

# Hidradenitis Suppurativa and Zinc: A New Therapeutic Approach

## A Pilot Study

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### Key Words

Hidradenitis suppurativa · Verneuil's disease · Zinc salts

### Abstract

**Background:** Hidradenitis suppurativa (Verneuil's disease) is a chronic suppurative dermatosis involving apocrine glands with a severe impact on the quality of life, which is enhanced by the fact that the drugs usually prescribed are poorly effective. **Objective:** We discuss a new therapeutic approach based on zinc salts. **Methods:** We performed a pilot study on 22 patients, mainly from grade I or II in Hurley's classification. All included patients had previously been prescribed a treatment (antibiotic, isotretinoin, surgery or anti-androgens), which was inefficient. They were then treated with 90 mg of zinc gluconate per day (15 mg zinc per Rubozinc<sup>®</sup> capsule). **Results:** We observed a clinical response in all patients, with 8 complete remissions (CR) and 14 partial remissions (PR). When CR was obtained, the treatment was progressively decreased (average of 3.5 capsules/day); 4/22 patients experienced side-effects, mainly gastro-intestinal. **Conclusion:** Zinc salts could provide a new therapeutic alternative for the treatment of hidradenitis suppurativa.

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### Introduction

Verneuil's disease, also called hidradenitis suppurativa or acne inversa, is a chronic, suppurative dermatosis. Its prevalence is estimated to be between 0.3 and 4% in industrialized countries [1]. The disease starts during youth and affects more frequently women (sex ratio about 4), with localizations restricted to apocrine gland areas. The aetiology is obscure, but suggested contributory factors include a genetic predisposition, comedones occluding the pilosebaceous apparatus, bacterial infections and hormonal factors [2]. A pre-existent hidradenitis may be worsened by obesity and localized irritations (deodorants, depilation, shaving), due to a mechanical phenomenon, occlusion and maceration. Lithium and smoking are recognized as worsening factors of the disease [3]. Recurrence of the disease is common, as the inflammatory and suppurative process spreads. Remission periods alternate with exacerbation. There is no standard treatment for hidradenitis suppurativa, and the therapeutic control of the disease remains difficult. Several molecules have been proposed as a treatment – local antiseptics and antibiotics, long-term antibiotherapy (doxycycline, minocycline), isotretinoin, oral oestrogenic contra-

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ception or anti-androgen (cyproterone acetate) – but results are often disappointing. Systemic corticoids are sometimes used as short-term treatment during an acute phase, for highly inflammatory and thus painful forms. Many molecules were tested in anecdotic reports, but their efficiency has still to be demonstrated (dapsons, acitretin, cyclosporin, methotrexate, infliximab). The main purpose of minor surgery (e.g. incision, limited resection, curettage, drainage) is to eliminate the pain associated with the disease and is often followed by relapses. Nevertheless, surgery remains, for many authors, the reference for acute and relapsing forms, resistant to medical treatments; it is the only treatment enabling a permanent response. However, the outcome is not always satisfying. In the present work, we discuss a new therapeutic approach based on zinc salts. Zinc is a trace element essential to human life, which plays a role in numerous metabolic pathways, in the immune system and in hormonal regulations, but which also acts as a membrane stabilizer.

## Methods

We performed a pilot study, including 22 consecutive patients suffering from hidradenitis suppurativa. Hurley's clinical staging was used for the classification of patients: stage I consists of abscess formation, single or multiple without sinus tracts and cicatrization; stage II consists of 1 or more widely separated recurrent abscesses, with tract formation and scars; stage III has multiple interconnected tracts and abscesses throughout an entire area. In this study, 11 patients were in Hurley's grade I, 10 in grade II and 1 in grade III. All included patients had previously been prescribed a treatment (systemic antibiotic, isotretinoin, surgery or anti-androgens), which was inefficient. Therapeutic responses ranged from complete remission (CR), defined by disappearance of cutaneous lesions or no new lesions during 6 months or more, to partial remission (PR), defined as a reduction of 50% or more of the number of nodules and/or a shorter cycle of each inflammatory lesion. No decrease or an increase in the number of nodules was defined as a non-response. Patients were treated with 90 mg of zinc gluconate (Rubozinc®) [4] per day. The initial treatment consisted of 6 zinc gluconate capsules per day (15 mg zinc per Rubozinc capsule). When CR and PR were maintained for 4 months, zinc gluconate was decreased by 15 mg every 2 months.

