of Health define erectile dysfunction (ED) as the inability to achieve, maintain or sustain an erection firm enough for sexual intercourse [1]. Studies have shown an increased incidence of ED in diabetes patients. In addition, ED appears to arise about 10 years earlier in diabetic patients than in the general population [2] and is more severe, decreasing the health-related quality of life. ED is most often a forewarning of cardiovascular disease; thus, the treatment of ED among diabetics is a priority. Diabetic ED is multifactorial in aetiology and more resistant to treatment compared with non-diabetic ED.

The aim of the present review is to provide an update on the epidemiology, risk factors, pathophysiology and management of diabetic ED.

## 2. Methods

The literature was reviewed using the National Library of Medicine database (<http://www.pubmed.gov>). A Medline search was performed with special emphasis on diabetes and ED, using combinations of the following terms: diabetes; erectile dysfunction; endothelial dysfunction; cardiovascular disease; phosphodiesterase inhibitors; intracavernous injection; and penile prosthesis. Only articles published between 2000 and 2011 were considered. Also, due to a paucity of randomized data regarding treatment results, articles for this review were selected with regards to the following criteria: evolution of concepts; development and refinement of techniques; intermediate and long-term clinical outcomes; and quality of the study and relevance. Older studies were included selectively if historically relevant or when the data were scanty in more recent publications.

### 2.1. Epidemiology

Type 2 diabetes, which is strongly associated with changing lifestyles, is reaching pandemic levels. Indeed, the world diabetic population is expected to reach 366 million by the year 2030 [3]. Among diabetic patients, more than 50% have sexual troubles caused by their disease. The incidence of ED is higher in patients receiving diabetes treatment; ED affects 35 to 90% of these patients and more than 65% of such patients who are 40 years old or more [4–10]. In a Massachusetts study of male ageing, men treated for diabetes had a 28% age-adjusted prevalence of complete ED (no erection), which was almost three times higher than the prevalence of complete ED observed in the entire study sample (10%) [2]. The findings also highlighted the

extremely deleterious epidemiological link between coronary artery disease (CAD), diabetes and ED.

As the majority of the studies did not distinguish between type 1 and type 2 diabetes, it is difficult to determine whether there are significant differences between the two major types of the disease. Contrary to Fedele et al. [8], two studies reported a similar likelihood of developing ED among patients with type 1 and 2 diabetes after adjusting for age [5,7].

### 2.2. Pathophysiology of diabetic erectile dysfunction (ED)

The development of ED in men with diabetes is a complex and multifactorial process. The process appears to be affected by vascular and neurogenic causes, endothelial dysfunction, oxidative processes and changes in the nitric-oxide system. Fig. 1 illustrates the multiple mechanisms involved in diabetic ED.

#### 2.2.1. Common risk factors

The risk factors of ED are well known; increasing age and the long-term evolution of diabetic disease [8,10,11] as well as a sedentary lifestyle have been shown to be associated with a higher prevalence of ED not only in the general population, but also in diabetic men [11]. A meta-analysis of population-based studies shows that higher levels of physical activity confer lower risks of ED. The adjusted reduction in the risk of having ED was 58% for men who engaged in greater physical activity and 37% for those who engaged in moderate physical activity compared with men who engaged in little physical activity [12].

There is a link between glycaemic control and ED in men with diabetes in that patients whose disease is poorly controlled are at a two- to fivefold increased risk of ED compared with patients whose disease is well controlled [13,14]. Recent studies have suggested that insulin resistance and the metabolic syndrome may also be strongly associated with the development of ED [15,16]. As is well known, both the metabolic syndrome and insulin resistance (the pathophysiological basis of the metabolic syndrome) are strong and independent risk factors for cardiovascular events and death [17]. Hyperlipidaemia [8,18], hypertension [6,19] and obesity [20] often coexist with diabetes, and are independent risk factors for ED among diabetic men. Other patient risk factors for ED include endocrine disorders, psychological disorders, previous surgery (such as prostatectomy), and the use of alcohol, tobacco and illicit drugs.

Pharmaceutical use is also a factor, as many commonly used drugs contribute to ED [21], including antihypertensives (alpha-adrenergic agonists, beta-blockers, calcium-channel blockers), diuretics (aldosterone antagonists, thiazide diuretics), psychiatric agents (benzodiazepines, butyrophenones, selective

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