Oral contraceptives did not increase risk for flare in women with systemic lupus erythematosus


**Clinical impact ratings:** GIM/FP/GP ★★★★★✩✩ Hematol/Thrombo ★★★★★✩ Rheumatology ★★★★★✩

**Question**
In young women with stable systemic lupus erythematosus (SLE), do combined oral contraceptives (OCs) increase risk for lupus flare?

**Methods**

**Design:** Randomized, placebo-controlled, noninferiority trial (OC study of the Safety of Estrogens in Lupus Erythematosus National Assessment [OC-SELENA] trial).

**Allocation:** [Concealed]†.*

**Blinding:** Blinded [clinicians, patients, data collectors, outcome assessors, data analysts, and data safety and monitoring committee]†.*

**Follow-up period:** 12 months.

**Setting:** 15 centers in the United States.

**Patients:** 183 women 18 to 39 years of age (<36 y if a smoker) (mean 30 y) with inactive (76%) or stable active (24%) SLE. Exclusion criteria included use of OCs for >1 month since SLE diagnosis, hypertension, uncontrolled diabetes, presence of antinuclear antibodies or lupus anticoagulant, and history of thrombosis or gynecologic or breast cancer.

**Intervention:** Triphasic ethinyl estradiol (35 μg) plus norethindrone (0.5, 0.75, and 1.0 mg) OC (n = 91) or placebo (n = 92).

**Outcomes:** Severe flare (>12 out of 105 on the SELENA revision of the SLE Disease Activity Index [SLEDAI], new or worsening disease activity, increase in prednisone to >0.5 mg/kg per d or new immunosuppressive drug for SLE, hospitalization for SLE, or Physician's Global Assessment score >2.5 out of 3), mild or moderate flare, and change from baseline in SELENA-SLEDAI score, assessed at 1, 2, 3, 6, 9, and 12 months.

**Patient follow-up:** 83% (100% included in intention-to-treat analysis).

**Main results**
OC did not differ from placebo for proportions of women having a severe lupus flare (7.7% vs 7.6%) or a mild-to-moderate flare (69% vs 60%) at 12 months, or for mean change in SELENA-SLEDAI score at any time point (Table). Groups did not differ for type or frequency of adverse events, including thrombosis.

**Conclusion**
In young women with stable systemic lupus erythematosus, combined oral contraceptives did not increase risk for severe or mild-to-moderate lupus flare.

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**For correspondence:** Dr. J.P. Buyon, Hospital for Joint Diseases, New York, NY, USA. E-mail jill.buyon@nyumc.org.

*See Glossary.
†Information provided by author.

Further reassurance on many points is needed from larger, longer-term studies. The trial patients had inactive or stable active disease defined by exact and well-validated criteria. However, one cannot assume that OCs would be equally well tolerated during periods of greater disease activity. Scoring systems have improved, but there is still the risk that the dangers of a major disease feature could be overlooked. For example, 37% of patients had "renal disorder" of unspecified severity. Ironically, "nephritis" was a feature in the disease flares of 4 of the 7 patients who received placebo but only in 1 of the 7 who received OCs.

It would be foolish to conclude from these limited data that OCs never exacerbate lupus nephritis. The overall conclusion must be that OCs can be safely prescribed to selected SLE patients, but it would be premature to relax our guard completely now as it was to make false deductions in an earlier era.

Michael Denman, MD
Northwick Park Hospital
Harrow, England, UK

**References**