## Results

A total of 15 women and 7 men were included in the study (the sex ratio was 2.14 females for 1 male). The mean age of these 22 patients was 38.3 years (range 18–71 years). The mean age at the onset of the lesions was 24.6

years (14–51 years), and the mean duration between the beginning of illness and the diagnosis was 6.5 years (4 months to 17 years). One patient had presented a family history of hidradenitis suppurativa. The average follow-up was 23.7 months (4–120). All patients had previously been prescribed treatments which appeared to be inefficient: 18/22 patients had received long-term antibiotherapy ( $\geq 3$  months) with cyclins – 9 improved but relapsed when cyclins were stopped; 6/22 had been treated by isotretinoin without improvement; 3/7 women had received cyproterone acetate without improvement. All patients had been treated by local antiseptics during a few months, without improvement. Five patients presented a single localization (4 females, 1 male) whereas the 17 others had several sites involved (11 females, 6 males). Lesions (opened or closed inflammatory nodules) were inguinal in 16 cases (10 females, 6 males), axillary in 12 (10 females, 2 males), on the buttocks in 8 (4 females, 4 males), the pubis in 5 (3 females, 2 males), the interbuttock fold in 4 (2 females, 2 males) and the breast in 3 (2 females, 1 male). The average dosage (decrease in doses after PR or CR) was 3.5 Rubozinc capsules per day. Among included patients, 8/22 (36%) experienced a CR. For those patients, a reduction of the treatment was tested, but relapses occurred when reaching 2–4 capsules/day. Recurrences disappeared when the dose of zinc salts was increased. Thus, this treatment appears to be suppressive rather than curative. PR were observed in 14/22 (63.6%) patients. None of the patients experienced deterioration of their hidradenitis suppurativa during the treatment. The average dose of zinc salts avoiding relapse after PR or CR (maintenance dose) was lower in patients with Hurley's grade I (2.9 capsules daily) than in patients with grade II (4.6 capsules daily). No correlation between the efficiency and the number of lesions was observed, nor according to the duration of the disease. Three patients presented adverse events: 1 patient presented diarrhoea, 1 suffered from abdominal distension, 1 from oesophagitis. One patient presented nausea and vomiting; the treatment had to be stopped.

## Discussion

Until now, there has been no report about zinc efficiency in hidradenitis suppurativa. We observed 8/22 CR. But most of the patients were affected by a moderate form of the disease (Hurley grade I). The delay in the diagnosis of hidradenitis suppurativa is important (6.5 years) explained by the lack of knowledge of this disease. The

treatment was well tolerated: 4 patients experienced side-effects, mainly gastro-intestinal; only 1 patient had to stop the treatment because of nausea and vomiting. The zinc gluconate dosage was higher than the one usually used in other cutaneous affections. Zinc salts have been used for a long time in the treatment of mild and moderate acne, and the usual dosage is between 30 and 60 mg of zinc metal per day (corresponding to 2 capsules of 15 mg zinc gluconate per day in France) [5, 6]. Clinical studies have shown a significant effect of zinc salts, mainly on inflammatory lesions (superficial and deep lesions). With such doses, side-effects are minor and consist of gastro-intestinal disturbances such as nausea, vomiting or epigastric pain. These effects are often transient and rarely require a treatment stop. Compared to isotretinoin and cyclins, side-effects of zinc salts are minor, which is important in the context of a chronic disease.

The activity of zinc in Verneuil's disease could be related to the anti-inflammatory activity of zinc salts, which may act on different steps of the cutaneous inflammatory reaction. Indeed, zinc inhibits the chemotaxis of polynuclear neutrophils, which has been demonstrated in vitro and in vivo in acne patients treated by zinc salts at the dosage of 2 capsules of 15 mg/day for 2 months [7]. Zinc activates natural killer cells and the phagocytotic function of granulocytes [8]. Zinc inhibits the expression of integ-

rins expressed by the keratinocytes in inflammatory diseases such as ICAM-1 and LFA-3 [9], which play an important role in the interactions between keratinocytes and lymphocytes. Zinc also modulates the production of 2 major pro-inflammatory cytokines by keratinocytes such as TNF- $\alpha$  and IL-6 [10]. In addition, it has an antioxidant activity by inducing the expression of the enzyme Zn-Cu superoxide dismutase which is present both in keratinocytes and fibroblasts. Thus, it increases the elimination of free radicals. Moreover, zinc is a cofactor for thymuline, a hormone playing a role in T lymphocyte maturation. At the extracellular matrix level, zinc also plays a role in the regulation of metalloproteinases. Another mechanism for zinc action could be its 'anti-androgen' [11] activity which modulates 5 $\alpha$ -reductase type I and II expression and activity (especially type I in vitro).

## Conclusion

Zinc salts could provide a new therapeutic alternative for the treatment of hidradenitis suppurativa, even if it seems to have a more suspensive than curative activity. Furthermore zinc salts are well tolerated, which is crucial in the context of a chronic disease strongly affecting quality of life.

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