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Disease activity during the premenopausal and postmenopausal periods in women with systemic lupus erythematosus

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ASUNTO: Autorización del trabajo de investigación del Dr. Armando Villegas Jiménez.

DR. ISIDRO AVILA MARTÍNEZ
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Presente.

Estimado Dr. Avila Martínez:

Me permito informar a usted que el **Dr. Armando Villegas Jiménez**, alumno del curso de especialización en **Medicina Interna** en el **Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán**, presenta el trabajo de investigación intitulado ***"Disease Activity during the Premenopausal and Postmenopausal periods in women with systemic lupus erythematosus".***

De conformidad con el artículo 23 capítulo 5º. de las Normas Operativas del Plan Unico de Especializaciones Médicas (PUEM) se considera que cumple con los requisitos para validarlo como el trabajo formal de Investigación que le otorga el derecho de la diplomación como especialista.

Sin otro particular de momento, reciba un cordial saludo.

Atentamente
"POR MI RAZA HABLARÁ EL ESPÍRITU"
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JEFE DE LA SUBDIVISIÓN

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Disease Activity during the Premenopausal and Postmenopausal Periods in Women with Systemic Lupus Erythematosus

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PURPOSE: Cyclophosphamide-induced ovarian failure has been reported to be protective against flares of systemic lupus erythematosus (SLE). We studied whether patients with SLE experience a decrease in disease activity after natural menopause.

SUBJECTS AND METHODS: We studied 30 SLE patients with natural menopause who had been observed at least 2 years before and after menopause and who did not receive hormone replacement therapy or danazol. Menopause was defined as the date of the last self-reported menstrual period. Disease activity was assessed retrospectively by medical chart review using standard measures (the SLE disease activity index) during the immediate premenopausal and postmenopausal periods, and 2 (n = 30 patients), 3 (n = 19), and 4 (n = 13) years before and after menopause. We also compared the use of health services and medications.

RESULTS: Patients were studied for a mean (± SD) of 6.4 ± 1.7 years (premenopausal, 3.3 ± 0.9 years; postmenopausal, 3.2 ± 0.9 years). During the premenopausal periods, the mean disease activity score was 2.3 ± 2.3 (range, 0 to 9 on a 0 to 105 scale), compared with 2.3 ± 2.9 (range, 0 to 12; $P = 0.37$) after menopause. The maximum disease activity score was somewhat greater in the premenopausal period (7.9 ± 6.0 [range, 0 to 22] vs. 5.8 ± 5.1 [range, 0 to 22]; $P = 0.04$). The incidence rates of flares (0.56 per year vs. 0.43 per year, $P = 0.20$) and severe flares (0.17 per year vs. 0.12 per year, $P = 0.33$) were similar in the premenopausal and postmenopausal periods. Differences in disease activity scores (mean and maximum) and the number of visits to a rheumatologist's office were only significant when the fourth year before menopause was compared with the fourth year after menopause.

CONCLUSION: Disease activity is mild during the premenopausal and postmenopausal periods in women with SLE. A modest decrease, especially in the maximum disease activity, is seen after natural menopause. **Am J Med. 2001;111:464–468.**

Systemic lupus erythematosus (SLE) is an autoimmune disease of unknown etiology. Several studies have shown the relevance of sex hormones in the pathogenesis, course, and treatment of SLE in humans and animal models (1–14). Women during their reproductive years are 9 to 13 times more prone to SLE development than are men. This ratio is lower before puberty or after menopause (1). Use of oral contraceptives and postmenopausal estrogen therapy are associated with an increased risk of developing SLE (2,3). It remains controversial, however, whether estrogens exacerbate disease activity in patients with SLE (4–10).

In murine models of SLE, orchiectomized NZB/NZW F1 mice that are treated with estrogen have a greater mortality (11). Conversely, the course of the disease is delayed considerably in female NZB/NZW F1 mice by prolonged exposure to 5α-dihydrotestosterone (12). Prepubertal castration of female NZB/NZW F1 mice in the absence of androgen administration does not affect the production of antibodies to DNA or mortality (13). These results suggest that sex hormones modulate immune function and that androgenic hormones are protective in murine lupus (13).

