Isotretinoin Treatment in Patients With Acne Vulgaris: Does It Impact Muscle Strength, Fatigue, and Endurance?

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PRACTICE **POINTS**

- Musculoskeletal adverse effects have been reported due to isotretinoin treatment.
- This study investigated the effects of isotretinoin on muscle strength, fatigue, and endurance in patients with acne vulgaris using an isokinetic dynamometer.
- Systemic isotretinoin treatment did not alter muscle strength, fatigue, or endurance.

The objective of this study was to evaluate the effects of isotretinoin on muscle strength, fatigue, and endurance in patients with acne vulgaris. The study included 27 patients with acne vulgaris who underwent treatment with isotretinoin as well as 26 control patients for comparison. Participants in the treatment group received oral isotretinoin 0.5 mg/kg once daily for 1 month followed by an increased dose of 1 mg/kg once daily for 2 months. Isokinetic measurements were obtained from the hamstrings and quadriceps on the nondominant side of the body at baseline and 3-month follow-up using an isokinetic dynamometer. Results indicated that systemic isotretinoin did not significantly alter muscle strength, fatigue, and endurance.

Cutis. 2015;96:33-36.

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The authors report no conflict of interest.

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Isotretinoin is a vitamin A derivative that frequently is used in the treatment of acne vulgaris.[1,2] Although isotretinoin generally is associated with favorable effects, adverse effects also have been reported.[3-5] Musculoskeletal side effects can include myalgia, sacroiliitis, back pain, diffuse idiopathic skeletal hyperostosis, ligament and tendon calcifications, bone resorption, and reduced collagen synthesis.[6,7] Elevated creatine kinase (CK) levels also have been reported in 15% to 50% of patients with isotretinoin-induced myalgia.[8] However, there are limited data available on the effects of isotretinoin treatment on muscle strength. The objective of this study was to evaluate the impact of isotretinoin on muscle strength, fatigue, and endurance using an isokinetic dynamometer.

Methods

Study Design and Participants—The study followed a pretest-posttest design including 27 patients with acne vulgaris who were treated with oral isotretinoin (age range, 18–40 years) as well as 26 control patients for comparison. Exclusion criteria were renal or liver disease, uncontrolled hypertension, heart failure, malignancy, thyroid and bone disorders (eg, parathyroid disease, osteomalacia), use of drugs that can affect skeletal metabolism (eg, corticosteroids, heparin, anticonvulsants), and history of trauma to and/or surgery of

the lower extremities. All patients were informed of the study procedure and informed consent was obtained. The study protocol was approved by the local ethics committee.

Data Collection—Participant demographics and clinical features (eg, sex, age, body mass index [BMI]) were obtained. Participants in the treatment group received oral isotretinoin 0.5 mg/kg once daily for 1 month, followed by an increased dose of 1 mg/kg once daily for 2 months. Isokinetic measurements of the knee muscles were performed on the nondominant side at baseline and at 3-month follow-up. Reports of muscular side effects were noted during the course of treatment.

Isokinetic Evaluation—A calibrated isokinetic dynamometer was used to conduct isokinetic evaluations. After performing 5 submaximal warm-up contractions, concentric peak torque (PT) values of the quadriceps and hamstrings at 60° and 180° per second angular velocities (AVs), hamstring strength to quadriceps strength ratio (H:Q ratio), and muscle fatigue were evaluated. The isokinetic test protocol included 10 repeats at 60° per second, 15 seconds of rest, and 15 repeats at 180° per second.

Statistical Analysis—Data analysis was conducted using SPSS software version 20.0. Data were expressed as mean (standard deviation [SD]). After checking normal distribution with the Kolmogorov-Smirnov test, independent *t* tests were used to compare the baseline parameters between the treatment and control groups. Paired *t* tests and Wilcoxon signed rank tests were used to compare

Table 1.

Demographic Characteristics and Isokinetic Values of the Treatment Group and Control Group

Characteristic	Treatment Group (n=26)	Control Group (n=26)	*P* Value
Sex, n			
Female	23	23	<.999
Male	3	3	<.999
Mean age (SD), y	20.6 (1.6)	21.3 (1.5)	.149
Mean BMI (SD), kg/m^2	21.8 (2.8)	21.5 (1.8)	.656
Mean concentric quadriceps PT (SD), Nm			
60°/s AV	113.5 (27.9)	119.9 (33.3)	.460
180°/s AV	66.7 (26.6)	64.7 (23.5)	.776
Mean concentric hamstring PT (SD), Nm			
60°/s AV	50.9 (17.1)	46.3 (13.8)	.287
180°/s AV	32.2 (17.2)	28.5 (12.9)	.378
Mean H:Q ratio (SD), %			
60°/s	44.6 (10.9)	40.6 (6.1)	.114
180°/s	49.6 (16.6)	43.9 (10.3)	.147
Mean muscle fatigue (SD)			
Hamstring	22.2 (15.5)	21.6 (10.4)	.876
Quadriceps	24.9 (21.5)	30.3 (14.0)	.284

Abbreviations: SD, standard deviation; BMI, body mass index; PT, peak torque; AV, angular velocity; H:Q, hamstring strength to quadriceps strength.

baseline and posttreatment values where appropriate. The results were for those who completed treatment. Statistical significance was set at $P<.05$.

