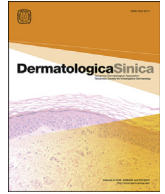




Contents lists available at ScienceDirect

Dermatologica Sinica

journal homepage: <http://www.derm-sinica.com>

## ORIGINAL ARTICLE

## Effects of acitretin on semen quality and reproductive hormone levels in patients with psoriasis vulgaris

Hui Liu\*, Jie Li, Li Yu

Department of Dermatology, 210 Hospital of People's Liberation Army, Dalian 116021, Liaoning, China

## ARTICLE INFO

## Article history:

Received: Aug 5, 2016

Revised: Sep 21, 2016

Accepted: Oct 31, 2016

## Keywords:

acitretin  
erythrocyte  
innate immune  
psoriasis  
semen quality  
sperm

## ABSTRACT

**Background:** The aim of this study was to investigate the effect of different doses of acitretin (ACI) on the main parameters of semen, sperm morphology, and reproductive hormone levels in patients with psoriasis vulgaris.

**Methods:** The main parameters of semen and the sperm morphology of 31 psoriatic patients were analyzed before and after treatment with different doses of ACI, and the changes in reproductive hormone levels were measured and compared with those of 14 healthy control individuals.

**Results:** At treatment doses of 20 mg/d ( $n = 15$ ) and 30 mg/d ( $n = 16$ ) of ACI, the semen volume, sperm motility, viability, concentration, and normal appearance percentage, and the serum reproductive hormone levels in the psoriatic patients showed no significant difference from those in healthy control individuals ( $n = 14$ ) after 1 month and 3 months of treatment, as well as after withdrawing the treatment for 3 months ( $p > 0.05$ ).

**Conclusion:** Different doses of ACI did not significantly affect semen quality in psoriatic patients at different treatment stages.

Copyright © 2016, Taiwanese Dermatological Association.

Published by Elsevier Taiwan LLC. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

## Introduction

Retinoids are a group of compounds that have similar structure and biological activity as vitamin A. Their bioactive isomers include all-trans retinoid and 9-cis retinoid, which regulate cell proliferation and differentiation, thus exhibiting bioactivities such as anti-keratosis, proliferation inhibition, antisebum synthesis, anti-inflammation, and immunomodulation.<sup>1</sup> Their molecular structure is composed of one cyclic group, one polyene side chain, and one terminal polar group. The change in any of the three parts could result in compounds with different bioactivities. Among the three generations of retinoids,<sup>2</sup> acitretin (ACI) is the second-generation derivative, and is suitable for treatment of all types of psoriasis and keratosis. Previously, the treatments of psoriasis with retinoids were mostly focused on severe erythrodermic psoriasis and pustular psoriasis,<sup>3,4</sup> which are types of psoriasis with significant side

effects. Their indications kept on expanding, and low dose long-term treatment protocols were more widely used for psoriasis vulgaris, with satisfactory results and minimal side effects.<sup>5</sup> Currently, it has been established that the major side effects of retinoids mainly manifest in muscle and bone, the central nervous system, liver, blood lipids, skin, and mucous membranes. They have particularly potent teratogenic effects in women and female animals, and women of childbearing age must use contraception during retinoid use and for at least 2 years after the withdrawal of retinoids.<sup>6</sup> The specific effects of retinoids occur mainly in the cardiovascular system, central nervous system, and auditory system, and the occurrence rate could be as high as approximately 30%. The embryotoxicity manifests as a high proportion of stillbirths and miscarriages, and the teratogenicity is still high a long time after withdrawal.<sup>6</sup> Thus, a consensus has been formed by today's medical community that women of childbearing age must strictly use contraception during retinoid use. The combination of sperm and egg, formation of a fertilized egg, and fetal development are all carried out *in utero*, so the effect of maternal factors on fetal development is self-evident. Sperm cells are one of the most active and damage-susceptible cells in humans. The father's sperm quality, especially the sperm concentration, mobility, and morphology, affects the formation and development of the fertilized egg and the

Conflicts of interest: The authors declare that they have no financial or non-financial conflicts of interest related to the subject matter or materials discussed in this article.

\* Corresponding author. Department of Dermatology, 210 Hospital of People's Liberation Army, Dalian 116021, Liaoning, China.

E-mail address: [huiliudoc@126.com](mailto:huiliudoc@126.com) (H. Liu).

<http://dx.doi.org/10.1016/j.dsi.2016.10.005>

1027-8117/Copyright © 2016, Taiwanese Dermatological Association. Published by Elsevier Taiwan LLC. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Please cite this article in press as: Liu H, et al., Effects of acitretin on semen quality and reproductive hormone levels in patients with psoriasis vulgaris, *Dermatologica Sinica* (2016), <http://dx.doi.org/10.1016/j.dsi.2016.10.005>