In women with SLE, the reduction of estradiol to testosterone ratio by the administration of cyproterone acetate reduces the episodes of exacerbation (14). In addition, menopause affects the onset of several autoimmune diseases, including SLE (1,15,16), and cyclophosphamide-induced ovarian failure may be protective against lupus flares (17). Given the improved prognosis for SLE (18), more women with SLE survive to undergo menopause. Therefore, we analyzed activity in a cohort of 30 women with SLE before and after menopause.

PATIENTS AND METHODS

From an SLE register of 157 postmenopausal patients, 30 women were identified who fulfilled inclusion criteria: a clinical diagnosis of SLE, development of natural menopause, and regular follow-up at our center at least 2 years

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before and after menopause. A woman was excluded if she developed SLE after menopause; had surgical, drug-induced, or premature menopause before the age of 35 years; received estrogens, progestins, or danazol at any time; had an estimated creatinine clearance ≤20 mL/min; or did not attend scheduled rheumatology appointments during the study period.

A standardized form with 46 variables, including demographic characteristics, health habits, reproductive history, SLE disease activity, and treatment, was completed for each patient after face-to-face interview and medical chart review.

A patient was considered postmenopausal if she had amenorrhea for more than 1 year and a serum follicle-stimulating hormone (FSH) level >20 mIU/mL. Menopause was defined as the date of the last self-reported menstrual period (19,20). Postmenopause was defined as dating from the final menstrual period. Premenopause was used to refer to the years immediately before menopause. SLE onset was defined as the time when at least one of the classification criteria for SLE was present (21); SLE diagnosis was defined as the time when the fourth classification criterion developed. A lupus flare was an increase of 3 or more points in the SLE disease activity index (22), compared with the previous visit or in a 93-day period (23). A severe lupus flare was defined as an increase of 10 or more points in the disease activity score. Duration of SLE was the time elapsed from SLE diagnosis until the beginning of the study period.

Outcome Measures

Disease activity was assessed retrospectively by medical chart review using the SLE disease activity index (maximum score, 105) (22) or a modified version of the index (maximum score, 32) (24). A physician trained to abstract data from medical records and who was uninvolved in the regular care of the patients derived these indexes from the clinical notes made by the treating physicians. Abnormalities that were not mentioned in the medical record were considered as not present and were scored as zero. Activity was estimated during the premenopausal and postmenopausal periods, as well as during the second, third, and fourth years before and after menopause as the mean (and maximum) SLE disease activity index and modified disease activity index, the number of lupus flares, and the number of severe lupus flares. A maximum of 2 flares in a 12-month period was scored. We also determined the number of visits to a rheumatologist's office, visits to an emergency room, number of hospitalizations related and not related to SLE, use and dose of prednisone, and use of chloroquine and immunosuppressant medications.

Statistical Analysis

Continuous variables were compared premenopausal and postmenopause using the Wilcoxon matched-pair signed-rank test. Categorical variables were analyzed using the chi-squared test or Fisher exact test. The analysis of lupus flares was based on incidence-density rates using patient-years of follow-up as the denominator. The incidence-rate ratio was expressed as relative risk (RR) of developing flares with 95% confidence intervals (CI). Statistical significance was set at $P < 0.05$ (two-sided). Analyses were performed using the STATA 5.0 computer program (Stata Corporation, College Station, Texas).

Table 1. Characteristics of the Sample

	Number (%) or Mean ± SD
Clinical characteristics	
Age (years)	53 ± 7
Education (years)	9 ± 5
Body mass index (kg/m^2)	23.6 ± 4.5
History of smoking	12 (40)
Age at menarche (years)	13 ± 2
Age at menopause (years)	45 ± 4
History of pregnancy	26 (87)
Number of pregnancies	4 ± 2
SLE characteristics	
≥4 criteria*	29 (97)
Number of criteria*	7 ± 2
Age at onset (years)	32 ± 9
Age at diagnosis (years)	34 ± 9
Duration (years)	7 ± 8
Length of follow-up (years)	7 ± 8

* Criteria of the American College of Rheumatology (21).
SLE = systemic lupus erythematosus.