Results

Twenty-seven participants (24 female; 3 male) with newly diagnosed acne vulgaris were enrolled in the treatment group along with 26 controls (23 female; 3 male). One of the participants in the treatment group did not tolerate isotretinoin due to headache and was excluded from the study. The mean (SD) age of the participants was 20.6 (1.6) years for the treatment group and 21.3 (1.5) years for the control group, and the mean (SD) BMI for both groups was 21.8 (2.8) and 21.5 (1.8), respectively. Participant demographics and isokinetic values at baseline are presented in Table 1. No significant differences between the treatment and control groups for participant sex, age, or BMI were noted ($P>.05$).

Of the 26 participants in the treatment group, 5 reported myalgia and nonspecific back pain. Isokinetic measurements of the treatment group obtained using the dynamometer are shown in Table 2. Although the PT of the hamstring and quadriceps at both 60° and 180° per second AV was decreased at 3-month follow-up, there was no significant difference compared to baseline ($P>.05$). Additionally, no significant difference in H:Q ratio or muscle fatigue was noted ($P>.05$), and no significant difference in isokinetic measurements was seen in participants with myalgia (n=5) at 3-month follow-up versus baseline ($P>.05$).

Comment

This study aimed to investigate the short-term effects of isotretinoin treatment on muscle strength, fatigue, and endurance in patients with acne vulgaris, which has not been widely evaluated in the literature. Although maximal PT of the hamstring and quadriceps in the isotretinoin treatment group was decreased at 3-month follow-up, there was no statistically significant difference in all parameters (ie, PT at 60° and 180° per second, H:Q ratio, muscle fatigue) versus baseline. These findings showed that systemic isotretinoin was not associated with muscle dysfunction in this patient population.

Myalgia, particularly associated with exercise, has been seen in approximately 50% of patients treated with isotretinoin.[6] Furthermore, Goulden et al[9] reported that patients with higher CK levels might be at an increased risk for developing rhabdomyolysis in the setting of isotretinoin treatment. High CK levels indicate serious muscular cell damage and are usually associated with release of

Table 2.

Isokinetic Measurements of Treatment Group at Baseline and 3-Month Follow-up

Measurement	Baseline	3-Month Follow-up	*P* Value
Mean concentric quadriceps PT (SD), Nm			
60°/s AV	113.5 (27.9)	105.1 (31.4)	.057
180°/s AV	66.7 (26.6)	63.1 (24.8)	.344
Mean concentric hamstring PT (SD), Nm			
60°/s AV	50.9 (17.1)	50.6 (17.4)	.933
180°/s AV	32.2 (17.2)	30.8 (13.5)	.629
Mean H:Q ratio (SD), %			
60°/s AV	44.6 (10.9)	48.0 (9.7)	.229
180°/s AV	49.6 (16.6)	48.8 (17.9)	.883
Mean muscle fatigue (SD)			
Hamstring	22.2 (15.5)	30.6 (19.6)	.075
Quadriceps	24.9 (21.5)	26.9 (15.0)	.703

Abbreviations: PT, peak torque; SD, standard deviation; AV, angular velocity; H:Q, hamstring strength to quadriceps strength.

myoglobin from muscular cells.[10] In the current study, 5 participants reported myalgia and nonspecific back pain at 3-month follow-up; however, no participants reported muscle weakness. Differences in the isokinetic measurements of participants with myalgia at baseline and at 3-month follow-up were not statistically significant.

Muscles mainly consist of type I (slow oxidative), type IIA (fast oxidative), and type IIB (fast glycolytic) muscle fibers. Type I fibers produce low force and high endurance, type IIB fibers produce high force and low endurance, and type IIA fibers fall in between the two. At low AVs (eg, 60° per second), only type II fibers contract. As the AV increases (eg, 180° per second), only type II fibers contract. Consequently, the observation of a decrease in the isokinetic test parameters at low or high AVs indicate the decrease in type I or type II contracting muscle fibers.[11,12] In our study, the isokinetic values did not significantly change. As such, we concluded that isotretinoin treatment did not result in the reduction of muscle fibers in our patient population.

The H:Q ratio is the indicator of muscle balance and dynamic stabilization of the knee. It is calculated by dividing the PT of the hamstrings by the PT of the quadriceps in concentric motion.[13] Additionally, muscle fatigue demonstrates the endurance of the contraction of type IIB fibers (anaerobic).[14] In our study, isotretinoin treatment did not impact the H:Q ratio or muscle fatigue.

This study included a few important limitations. The sample size was small, particularly concerning the number of participants who reported myalgia. The lack of laboratory evaluations (eg, creatinine kinase) also was a limitation. Finally, the short study period limited the conclusions that could be drawn from the data.

Conclusion

Results from the current study revealed that systemic isotretinoin treatment did not alter muscle strength, fatigue, or endurance. Further studies taking into account histologic evaluations with larger sample sizes and long-term follow-up are needed.

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