Erectile dysfunction in aging male

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Abstract. With the increasing longevity in men and women, sexual health concerns have become more and more important and demands for help are far more common than in the past. Erectile dysfunction's severity and prevalence both increase with aging: since erectile dysfunction is a symptom, physicians should diagnose underlying pathologies that might lead to it instead of focusing on finding a viable treatment. Cardiovascular alterations occur in the elderly, and might lead to erectile dysfunction because of penile blood flow impairment: diabetes, smoking, and sedentary life-style, being risk factors for vascular pathologies, can affect erectile function. Metabolic syndrome and psychological factors are highly prevalent in aging men, and might be other important determinants of erectile dysfunction. Drugs play a role in the pathogenesis of erectile dysfunction, as they can alter hormonal or vascular mechanics needed for achieving or maintaining erection. Alterations in penile vessels can be observed in the elderly: lack of androgens might lead to a reduction of smooth muscle cells content in the penis and an increase in the caliber of vascular spaces. Hypogonadism, when present, should be treated regardless of age; furthermore, synergistic effects have been found during testosterone replacement therapy when using an oral therapy with a PDE-5 inhibitor (sildenafil, vardenafil or tadalafil). These therapies are effective in the elderly, with no increase in the frequency of adverse events, and might also help in providing relief from lower urinary tract symptoms. (www.actabiomedica.it)

Key words: Aging, erectile dysfunction, sexual health

In 1993, the NIH Consensus Development Panel on Impotence defined erectile dysfunction (ED) as the inability of a man to achieve or maintain an erection sufficient for satisfactory sexual function (1); similarly, in 1994, the DSM-IV defined erectile disorder as the recurrent inability to achieve or maintain an adequate erection until completion of sexual activity while simultaneously causing distress and interpersonal problems (2). Aging is commonly associated with a decline in several aspects of a man's health: androgen deficiency in the elderly leads to a reduction in the sense of well-being and to an overall decline in the subject's quality of life. Many clinical features are closely related to testosterone deficiency, as this hormone has effects on muscle mass and strength, on blood formation, on bone mineral density, on physical performance and, last but not least, on libido and sex-

ual health (3). Not surprisingly, men of all ages seems afraid to discuss this topic with their physicians: for many people, sex is a sort of "taboo", and as such sexual health is seldom discussed, and its problems are often under-diagnosed.

Epidemiology of ED

In the elderly, prevalence of ED seems to be higher than in younger people. The Massachusetts Male Aging Study (MMAS) (4), conducted from 1987 to 1989 in cities and towns near Boston (USA) on 1290 men aged 40 to 70 years, underlined the existence of a relationship between aging and ED, as younger men suffered less, and less severely, from ED than older people: the total prevalence of all degrees of impotence

was 52% (minimal 17.2%, moderate 25.5%, and complete 9.6%). However, the study also showed that 50% of men in their seventies suffered from either a moderate or a severe form of ED and another 20% showed signs of mild ED, whereas more than half of people in their forties did not complain about ED. Complete impotence tripled from 5 to 15%, while moderate impotence increased from 17% to 34% for subjects between the ages of 40 and 70 years. The prevalence of minimal impotence remained constant at approximately 17% over the same age range.

An Italian study (Parazzini et al., 2000) (5) on 2010 men stressed how the total prevalence for ED was about 12,8%, but it increased with age, from 2% in men aged 18 to 39 to 48% in those over 70 years. This study also underlined that the risk of ED tended to decrease when educational levels increased and that smoking was associated with an increased risk of ED, with risk increasing with duration of the habit. No association emerged in this study between marital status, alcohol consumption, age at first intercourse and risk of ED.

Braun et al., in 2000 (6), sent a questionnaire on ED to a representative population sample of 8000 men in the Cologne urban district, aged 30 to 80 years. The so-called "Cologne Male Survey", based on the 4489 answered questionnaires, showed that ninety-six per cent of the subjects aged 30 to 39 years reported regular sexual activity, including auto-erotic activity and exchange of caresses without sexual intercourse, compared to 71.3% of people aged 70 to 80 years. In this study, ED was present in 2.3% of men aged 30 to 39, with increasing percentages in all age groups (9.5% of men aged 40-49, 15.7% of men aged 50-59, 34.4% of men aged 60-69, and 53.4% of men aged 70-80), with an overall prevalence of 19.2%. Only 6.9% of respondents suffering from ED would start a therapy, with a peak for people aged 60 to 69 years (14.3%). Compared with the youngest age group, people aged 70 to 80 years have a 22-fold higher risk for ED; the same risk for the 40-49 age group is still nearly 4-fold higher.