RESULTS

The 30 women included in the study were a mean (± SD) of 7.2 ± 5.3 years from menopause (Table 1). They were studied for a mean of 6.4 ± 1.7 years (range, 4 to 8 years). The mean premenopausal period was 3.3 ± 0.9 years (range, 2 to 4 years), and the mean postmenopausal period was 3.2 ± 0.9 years (range, 2 to 4 years). Thirteen patients were seen during the fourth years before and after menopause, 19 patients during the third years, and all 30 patients during the second years.

SLE Activity

Mean disease activity was similar in the premenopausal and postmenopausal periods, but maximum disease activity was slightly, albeit significantly, greater in the premenopausal period (Table 2). Most patients had relatively mild disease. There were 55 disease flares during 98 patient-years in the premenopausal period, compared with 40 flares during 93 patient-years in the postmenopausal period (RR = 1.3; 95% CI: 0.9 to 2.0). There were 17 severe flares in the premenopausal period, and 11 dur-

ing the postmenopausal period (RR = 1.5; 95% CI: 0.7 to 3.5). Twenty-seven (49%) of the premenopausal flares and 22 (55%) of the postmenopausal flares prompted a change in treatment ($P = 0.57$). When specific premenopausal and postmenopausal years were compared, disease activity was greater during the fourth year before menopause than during the fourth year after menopause (Table 2), but not for the other years.

The use of health services and medications showed no difference during the premenopausal and postmenopausal periods (Table 3). As with the measures of disease activity, patients had more visits to a rheumatologist's office during the fourth premenopausal year (4.9 ± 2.7) than during the fourth postmenopausal year (3.2 ± 2.3, $P = 0.03$). No other differences were noted for year-to-year comparisons.

DISCUSSION

We found that women with SLE had relatively mild disease activity during the premenopausal and postmenopausal periods. There was a modest decrease in maximum disease activity after natural menopause, especially when the disease activity in the fourth year before menopause was compared with the fourth year after menopause. These findings suggest that natural menopause has a mild protective effect on SLE activity, as has been found following cyclophosphamide-induced ovarian failure (17).

Although hypoestrogenemia is a consequence of both induced and natural menopause, there are important differences in these conditions. Whereas induced menopause leads to a sudden decrease in circulating ovarian steroids (both androgens and estrogens), there are inconsistent and gradual changes during the several years that precede natural menopause (25). Throughout this menopausal transition, serum concentrations of estradiol are lower than in younger women (26). During the early postmenopausal period, some women have ovarian follicles that are capable of secreting estrogen, as well as have declining concentrations of estrone, estradiol, and estrone sulfate that stabilize within 12 months after the last menses (27). Studies suggest that 25% to 50% of women have estrogen levels indicative of some follicular activity during the first 6 to 12 months after the cessation of menses (28,29), and approximately 10% of women will retain estrogenic activity up to 10 years after menopause (30,31). Given this gradual transition, the decrease in SLE activity after natural menopause would not be as great as that after induced menopause in women (17) or in animal models (11–13). Perhaps greater differences in SLE activity would be observed if women before the initiation of the menopausal transition were compared with those who have a more advanced postmenopausal state.

Table 2. Comparisons of Systemic Lupus Erythematosus (SLE) Activity 2, 3, and 4 Years before and after Menopause, and during the Premenopausal and Postmenopausal Periods

