VOLUME 41 PART 3 pp 264–267 JUNE 1997

Early menopause in women with Down's syndrome

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Abstract

We used the AAMR's Adaptive Behavior Scale to ascertain current menstrual status in a population-based sample of 157 women with Down's syndrome (DS) and 187 women with other intellectual disability, all 40 years of age or older. The age-adjusted likelihood of menopause was twice as high in women with DS syndrome as in women with other intellectual disability (OR=2.3; 95% CI=1.1–4.9). Treated thyroid conditions did not influence menstrual status and did not modify the relationship between DS and menstrual status. These findings support the hypothesis that women with DS experience menopause at an earlier age and that this may be associated with accelerated aging.

Keywords menopause, women, Down's syndrome

Introduction

Recent studies of gonadal function in women with Down's syndrome (DS) living in the community suggest that menstrual function as indicated by age at menarche and regular menses are much closer to that of the general population than indicated by earlier studies of institutionalized women (Oster 1953; Bellone *et al.* 1980; Goldstein 1988). For example, Scola & Pueschel (1992) found that 76% of women with DS from 13 to 27 years of age (n=51) had regular menstrual cycles compared with 73% of a general high school population. In addition, studies of hormonal status during menstrual cycles, although based on small numbers of persons and only a few cycles per person, have generally supported the conclusion that most cycles show evidence of ovulation and formation of a corpus luteum (Tricomi *et al.* 1964; Bock 1974; Hasen *et al.* 1980; Hsiang *et al.* 1987).

Older individuals with DS show age-related changes in health and functional capacities suggestive of premature or accelerated aging (Martin 1978; Oliver & Holland 1986). The most extensively studied aspect of aging in middle aged and elderly people with DS is their high risk of Alzheimer's disease (Lai & Williams 1989). Early menopause in women with DS would be consistent with the hypothesis of accelerated aging.

Only one paper has reported on menopause in women with DS. Carr & Hollins (1995) surveyed the menstrual histories of 45 women with DS and 126 women with learning disabilities aged 36 to 61 years. Their data suggest that women with DS are younger at the onset of menopause than women with other learning disabilities. In this report, we confirm and extend the findings of Carr & Hollins (1995). We studied a large population-based sample of women

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with and without DS to estimate the median age at onset of menopause, and to determine the influence of hypothyroidism on menstrual status.

Methods

Women with DS residing in the nine-county downstate region of New York, USA, were identified from a registry of people with DS in New York State developed from the Developmental Disabilities Profile, a computerized database maintained by the New York State Office of Mental Retardation and Developmental Disabilities and supplemented by an independent survey of all state and voluntary service providers (Schupf *et al.* 1994; Zigman *et al.* 1996). We selected a random sample of adults with DS, 30–70 years of age, and a sample of adults with other forms of intellectual disability, frequency matched to the age distribution of the adults with DS. Informed consent to participate was provided by a responsible family member.

A semi-structured interview was conducted at the individual's residential or day-treatment facility with a caregiver (direct care staff or staff supervisor) familiar with the individual being assessed. The interview obtained information on age, sex, race, DS status and functional diagnoses, and medical history. Menstrual status was ascertained using the American Association on Mental Retardation' s Adaptive Behavior Scale (ABS; Nihira *et al.* 1974). The ABS is a standardized scale of adaptive competence designed specifically for use with individuals with intellectual disability. The section of the ABS concerned with menstruation includes a question on whether or not the individual is currently menstruating, and for those who are, questions about the extent of assistance required. We used data from the first question to define current menstrual status.

The sample comprised 191 women with DS and 215 women with other forms of intellectual disability. Preliminary analyses used cross-tabulations and χ^2 tests to compare the prevalence of menstruation by 5 year age groups in women with and without DS. Among women from 30 to 39 years of age, 20% of the women with DS and 4% of the women with other forms of intellectual disability were not currently menstruating (Table 1). This may include a proportion of women who had never menstruated in each group. Because the inclusion of this group might lead us to underestimate the median age at menopause, we restricted our analyses to women ≥40 years of age (157 women DS and 187 women with other intellectual disability) in whom we assume that the majority of women not currently menstruating had done so in the past, and thus, had reached menopause.

We used maximum likelihood logistic regression analysis to estimate the odds of not menstruating ('menopause') among women with DS compared with women with other forms of intellectual disability, adjusting for current age. We used the methods developed by MacMahon & Worcester (1966) to estimate median at age at onset of menopause from cross-sectional data. Analyses were repeated for the 159 women (78 with DS, 81 with other intellectual disability) with information on thyroid conditions because of the possibility that specific autoimmune conditions, including thyroid disorders, are associated with premature ovarian failure (Coulam 1983; LaBarbera *et al.* 1988). All

Table 1 Age distribution and menstrual status of women with Down's syndrome and with other forms of intellectual disability

Age group (years)	Number		Not currently menstruating (%)	
	Down's syndrome	Other intellectual disability	Down's syndrome	Other intellectual disability
30–39	34	28	7 (20.0)	1 (3.6)
40–44	31	29	2 (6.5)	3 (10.3)
45–49	25	35	13 (52.0)	11 (31.4)
50–54	33	26	30 (90.9)	17 (65.4)
55–59	18	32	18 (100)	30 (93.7)
60+	50	65	50 (100)	65 (100)

women with thyroid conditions were diagnosed as hypothyroid and all were receiving synthroid treatment (n=37). As expected, hypothyroidism was more common in women with DS than in women in the comparison group (34.6% versus 12.3%, P=0.0009).