An Australian survey, conducted in 2003, gathered data on 5990 men over 40 years of age (Holden et al., 2005) (7): the total prevalence of both moderate and severe erectile problems was 21% among all ages, but these symptoms occurred in 3% of people aged 40 to 49, in 11% of people aged 50 to 59, in 32% of people aged 60 to 69 and in 68% of people over 70. Furthermore, 37% of people in the last age group had no sexual activity in the 12 months prior to the interview, whereas 93% of people aged 40 to 49 did have sexual activity of some kind. However, only one fifth of the interviewed subjects older than 70 years had sought medical advice for ED; the awareness seemed higher in younger man, as nearly half of participants aged 40 to 49 years with an erectile problem had spoken with their physicians. Major reasons for not seeking medical help were the belief the problem was due to other medication or disorders, relationship or other sexual difficulties, and inability to talk about erectile problems.

A more recent study (Englert, 2006) (8) collected data from 490 patients living in Germany, and showed similar results, with just 26% of people older than 70 having very high to moderate confidence in achieving and/or maintaining an erection sufficient for intercourse. The decline was more and more relevant with aging: only 12% of people aged 40 to 49 seemed to have very low or low confidence, but this estimate rises to 30% in people aged 50 to 59 and to 50% in people aged 60 to 69, up to 74% in the group of people aged 70 to 79. This study also stressed how severity was proportional with age: people aged 40 to 49 defined their ED as "mild" in 51% of cases and as "severe" in up to 16%; on the other hand, people aged 70 to 79 suffered from "mild" ED in only 18% of cases and from "severe" ED in up to 61% of cases.

In all these studies, it is not possible to directly compare their results, as different criteria, age ranges and questionnaires were used. Nevertheless, prevalence of ED seems to be strongly associated with aging, as all studies point in the same direction.

Aging and ED

Age-related modifications of endocrine functions, but also the increased prevalence of cardiovascular and metabolic diseases, are important determinants of erectile dysfunction in the elderly (4, 9-14). Adequate blood inflow and outflow through penile vessels

are needed to achieve and maintain erection: hemodynamic changes due to aging might lead to a reduction in the peak systolic velocity (PSV) and to an increase in the end-diastolic velocity (EDV) in the cavernous arteries. Doppler ultrasound of these arteries, after the intracavernous injection of a pro-erectile drug (like prostaglandin E_1), allows evaluation of PSV and EDV; resistive index (RI) can be obtained by a simple formula [RI = (PSV- EDV) / PSV]. In the elderly, all flow parameters lean more frequently towards pathological values, although no consensus exists about which velocities should be considered as cut-offs. Nevertheless, most authors consider a maximum PSV greater than 35 cm/s and a minimum EDV of 5 cm/s or less an index of normal arterial function (15-17). Arterial impotence occurs with a PSV of 25 cm/s or less; corporal veno-occlusive dysfunction (CVOD) is diagnosed by an EDV > 5 cm/s or by a RI of 0.80 or less.

Erectile dysfunction is closely related to endothelial dysfunction: alterations in the production of nitric oxide (NO) or in the regulation of the NO syntase (NOS) activity lead to neurogenic ED, whereas the loss of smooth muscle cells and their replacement by collagen fibers (fibrosis) leads to vasculogenic ED, mostly because of venous leaking. Both forms of ED might coexist in the same patient: neurogenic ED is in many instances associated with CVOD because of the relative atrophy of the trabecular smooth muscle. These alterations are more frequent in the elderly (17); furthermore, a reduction of smooth muscle cells content and an increase in the caliber of vascular spaces are evident in the elderly and these changes may limit the basic function of the penile vascular tree.

Caretta et al. (18) studied 179 consecutive subjects, aged 23 to 79 years, and underlined the relationship between VPS and carotid wall alterations: their research shows how penile vessels, because of their smaller diameter, are affected by systemic vascular diseases before other symptoms might appear.

Hypogonadism is more frequent in the elderly than in younger people (3): the decline in testosterone levels might lead to loss of libido, although it has been shown that androgens are also needed in order to maintain penile tissue architecture by acting on post-ganglionic parasympathethic neurons (18). Androgens also play a role in avoiding structural changes in tissue components (mostly on smooth muscle cells, but also on nerve fibers and connective tissue) involved in CVOD (19). As such, testosterone treatment in elderly patients suffering from androgen deficiency might also improve erectile function. It should also be noted that a previous study about the relationship between sex hormones and ED showed little to no correlation with total or bioavailable testosterone, but a strong association between ED and higher than normal levels of LH (20).

Koskimäki et al showed that among men aged 55 to 75 years regular intercourse (at least once per week) protects against the development of ED (21). Testosterone replacement therapy also restores libido: this might lead to an increase in the frequency of sexual intercourse, which would thus prevent ED on its own (22).

