Influence of Work on Andropause and Menopause

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Work-related factors, such as stress and pollutant exposure, affect gonadal function and can interfere with reproduction in both genders. Work-related factors, such as psychological stress, physical effort, and sleep disorders, showed a significant correlation with andropause manifestations, whereas age at menopause and severity of menopausal symptoms were both influenced by factors such as pesticide exposure, high job strain, and repetitive work.

Keywords: testosterone ; estradiol ; workplace ; workers ; job ; late-onset hypogonadism

1. Introduction

Aging is associated with modifications of the hypothalamic–pituitary–gonadal (HPG) axis, which in females lead to menopause and in a variable proportion of males lead to a clinical entity called andropause or, according to more recent terminology, late-onset hypogonadism (LOH).

The physiological age of menopause is on average 46 years; the diagnosis is made retrospectively after at least 12 months of amenorrhea [1]. The Stages of Reproductive Aging Workshop + 10 (STRAW + 10) criteria, which are based on menstrual bleeding patterns, were established in 2001 and updated in 2012 [2]. Vasomotor symptoms affect 80% of women, but their pathophysiology is not clearly understood. Notably, aside from reduced circulating estrogen, increased responsiveness of the hypothalamic thermoregulatory zone to changes in body temperature are believed to be affected by central mechanisms mediated by hormonal stimuli (e.g., high levels of luteinizing hormone (LH) from the pituitary gland) or local factors (e.g., hypothalamic neurokinin B) [2].

Unlike aging women, most men do not experience a dramatic decline in gonadal function. In fact, although morning serum testosterone (T) levels decline progressively over time, only 20% of adults aged 65 years or more have T levels below the normal range for young men [1]. In addition, unlike menopausal symptoms, most of the signs and symptoms of LOH are mild and difficult to distinguish from the effect of aging per se. From a pathophysiological point of view, aging is associated with a progressive reduction in testicular T production as an effect of Leydig cell degeneration and of atherosclerosis of testicular arterioles. However, in most men, an increase in LH compensates for the reduced function of the testis and maintains adequate T levels, preventing the appearance of signs of hypogonadism. Additional factors, such as chronic diseases or obesity, which become more frequent with aging, can reduce HPG axis activity, disrupting the compensatory mechanisms and making hypogonadism clinically evident [3].

Work accompanies individuals of both genders for much of their lives and through all stages of adult life. The effects of the work environment combine with those of aging and of chronic conditions to determine the ultimate health status of the older person; occupational stress is an additive factor in the perception of menopause and LOH symptoms [4][5]. Menopause and LOH are both associated with increased cardiovascular mortality [6][7] and the loss of sex hormones; combined with age-associated immunosuppression and chronic inflammation, they may contribute to define the patterns of cancer incidence and mortality in the elderly [8].

In recent years, a longer life expectancy has been paralleled by a later retirement age, increasing the proportion of older people in the workforce. Since work, aging, and hormonal changes appear to be closely linked in the later stages of life, it is essential to understand the influence of work on menopause and LOH and the mechanisms underlying these phenomena.

2. Influence of Work on Andropause and Menopause

2.1. Aging and Gonadal Status in Male Workers

In a study of 664 blue-collar workers aged 40–60 years, Kratzik et al. explored the risk factors for hypogonadism by assessing a hormone panel in relation to age, body mass index (BMI), and the Aging Males' Symptoms (AMS) questionnaire. The results were presented by AMS domain. For the psychological domain, the risk of a moderate-to-severe score significantly decreased with higher bioavailable T or total T (TT) levels; a similar result was described for the somatovegetative domain, where each year of age also significantly augmented ($p < 0.001$) the risk of a severe score; finally, age was the only significant predictor for the sexual domain [9].