Results

Women with and without DS were similar in age (mean age=54.1 and 55.0 years, respectively; P=0.332). The age-adjusted likelihood of menopause was twice as great in women with DS compared with women with other intellectual disabilities (odds ratio (OR)=2.3; 95% CI=1.1–4.9, P<0.05; Table 1). The estimated median age at menopause was 2.2 years earlier for women with DS (47.1 years) than for women with other forms of intellectual disability (49.3 years) (Fig. 1).

Results were similar in analyses limited to women with information on thyroid conditions. Adjusting for the effects of age and thyroid conditions, the likelihood of menopause was three times higher in women with DS than in women with other intellectual disability (OR=3.4; 95% CI=0.77–14.9). In addition, treated hypothyroidism was not significantly associated with age at menopause (OR=1.3; 95% CI=0.24–6.8; ns).

Discussion

Our findings are consistent with those of Carr & Hollins (1995) in showing earlier menopause in women with DS than in women with other forms of intellectual disability. Carr & Hollins (1995) reported that 88% of women with DS and 62% of women with learning disabilities were no longer menstruating in the 46–50-years-old age-group. The corresponding proportions in our study were 62% and 33% for women with and without DS, respectively. Differences in subject characteristics (e.g. the proportion of women in institutional residence) or in the manner of collecting data may account for the variation in estimates. We estimated the median age at menopause as 47.1 for women with DS and 49.3 for women with other intellectual disability. In a population-based prospective study, Brambilla & McKinlay (1989) estimated median age at menopause as 50.7 years for women without intellectual disability (later modified to 51.2 years to account for the fact that, on average, women are 6 months older than reported age at last birthday). However, differences in the methods of collecting data on menstrual periods preclude inferences about age at menopause in women with intellectual disability compared with women in the general population.

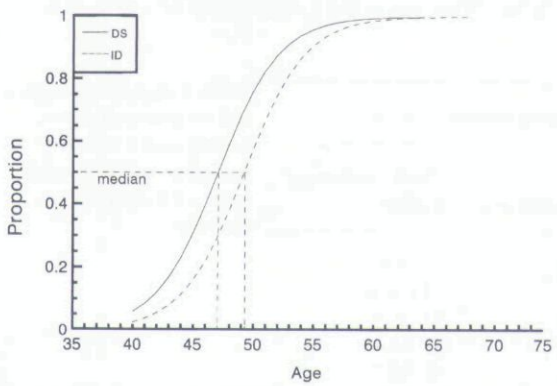

Figure 1 Logistic regression model of proportion of women not menstruating. DS: Down's Syndrome, ID: Intellectual disability.

Carr & Hollins (1995) noted that thyroid deficiency might predispose to earlier menopause. In our sample, all women with thyroid conditions were treated. Nonetheless, we examined the influence of hypothyroidism on menstrual status. Treated hypothyroidism was not associated with age at menopause among women with or without DS nor did the occurrence of hypothyroidism modify the association between DS and early menopause. We cannot rule out the possibility that age at menopause might be earlier in women with untreated hypothyroidism or with other endocrine irregularities.

Our data have two limitations with respect to the estimated age at menopause. First, we could not identify women who had never menstruated. Thus, there is the possibility that some women who are not currently menstruating are incorrectly classified as having reached menopause and that the median age at menopause is underestimated. For example, the proportion of women with DS who are not menstruating at 30–39 years of age is higher than at 40–44 years of age, (20% versus 6%), which may reflect the inclusion of women who never menstruated. These women are likely to be a larger

proportion of women aged 30–39 years than of women aged 40–44 years. To address this limitation, we restricted the analysis to women aged 40 years or older to reduce the proportion of women who had never menstruated. Secondly, we did not ascertain menopause directly through prospective study. Further longitudinal study will provide more precise estimates of age at menopause and more detailed information on the nature of aging in women with DS.

Acknowledgements

This work was supported by Federal Grants AG09400 and R29 HD24170, by grant IIRG-90-067 from the Alzheimer's Association, and by funds provided by the New York State Office of Mental Retardation and Developmental Disabilities. We thank Dr Wayne Silverman for his valuable comments on the manuscript.

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Received 15 July 1996; revised 4 September 1996