fetus. It was reported that infertility caused by male factors accounted for about half of the total number of cases of infertility.<sup>7</sup> Thus, we must determine whether the increasingly widespread usage of retinoids influences the reproductive system of male patients. This has not received enough attention for a long time, and the effect of retinoids on the semen quality and genital safety in male psoriatic patients of childbearing age in China and abroad is rarely reported. Reproductive safety-targeted research was firstly done by Parsch et al<sup>8</sup> in 1990, who used a manual method to detect the semen quality changes in five patients after one retinoid treatment (50 mg/d, 3–4 months) and concluded that retinoids had no impact on sperm quality. However, it is concerning that the majority of the literature on the effects of retinoids on male genital safety thereafter cited this report. In recent years, foreign scholars have begun to focus on the issue of retinoids' application toward male genital safety. Because of ethical reasons, direct intervention studies of ACI on the human male reproductive system in psoriatic patients are very difficult. Choosing animal models to obtain teratogenicity data and referring to the results of oral administration of vitamin A and its major metabolites in the volunteers are the new methods being used by certain research institutes to solve this problem; however, the conclusions were different.<sup>9,10</sup> Using *in vitro* tests, Pilkington and Brogden<sup>11</sup> found that high concentrations of ACI could inhibit the fructose decomposition inside sperm, significantly decreasing the contents of lactic acid and CO<sub>2</sub>. Sigg et al<sup>12</sup> conducted a small study on the effect of ACI on eight male patients, and reported no change in sperm concentration. Although it is still unknown whether ACI has residual effects in the semen of male patients taking ACI during or after the treatment, it would not constitute a risk to the fetus. The maximum concentration of ACI observed in human semen after taking ACI or etretinate was 12.5 ng/mL, namely about 125 ng/10 mL in semen. However, there is a warning that women of childbearing age and their spouses must use contraception for at least 3 months before or after taking isotretinoin in its package inserts. Therefore, the aim of this study was to investigate the changes of semen quality in 31 psoriatic patients of childbearing age before and after treatment with different doses of ACI. Parameters analyzed included sperm concentration, motility, viability, and morphology, as well as levels of three serum reproductive hormones: luteinizing hormone (LH), follicle stimulating hormone (FSH), and serum testosterone (T). The aim was to preliminarily explore the reproductive safety issues in male patients using this kind of drug. In this study, the detection of physical indicators and parameters was done using a manual method, and the sperm concentration and motility were analyzed using a computerized automatic semen analysis system.

## Methods

### General information

Thirty-one psoriatic patients were recruited from the in-patient department of our hospital. All were: young soldiers, aged 18–24 years, without any history of contact with radar or nuclear radiation; unmarried with no children; with their primary disease as psoriasis without orchitis, prostatitis, or varicocele; without infectious diseases (such as hepatitis B, hepatitis C, or human immunodeficiency virus); without endocrine or genetic diseases; without familial high incidence of cancer; with a disease duration of 3–48 months; and with a Psoriasis Area and Severity Index (PASI) score of over eight points. All of the patients were in the progressive or stationary phase when semen examination was performed. The 31 patients were randomly divided into two groups according to the doses of ACI. The major parameters of semen [sperm morphology and serum reproductive hormone levels (T,

FSH, and LH)] were observed before the treatment, 1 month after the treatment, 3 months after the treatment, and 3 months after withdrawal. Group A: 15 cases, orally administered 20 mg once a day; Group B: 16 cases, orally administered 30 mg once a day. The PASI score, age, disease duration, and body weight of the two groups showed no statistically significant difference ( $p > 0.05$ ). All of the patients were prohibited from undergoing any treatment during the withdrawal, except for external ointment therapy such as tazarotene or mometasone. The 14 healthy volunteers in the control group were young soldiers recruited from the surrounding area. All were unmarried, without children, healthy, and aged 20–25 years. All of the patients and volunteers were familiar with the study contents and gave informed consent.

### Semen tests

All participants were asked to abstain from sexual activity for 2–7 days before the semen collection. During the sampling, benzalkonium bromide solution and saline were used to swab the urethra and surrounding skin. Then, the semen was obtained in a sterile wide-mouth glass bottle by masturbation so as to avoid contamination and leakage. The semen was liquefied, and the sperm count, motility, and morphological analyses were measured according to the standards described in the Laboratory Manual of WHO human semen and sperm—cervical mucus interactions (fifth edition).<sup>13</sup>

The semen volume was measured, and the color, sticky degree, or liquefaction were observed. The pH was determined using pH test strips after the semen was liquefied. A sperm quality automatic analyzer (SCA 5.2; Microptic, Barcelona, Spain) was used to measure the sperm concentration, viability, and motility.<sup>14</sup>

### Sperm morphology observations

The results of sperm morphology observations were manually counted using the Diff-Quik method.<sup>15</sup>

### Detection of sperm nuclear DNA fragments

Sperm nuclear DNA fragments were detected using flow cytometry (Accuri C6; Becton Dickinson Immunocytometry Systems, San Jose, CA, USA).<sup>16</sup>

### Detection of reproductive hormones by radioimmunoassay

The levels of T, FSH, and LH were detected using the BHP9507 chemiluminescence immunoassay analyzer and kit (Yamasa Shoyu Co., Ltd., Chiba, Japan),<sup>17</sup> with the intrabatch error < 5%.

### Statistical analysis

The comparison between different ACI dose groups, different treatment period groups, and the control group was performed using the *t* test. The measurement data were expressed as  $\bar{x} \pm SD$ , and all the data were processed using SPSS13.0 statistical package (SPSS Company, Chicago, Illinois, USA), with  $\alpha = 0.05$  set as the test level.

### Ethical approval

This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethics Committee of 210 Hospital of People's Liberation Army. Written informed consent was obtained from all participants.

Download English Version:

<https://daneshyari.com/en/article/5645890>

Download Persian Version:

<https://daneshyari.com/article/5645890>

[Daneshyari.com](https://daneshyari.com)