Activity Measure	Years from Menopause*											
	−4	+4	P	−3	+3	P	−2	+2	P			P
	(n = 13)		Value	(n = 19)		Value	(n = 30)		Value	Premenopausal	Postmenopausal	Value
SLE disease activity index†												
Mean	1.9 ± 2.0	0.7 ± 1.5	0.03	2.4 ± 2.7	1.6 ± 1.8	0.26	1.8 ± 2.7	1.8 ± 2.8	0.92	2.3 ± 2.3	2.3 ± 2.9	0.37
Maximum	5.0 ± 5.2	1.9 ± 3.3	0.04	5.9 ± 6.1	3.9 ± 3.9	0.20	4.3 ± 5.8	3.6 ± 4.9	0.62	7.9 ± 6.0	5.8 ± 5.1	0.04
Modified SLE disease activity index‡												
Mean	1.1 ± 1.2	0.5 ± 0.9	0.10	1.3 ± 1.5	1.1 ± 1.1	0.33	1.0 ± 1.4	0.9 ± 1.2	0.48	1.4 ± 1.4	1.2 ± 1.3	0.34
Maximum	3.0 ± 3.2	1.1 ± 1.8	0.03	3.7 ± 3.9	2.6 ± 2.9	0.24	2.9 ± 4.1	2.0 ± 2.7	0.05	5.3 ± 4.4	4.1 ± 3.4	0.03
Any flare (rate per patient-year)	0.54	0.15	0.11	0.67	0.56	0.68	0.5	0.5	1.0	0.56	0.43	0.20
Severe flares (rate per patient-year)	0.15	—	0.25	0.17	0.11	0.69	0.10	0.13	0.73	0.17	0.12	0.33
Patients who flared (n [%])	5 (38)	2 (13)	0.38	9 (47)	8 (42)	0.74	12 (40)	11 (37)	0.79	22 (73)	17 (57)	0.18

* Negative numbers indicate before menopause; positive numbers indicate after menopause.
† From reference 22. Plus-minus values indicate mean ± SD.
‡ From reference 24. Plus-minus values indicate mean ± SD.

Table 3. Use of Health Services and Medications in Patients with Systemic Lupus Erythematosus during the Premenopausal and Postmenopausal Periods

Measurement	Premenopausal	Postmenopausal	*P* Value
	Number (%) or Mean ± SD		
Health services utilization			
Rhematology visit	14.3 ± 8.5	12.4 ± 7.5	0.12
Emergency room visit	1.7 ± 2.6	1.8 ± 2.8	0.79
Hospitalization	0.1 ± 0.3	0.1 ± 0.3	1.00
Medication Use			
Prednisone	25 (83)	21 (70)	0.36
Prednisone dose (mg)	8 ± 10	7 ± 8	0.15
Chloroquine	16 (53)	13 (43)	0.44
Azathioprine	9 (30)	7 (23)	0.56
6-Mercaptopurine	1 (3)	0	1.00
Intravenous cyclophosphamide	2 (7)	2 (7)	1.00
Oral cyclophosphamide	3 (10)	3 (10)	1.00
Methotrexate	1 (3)	0	1.00

Because disease activity was mild during the premenopausal period, an additional decrease in clinical activity would be difficult to detect with available instruments. Thus, our results may be limited to premenopausal patients with mild disease. Indeed, women with SLE who reach natural menopause are a select group. In our sample, they had a relatively late onset of disease and a prolonged course, factors that might be associated with milder disease (32). Some patients with more severe disease do not reach natural menopause, either because of premature mortality or the development of early menopause induced by chemotherapy or immunologic damage to the ovaries. Thus, the mildness of disease activity during the premenopausal period might be due to factors associated with reaching natural menopause, as well as the hypoestrogenemia that occurs in the premenopausal period.

Few studies have explored SLE activity in postmenopausal patients. Mok et al. reported significantly fewer flares ($P = 0.03$) and severe flares ($P = 0.01$) among patients with cyclophosphamide-induced ovarian failure when compared with patients who were still menstruating, and concluded that ovarian failure with hypoestrogenemia was protective against lupus flares (17).

Some limitations of the study need to be considered. Age at menopause was defined retrospectively as the self-reported date of the last menstrual period because this information was not uniformly noted in medical records. The reproducibility and validity of self-reported age at menopause has wide variability, especially for natural menopause (33–36). Among the 157 postmenopausal SLE patients in our center, the reproducibility of this information was 62% within 1 year and 76% within 2 years when women were reinterviewed 22 months after the initial questionnaire.

