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Spironolactone use for acne is not associated with an increased risk of venous thromboembolism: A matched, retrospective cohort study

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Keywords

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Combined oral contraceptives (COCs) are associated with an increased risk of venous thromboembolism (VTE), and there have been concerns about whether the risk is even greater with drospirenone containing combined oral contraceptives.[1] Drospirenone has anti-mineralocorticoid properties that may modify hemostasis leading to decreased coagulability.[2] This provides a potential mechanism by which drospirenone containing COCs could result in an increased risk of thrombosis compared to other COCs. Since drospirenone is molecularly related to spironolactone, it is possible that spironolactone might also be associated with an increased risk for VTE. The purpose of this study was to evaluate whether patients with acne treated with spironolactone are at increased risk for VTE.

Using a new-user active comparator design with the Truven Health MarketScan Commercial Claims Database from January 1, 2017-December 31, 2020, this retrospective cohort study sought to compare the risk of developing a deep venous thrombosis (DVT) or pulmonary embolism (PE) in patients with acne treated with spironolactone versus tetracycline-class antibiotic (i.e., doxycycline, minocycline, sarecycline). The MarketScan database includes individuals from more than 160 large employers and health plans across the United States and includes health care claims with diagnosis and procedure codes for medical encounters and all prescription medication fills. These data are de-identified in compliance with the Health Insurance Portability and Accountability Act regulations.

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Patients were identified according to the following criteria: (1) female sex, (2) at least 1 diagnosis of acne by a dermatologist[2], and (3) a minimum of 60 days of treatment with spironolactone or tetracycline-class antibiotic. The cohorts were matched for age and combined oral contraceptive use, since these can be risk factors for VTE[3]. Incident venous thromboembolism, deep venous thrombosis, or pulmonary embolism events were identified using ICD-10 codes: I80.1x, I80.2x, I82.4x, I82.6, and I26x.[4] Logistic regression was used to analyze the relationship between spironolactone and tetracycline-class antibiotics on the probability of developing a PE/DVT within 60 days. Analyses were performed using Stata 17. Given the use of de-identified data, this study was exempt from Institutional Review Board review.

Among 33,543 patients started on spironolactone, who were matched with 33,543 patients started on a tetracycline-class antibiotic, the mean age was 30.9 (SD 11.3) and 8.6% were current combined oral contraceptive users (Table 1). Those treated with spironolactone were not more likely to develop DVT (OR 0.57; 95% CI 0.31–1.06) or PE (OR 0.60; 95% CI 0.26–1.37) than those treated with tetracycline-class antibiotics (Table 1).

These results highlight that spironolactone is not associated with an increased risk of DVT or PE when used among patients being treated for acne. The findings of this study should be interpreted in the context of its design. There is potential for unmeasured confounding, though the use of matching and consideration of potential confounders such as combined oral contraceptive use decreases this risk. While there is a need to further study whether these findings generalize to other populations, this study provides reassurance that spironolactone use for acne is not associated with an increased risk for VTE.

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Table 1.

Cohort Characteristics and Outcomes

	Spironolactone (n=33,543)	**Tetracyclines (n=33,543)**
Age, y, mean (SD)	30.9 (11.3)	30.9 (11.3)
Age, y, median (IQR)	27 (22–38)	27 (22–38)
Oral contraceptive use, n (%)	3143 (8.6)	3143 (8.6)
DVT within 60 days, n (%)	16 (0.04)	28 (0.08)
PE within 60 days, n (%)	9 (0.02)	15 (0.04)

SD: standard deviation; IQR: interquartile range