Fukai et al. studied middle-aged Japanese office workers who had undergone an annual health check in 2002 and 2007. Their data were subjected to cross-sectional (96 and 76 men, respectively) as well as longitudinal analyses (33 men). Age was negatively associated with free T (FT; r = −0.399, $p < 0.001$ in 2002; r = −0.458, $p < 0.001$ in 2007) and dehydroepiandrosterone sulfate (DHEAS) (r = −0.233, $p = 0.002$ in 2002 and r = −0.336, $p < 0.01$ in 2007) levels, but not with TT. Moreover, in the longitudinal analysis, the 5-year changes in androgen levels were not significant [10].

The association between hypogonadism symptoms and sex hormone levels in relation to anthropometric and socioeconomic parameters was explored by Samipoor et al. in 140 men aged more than 40 years. The total AMS score was significantly related to occupation ($p = 0.005$), with more severe symptoms in self-employed subjects, compared to employees and workers. A similar relationship was observed for the somatic and psychological (but not the sexual) symptoms. The levels of LH and follicle stimulating hormone (FSH) increased with age, whereas there was no association between TT and FT levels and andropause symptoms [11].

Balasubramanian et al. examined the association between sleep disorders and hypogonadism symptoms in 619 non-standard shift workers (who began work before 7:00 a.m. or after 2:00 p.m., worked regularly outside the 7:00 a.m.-to-6:00 p.m. workday, or regularly rotated between standard and non-standard shifts) and 1952 daytime shift workers. A multivariate regression model (corrected for age, burden of comorbidities, T supplement use in the 2 weeks prior to the survey, and TT levels) indicated that non-standard shift workers at high risk of sleep disorders ($n = 196$) had significantly worse ($p < 0.01$) hypogonadism symptoms than non-standard shift workers without sleep disorders ($n = 423$) and that non-standard shift workers (regardless of the presence of sleep disorders) had significantly worse ($p < 0.01$) hypogonadism symptoms than daytime workers. In non-standard shift workers, sleep disorders were independently associated with lower TT levels (mean decrease, 100.4 ng/dL; $p < 0.01$) when controlling for age, comorbidities, and prior T supplementation. Moreover, age was a significant independent predictor of T level in shift workers with or without sleep disorders [12].

2.2. Aging and Gonadal Status in Female Workers

Whereas aging men who experience hypogonadism are a minority, all women exhaust ovarian function over time. The diagnosis of menopause can be confirmed by reduced blood estradiol, although it is more commonly based on at least 12 months of amenorrhea. Work influences menopausal status in two ways: age at onset and symptoms.

2.2.1. Influence of Work on Menopause Onset

Physiological menopause occurs at an average age of 46 years [1], but some work-associated conditions can significantly modify age at onset.

According to Zhao et al., professional city women experience menopause at a later age (mean age, 48.2 ± 4.1 years) than women farmers living in rural areas (mean age, 46.5 ± 4.9 years). The effect of work on menopausal symptoms is also considered in their article [13] and is discussed below.

Based on experimental evidence of the ovotoxicity of some hormone-active pesticides, Farr et al. examined 8038 premenopausal women living or working on a farm and compared the age at menopause onset in those who had mixed or applied any pesticide (62%) versus unexposed women. Surprisingly, exposure to any pesticide was associated with a later age at menopause (hazard ratio (HR), 0.87), with an average increase of approximately 3 months in the median time to menopause, whereas exposure to hormonally active pesticides alone further increased this time by approximately 5 months [14].

The French ESTEV study, a prospective longitudinal epidemiological investigation that took place in 1990 and 1995, involved 1594 gainfully employed French women born in 1938, who experienced menopause at a median age of 52

years. In a recent analysis of these data, after distinguishing for a self-reported history of depression, the authors found that earlier age at menopause was associated with high job control ($p = 0.03$) and high school education ($p < 0.01$) in women with previous depression, whereas in those without previous depression, earlier age at menopause was associated with a high-strain job ($p = 0.01$) and difficult schedules ($p = 0.03$). Interestingly, in women without previous depression, later age at menopause was associated with repetitive work ($p = 0.05$), whereas depression itself was more frequent among women who reported exposure to high job strain ($p < 0.04$) and repetitive work ($p < 0.004$). Smoking (>10 cigarettes/day) was associated with an increased risk of earlier menopause in the entire sample ($p < 0.001$) [15].

