

Treatment of Vulvar Lichen Sclerosis

Subjects: **Dermatology**

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Vulvar lichen sclerosis (VLS) is a chronic inflammatory disease involving the genital skin and mucous membrane.

vulvar lichen sclerosis

VLS

photodynamic therapy

PDT

1. Introduction

Vulvar lichen sclerosis (VLS) is a chronic inflammatory disease involving the genital skin and mucous membrane. The first description of lichen sclerosis lesions became known in 1887 ^[1]. Initially, no uniform terminology existed, with many synonyms being used. Nowadays, the term “vulvar lichen sclerosis” is widely applied ^[2]. VLS is a chronic disease with a pattern of recurrent lesions. Patients exhibit focal atrophy, destructive scarring, and associated functional impairment, with an increased risk of malignant transformation ^[3]. Worth mentioning, lichen sclerosis may also interest other body areas, and the genital area of the opposite sex ^[4].

The worldwide prevalence of lichen sclerosis ranges from 0.1% to 1.67% ^[5]. Of note, the exact prevalence of VLS has not been established and is probably underestimated, particularly in young women ^[6]. Several papers report a bimodal onset of disease, that is, in prepubertal children and postmenopausal women ^{[2][7]}. However, recent studies suggest that VLS may also affect some other age groups ^[5]. In terms of incidence, elderly women predominate (3%), while lichen sclerosis affects about 0.07% of men ^{[8][9]}. The ratio of men to women varies between 1:3 and 1:10, and only rarely is an equal split observed ^[9]. Approximately 0.3% of children are estimated to be involved ^[10]. The etiology of VLS remains unknown, but several mechanisms have been investigated ^[11]. Studies suggest a multifactorial origin of the etiology, such as autoimmune mechanisms, genetic predisposition, association with viral diseases, trauma, chronic irritation, and endocrine disorders ^{[3][12]}.

In the early stages of VLS, well-demarcated, thin, glistening, ivory-white areas are seen, usually located in the labia minora, vaginal introitus, and fork. Tenderness and fragility, characteristic features of VLS, lead to the development of erosions, fissures, purpura, and petechiae. Fissures are particularly common between the clitoris and urethra, in the interlabial sulci, and at the base of the posterior fourchette. In addition, these lesions often occur during sexual intercourse or aggressive physical examination. With time, late complications resulting from the development of atrophic changes and scarring may appear. Mucocutaneous lesions are accompanied by itching, which is particularly severe at night and therefore worsens the quality of sleep, as well as intense pain, dyspareunia, or even apareunia, and impeded urinary flow. Furthermore, when the perianal area is involved, which occurs in about one-third of women, problems with defecation may occur ^{[2][8][11][13]}. Of concern is the association between VLS and subsequent vulvar squamous cell carcinoma (SCC). In their systematic review, Spekreijse et al. reported that

the absolute risk of developing SCC in women with VLS varied between 0.21% and 3.88%. Contributing factors to this risk included age, presence of vulvar intraepithelial neoplasia, long medical history of VLS, delayed diagnosis of VLS, and only partial compliance in terms of use of the topical treatment [14].

According to the guidelines published, the diagnosis of VLS is based on clinical and histopathologic features. In addition, it is necessary to exclude several other disorders [9][15]. Noteworthy is the possibility of employing dermoscopy as a non-invasive diagnostic method [16][17].

2. Discussion

Currently, PDT has many applications in the treatment of a variety of skin disorders, mainly non-melanoma skin cancers [18]. Of note, this method in dermatology was used by Kennedy et al. for the first time [19]. The mechanism of PDT is based on the interaction of three elements: photosensitizer, the light of the appropriate wavelength, and oxygen. The purpose of this interaction is the production of cytotoxic reactive oxygen species that selectively destroy damaged tissue while leaving normal skin intact [19]. However, the exact mechanism of action of PDT in the treatment of VLS remains uncertain. It is thought to primarily target skin sclerosis as PDT has been shown to induce apoptosis of lymphocytes and keratinocytes and to alter the expression of both cytokines and metalloproteinases that play a role in skin remodeling [20]. However, Olejek et al. described the effect of PDT on the immune status of patients after the procedures, that is, a significant reduction in antinuclear antibody titers, which places PDT as a method with immuno-modulatory potential [21]. Moreover, Maździarz et al. presented the efficacy of PDT in concomitant infection with high-risk HPV types, which establishes PDT as a prophylactic method in cancer development [22]. According to Zielińska et al., treatment of VLS in the absence or confirmed presence of HPV infection is equally effective [23].