In our study on 1180 men aged 18 to 91 years, we noticed how EDV increased with age, from 1.525 ± 0.13 cm/s in people under 30 up to 6.23 ± 0.5 cm/s in men over 70 years; similarly, PSV in people aged 30 to 39 years was 86.125 ± 4.31 cm/s, but in people over 70 years of age it was 54.79 ± 2.8 cm/s, with an overall decrease of 36%. A similar decrease in androgen levels has been observed in the same subjects: total testosterone levels decrease by 1.6% per year, up to an overall reduction of 35% between men aged 25 and 75 years (respectively 5.4 ± 0.3 and 3.3 ± 0.3 ng/ml), and bioavailable testosterone levels decreased by almost 50%, from 25.1 ± 0.3 to 12.0 ± 0.5 (23-25). These data are a further confirmation of the effect of androgens on penile blood vessels.

In the elderly, metabolic syndrome affects about 22% of the US population, with prevalence increasing from 6.7% among men aged 20 through 29 years to 43.5% and 42.0% for men aged 60 through 69 years and aged at least 70 years, respectively (26-27). Obesity, hypertension, insulin resistance and hypertriglyceridaemia, together with an unfit lifestyle, have negative effects on penile hemodynamics; cross-sectional studies have also underlined that metabolic syndrome is associated with an impairment in penile blood flow, leading to an increased prevalence of ED. Furthermore, hypogonadism and metabolic syndrome are

closely related: hypogonadism could be an adverse consequence of obesity, but on the other hand low testosterone levels could contribute to the accumulation of excess fat (27).

Psychological factors should not be forgotten in the elderly: ED is closely related to mental health, with an increase of ED in men with poorer mental health and vice-versa. Depression is an important risk factor for sexual dysfunction, and its increased prevalence with age is another cause of ED in aged men.

Polipathology in geriatric patients requires different therapies: some drugs might impair erectile function, because of their direct effects on circulation (anti-hypertensive drugs) or on hormones (anti-androgens). However, other medications, like prokinetic or psychiatric drugs (mostly antidepressants and antipsychotics) interact with mediators of erection, and as such might lead to ED.

Therapy of ED in the elderly

International recommendations suggest that the initial assessment of men suffering from ED or diminished libido should include determination of serum testosterone: there is also evidence of therapeutic synergism with the combined use of testosterone and oral proerectile drugs (phosphodiesterase-5 [PDE-5] inhibitors), a treatment which should be considered in hypogonadal patients with ED failing to respond to either treatment alone. In the elderly, both treatments are viable: PDE-5 inhibitors sildenafil (28), tadalafil (29) and vardenafil (30) are well tolerated in aged men, although their efficacy rate seems to be lower in the elderly (28). The incidence of adverse events in the elderly seems to be similar in all age groups (28). There is a tendency for younger men to choose tadalafil because it gives them a broader window of opportunity, while older men tend to prefer vardenafil or sildenafil because of their quicker action (31). Therapy with sildenafil citrate has also led to an improvement in the symptomatology of androgen decline in aging men: even without any alterations in hormonal pattern, sildenafil citrate caused an improvement in AMS score compared to pretreatment levels (33.5 ± 1.3 vs 28.6 ± 1.3) (32).

Lower urinary tract symptoms (LUTS) are highly prevalent in the aging population: autonomic hyperactivity, pelvic atherosclerosis, Rho-kinase activation and altered nitric oxide levels prove the existence of a relationship between LUTS and ED. PDE-5 inhibitors have been used in the prophylaxis for LUTS in people having concurrent ED, because of their positive effects on detrusor activity (33).

Even in the elderly, counseling has a pivotal role: sexual dysfunction is highly prevalent in the aging population, and interactions of physical and mental morbidity should always be considered when dealing with aging men. In order to achieve and maintain sexual health, therapy should include biomedical, individual psychotherapeutic, and systemic interventions (34).

Conclusion

Sexual health is an important aspect of quality of life, in the aging male as in younger men. Even if the prevalence and the severity of erectile dysfunction increases with age, many men prefer not to speak with their physicians about their sexual concerns: however, sexual health should be a primary concern, since erectile dysfunction and other sexual dysfunctions can be a warning of cardiovascular diseases. Penile dynamic ultrasound should be performed to diagnose vascular alterations in the penile arteries, including reduced blood inflow and corporal veno-occlusive dysfunction.

Oral therapy with PDE-5 inhibitors for ED is viable even in aging men: sildenafil, vardenafil and tadalafil are effective in all age groups, with no increase in adverse events with aging. Furthermore, therapy with PDE-5 inhibitors might prevent lower urinary tract symptoms, thus preserving quality of life in the elderly.

Hypogonadism should be treated in all men, regardless of age: combination with PDE-5 inhibitors should be considered in hypogonadal patients not responding to single treatment.

However, treatment with these medications should only be started after the assessment of other conditions: all comorbidities, including metabolic syndrome, diabetes, hypertension, drugs, psychiatric fac-

tors and life-style behaviors, should be carefully evaluated before starting a therapy with PDE-5 inhibitors.

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