We assessed SLE activity retrospectively by chart review. Two studies have reported that chart-based evaluation is reasonably accurate, but tends to minimize activity, especially if the disease is mild or non–life-threatening (37,38). To the extent that disease activity was underestimated (or wrongly estimated) to similar degrees in the premenopausal and postmenopausal periods, this would have biased our results toward finding no difference between the two periods. Moreover, the mean disease activity scores that we observed and the numbers of flares were similar to those previously reported (23,37). The lower incidence of flares reported by Mok et al. (17) might be because they modified the disease activity score to prevent overestimation of scores. Whether chart-derived assessments can detect changes in disease activity is unknown. We did not study the intrarater reliability of the physician who performed the chart abstractions. Nevertheless, disease activity assessment was identical during the premenopausal and postmenopausal period.

We conclude that disease activity is mild and similar during the premenopausal and postmenopausal periods in women with SLE. There is a modest decrease in maximum disease activity after natural menopause.

REFERENCES

1. Masi AT, Kaslow RA. Sex effects in systemic lupus erythematosus: a clue to pathogenesis. *Arthritis Rheum.* 1978;21:480–484.
2. Sánchez-Guerrero J, Liang MH, Karlson EW, et al. Postmenopausal estrogen therapy and the risk for developing systemic lupus erythematosus. *Ann Intern Med.* 1995;122:430–433.
3. Sánchez-Guerrero J, Karlson EW, Liang MH, et al. Past use of oral contraceptives and the risk of developing systemic lupus erythematosus. *Arthritis Rheum.* 1997;40:804–808.
4. Mund A, Simson J, Rothfield NF. Effect of pregnancy on course of systemic lupus erythematosus. *JAMA.* 1963;183:917–922.