The first-line treatment for VLS is topical corticosteroids. When used chronically, these agents possess numerous side effects [24]. Moreover, the risk of VLS recurrence after their use is very high [25]. Noteworthy are the results of a single open-label study comparing ALA-PDT and the application of clobetasol propionate 0.05% ointment by 43 patients with VLS [26]. PDT treatments were performed four times every 2 weeks, and clobetasol was applied once daily for 8 weeks. It was found that clinical symptoms and subjective complaints improved in both groups. However, it was ALA-PDT that led to a higher clinical response rate and a longer remission period [26].

Biniszkiwicz et al. stated that PDT, because of its excellent cosmetic effect, lack of complications in the form of scarring, or changes in the structure and function of the treated tissues, should be performed as a therapy preceding more invasive procedures [27]. In view of the above and the lack of effect on reproductive capacity, PDT stands as a method also for the treatment of young women of childbearing potential [28]. PDT is considered an affordable method [27]. In addition, thanks to the possibility of using a form of a patch containing photosensitizer, it becomes an outpatient procedure, which is convenient and timesaving for patients [29].

Undoubtedly, VLS significantly affects the mental and physical health of female patients. Not only is the architecture and morphology of the vulva altered, but a wide range of subjective complaints are also experienced.

The effectiveness of PDT in remission of symptoms of the disease, improvement of sexual life, and mood disorders allows making patients' quality of life better. Based on the literature review, PDT for VLS apparently represents a promising therapeutic modality. In all of the papers, there was an improvement, reflected in the resolution of subjective and/or objective symptoms. Although some of the publications did not demonstrate the clinical efficacy of PDT in the treatment of VLS, none of them reported lesion exacerbation. However, a significant limitation in terms of assessing the efficacy of PDT was the paucity of controlled studies.

The histopathological findings considered demand a careful approach. The reported lack of improvement indicates the need for continued follow-up of patients for progression of lesions to malignancy. Of note, VLS, as an intractable dermatosis in some cases, will not change histologically. However, the reported evidence of apoptosis indicates the therapeutic effect of PDT [\[29\]](#).

In all reported cases, PDT was performed as the next step, not as first-line treatment. This emphasizes the role of PDT to be a therapeutic option for refractory lesions to the previous treatments. It may also be safely repeated a number of times as it is not associated with the development of resistance [\[30\]](#). However, in order to reduce the number of procedures, to shorten the treatment period, and to avoid the side effects that accompany the interventions, it is worth considering the addition of a holmium laser treatment [\[31\]](#).

There was certainly a notable heterogeneity in the publications in regard to the photosensitizing substance and its retention length on the skin, the treatment parameters, their number, and the time intervals between them. In addition, the studies used different indices to assess clinical improvement. In our opinion, dermoscopy deserves special attention, which, as a non-invasive, available, and inexpensive method, allowed the evaluation of the therapeutic response at early stages [\[32\]](#). In contrast, concordance was seen for the study cohort, which consisted of peri-menopausal women.

Interestingly, Declercq et al. recently reported a PDT protocol for VLS on the basis of a systematic review of the literature [\[33\]](#). Patients should urinate before the procedure; then, the vulva is to be washed with 0.9% NaCl. The photosensitizer, 5% ALA, has to be applied under the occlusion with a margin of 1 cm. The incubation period is supposed to be 3 h, and red light of 590–760 nm, at a dose of 120 J/cm², and an intensity of 204 mW/cm² should be used for irradiation. In addition, the authors suggested the practice of blue light photodiagnostics and xylocaine or water spray alleviate side effects during the procedure [\[33\]](#).

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