A large cross-sectional survey conducted across Poland investigated 7183 women from all social strata to assess the correlation between menopausal age and demographic, social and lifestyle behavior. The median age at natural menopause was 51.25 years. Univariate Cox models were fitted to the age at menopause for all individual covariates before the multivariate analysis. Since employment was not significantly associated with age at menopause (HR, 0.92; 95% confidence interval [CI], 0.38–2.21), it was not included in the multiple Cox model. Cigarette smoking, low level of education, and a negative health perception were the only lifestyle behaviors that significantly correlated with earlier age at menopause [16].

In the NHANES III population, tobacco use (both primary and secondhand smoking) was associated with earlier age at menopause. Moreover, analysis of the employment status indicated that, although the difference was not statistically significant, service workers experienced the earliest age at menopause (46.95 years) and white-collar workers the latest (48.75 years). The authors suggested that secondhand smoking (which was frequent for service jobs) could play a role in earlier age at menopause onset [17]. Wang et al. also found an earlier age at menopause in blue-collar (49.0 years) than in white-collar workers (49.5 years), which they attributed to sulfur dioxide (SO_2) exposure since occupational exposure to SO_2 for more than 20 years was the only factor that remained significant on multivariate analysis [18].

The association between rotating night shift work and menopausal age was assessed by Stock et al. in a cohort of 80,840 nurses, with a follow-up of 22 years (1991–2013). During follow-up, 27,456 women (34%) experienced natural menopause at a mean age of 50 ± 4.0 years; those who in the previous 2 years had worked 20 or more months in rotating shifts had an increased risk of earlier age at menopause (HR, 1.09, 95% CI, 1.02–1.16), compared to non-shift working nurses. Cumulative rotating nightwork also exerted an effect since the younger nurses (<45 years) were at increased risk of earlier menopause (11–20 years: HR, 1.22, 95% CI, 1.03–1.44; ≥20 years: HR, 1.73, 95% CI, 0.90–3.35) than the older nurses [19].

2.2.2. Influence of Work on Menopausal Symptoms

In the study by Zhao et al., the prevalence of vasomotor symptoms was 35.1%; the prevalence of psychological symptoms was 78.5%; and the prevalence of bone/joint pain was 45.8%. After excluding premenopausal women, the prevalence of all symptoms was lower among postmenopausal women with farming jobs than among postmenopausal professional women; the prevalence of vasomotor symptoms was even lower among perimenopausal women with farming jobs [13].

A cross-sectional survey by Olaolorun et al. found a high prevalence of any menopausal symptom (84.5%); joint and muscular discomfort was the most common symptom (59.0%), followed by physical and mental exhaustion (43.0%), sexual problems (40.4%), and hot flashes (39.0%). Symptom perception was quantified using a structured questionnaire that included a standardized Menopause Rating Scale (MRS). Occupational status was defined as managerial and professional, intermediate, or routine and material. On multiple linear regression, occupation significantly predicted the total MRS score (HR, 0.76, 95% CI, 0.10–1.42) and the psychological subscale score (HR, 0.45, 95% CI, 0.16–0.75) [20].

Hammam et al. investigated the relationship between work and menopausal symptoms in 131 middle-aged medical teaching staff workers. They found that several workplace factors, such as poor physical environment (91.6%), confined spaces/crowding (84.7%), insufficient sanitary/rest/refreshment facilities (83.2%), and poor workstation design (63.4%), worsened symptoms [21].

3. Conclusions

The available information on the correlation between work and aging-related hormonal alterations is limited. The studies conducted to date do not rule out an influence of work on andropause or menopause. Some occupational factors, such as job-related stress, sleep disorders related to shift work, and pesticide exposure, are implicated in aging-related hormonal alterations. The possible role of work on andropause/menopause warrants further investigation and greater attention by the scientific community.

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