5. Rose E, Pillsbury DM. Lupus erythematosus and ovarian function: observations on a possible relationship with a report of 6 cases. *Ann Intern Med.* 1944;21:1022–1034.
6. Jungers P, Dougados M, Pelissier C, et al. Influence of oral contraceptive therapy on the activity of systemic lupus erythematosus. *Arthritis Rheum.* 1982;25:618–623.
7. Barret C, Neylon N, Snaith ML. Oestrogen-induced systemic lupus erythematosus. *Br J Rheumatol.* 1986;25:300–301.
8. Arden NK, Lloyd ME, Spector TD, Hughes GRV. Safety of hormone replacement therapy (HRT) in systemic lupus erythematosus (SLE). *Lupus.* 1994;3:11–13.
9. Kreidstein SH, Urowitz MB, Gladman DD, Gough J. Hormonal replacement therapy in systemic lupus erythematosus. *J Rheumatol.* 1997;24:2149–2152.
10. Mok CC, Lau CS, Ho CTK, et al. Safety of hormonal replacement therapy in postmenopausal patients with systemic lupus erythematosus. *Scand J Rheumatol.* 1998;27:342–346.
11. Roubinian JR, Talal N, Greenspan JS, et al. Effect of castration and sex hormone treatment on survival, anti-nucleic acid antibodies and glomerulonephritis in NZB/NZW F1 mice. *J Exp Med.* 1978;147:1568–1583.
12. Roubinian JR, Talal N, Greenspan JS, et al. Delayed androgen treatment prolongs survival in murine lupus. *J Clin Invest.* 1979;63: 902–911.
13. Roubinian JR, Papoian R, Talal N. Androgenic hormones modulate autoantibody responses and improve survival in murine lupus. *J Clin Invest.* 1977;59:1066–1070.
14. Jungers P, Kuttenn F, Liote F, et al. Hormonal modulation in systemic lupus erythematosus. Preliminary clinical and hormonal results with cyproterone acetate. *Arthritis Rheum.* 1985;28:1243–1250.
15. Goemaere S, Ackerman C, Goethals K, et al. Onset of symptoms of rheumatoid arthritis in relation to age, sex, and menopausal transition. *J Rheumatol.* 1990;17:1620–1622.
16. Sullivan DA. Sex hormones and Sjogren's syndrome. *J Rheumatol.* 1997;24((suppl 50)):S17–S32.
17. Mok CC, Wong RWS, Lau CS. Ovarian failure and flares of systemic lupus erythematosus. *Arthritis Rheum.* 1999;42:1274–1280.
18. Systemic lupus erythematosus. In: Silman AJ and Hochberg MC, eds. *Epidemiology of the Rheumatic Diseases*. New York: Oxford University Press; 1993:163–191.
19. *Report of a WHO Scientific Group. Research on the Menopause in the 1990s*. Geneva: World Health Organization; 1996. WHO Technical Report Series, No. 866.
20. Utian WH. The International Menopause Society menopause-related terminology definitions. *Climacteric.* 1999;2:284–286.
21. Tan EM, Cohen AS, Fries JF, et al. The 1982 revised criteria for the classification of systemic lupus erythematosus. *Arthritis Rheum.* 1982;25:1271–1277.
22. Bombardier C, Gladman DD, Urowitz MB. Derivation of the SLEDAI. A disease activity index for lupus patients. *Arthritis Rheum.* 1992;35:630–640.
23. Petri M, Genovese M, Engle E, Hochberg M. Definition, incidence, and clinical description of flare in systemic lupus erythematosus. A prospective cohort study. *Arthritis Rheum.* 1991;34:937–944.
24. Guzman J, Cardiel MH, Arce-Salinas A, et al. Measurement of disease activity in systemic lupus erythematosus. Prospective validation of 3 clinical indices. *J Rheumatol.* 1992;19:1551–1558.
25. Greendale GA, Lee NP, Arriola ER. The menopause. *Lancet.* 1999;353:571–580.
26. Sherman BM, West JH, Korenman SG. The menopausal transition: analysis of LH, FSH, estradiol and progesterone concentrations during menstrual cycles of older women. *J Clin Endocrinol Metab.* 1976;42:629–636.
27. Longcope C, Franz C, Morello C. Steroid and gonadotropin levels in women during the peri-menopausal years. *Maturitas.* 1986;8: 189–196.
28. Rannevik G, Carlstrom K, Jeppsson S. A prospective long-term study of women from pre-menopause to post-menopause: changing profiles of gonadotropins, oestrogens, and androgens. *Maturitas.* 1986;8:297–307.
29. Trevoux R, De Brux J, Castanier M. Endometrium and plasma hormone profile in the peri-menopause to post-menopause. *Maturitas.* 1986;8:309–326.
30. De Waard F, Pot H, Tonckens-Nanninga NE. Longitudinal studies on the phenomenon of postmenopausal estrogen production. *Acta Cytol.* 1972;16:273–278.
31. Grattarola R, Secreto G, Recchione C. Correlation between urinary testosterone or estrogen excretion levels and interstitial cell-stimulating hormone concentrations in normal postmenopausal women. *Am J Obstet Gynecol.* 1975;121:380–381.
32. Swaak AJG, Nossent JC, Bronsveld W, et al. Systemic lupus erythematosus. II. Observations on the occurrence of exacerbations in the disease course: Dutch experience with 110 patients studied prospectively. *Ann Rheum Dis.* 1989;48:455–460.
33. Paganini-Hill A, Ross RK. Reliability of recall of drug usage and other health-related information. *Am J Epidemiol.* 1982;11:114–122.
34. Horwitz RI, Yu EC. Problems and proposals for interview data in epidemiological research. *Int J Epidemiol.* 1985;14:463–467.
35. Bean JA, Leeper JD, Wallace RB. Variations in reporting of menstrual histories. *Am J Epidemiol.* 1979;109:181–185.
36. Colditz GA, Stampfer MJ, Willett WC, et al. Reproducibility and validity of self-reported menopausal status in a prospective cohort study. *Am J Epidemiol.* 1987;126:319–325.
37. Arce-Salinas A, Cardiel MH, Guzmán J, Alcocer-Varela J. Validity of retrospective disease activity assessment in systemic lupus erythematosus. *J Rheumatol.* 1996;23:846–849.
38. Wluka AE, Liang MH, Partridge AJ, et al. Assessment of systemic lupus erythematosus disease activity by medical record review compared with direct standardized evaluation. *Arthritis Rheum.* 1997; 40:57–61.