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REVIEW ARTICLE

Hidradenitis Suppurativa in Children and Adolescents: A Review of Treatment Options

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Abstract Hidradenitis suppurativa (HS) is a burdensome disease and has the potential to affect the life course of patients. It is a rare disease in children, and the recorded literature is correspondingly scarce. This article reviews the therapeutic options for HS in children and adolescents, and highlights particular differences or challenges with treating patients in this age group compared with adults. The work-up of paediatric patients with HS should include considerations of possible endocrine co-morbidities and obesity. Medical therapy of lesions may include topical clindamycin. Systemic therapy may include analgesics, clindamycin and rifampicin, finasteride, corticosteroids or tumour necrosis factor alpha (TNFα) blockers. Superinfections should be appropriately treated. Scarring lesions generally require surgery.

Key Points

No therapeutic trials have been published in paediatric hidradenitis suppurativa, and treatment recommendations are based on case reports and extrapolation of therapies tested in adult patients.

Topical treatment (clindamycin 10 mg/mL lotion twice daily for 3 months) is recommended for patients with mild or moderate disease.

Systemic therapy requires appropriate paediatric dosing. Options include oral antibiotics (clindamycin and rifampicin), antiandrogens (finasteride), and immunosuppressants (TNFα blockers).

1 Introduction

Hidradenitis suppurativa (HS) is defined by its history and clinical presentation. It is a chronic, inflammatory, recurring, debilitating skin disease of the hair follicles that usually presents after puberty with painful, deep-seated, inflamed lesions in the apocrine gland-bearing areas of the body, most commonly the axillae, inguinal and anogenital regions (Dessau definition, First International Conference on Hidradenitis Suppurativa/Acne Inversa, March 30–April 1, 2006, Dessau, Germany) [1, 2]. The diagnosis is based on the history of the disease (recurrent), the topography (axillae, inguinal and anogenital regions) and the clinical presentation (painful deep-seated, inflamed lesions), often supplemented by scars into a recognisable presentation.

The usual age at onset is in the third decade of life, but on rare occasions it may occur as a pre-pubertal disease,

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and in the adult population the prevalence rates have been reported to range between 0.05 and 4 %, depending on the population and on how the data were gathered [3–11]. Generally, low prevalence rates are found in the US and in registry studies from, for example, insurance databases, whereas higher prevalence rates have been reported from Europe and studies depending on questionnaires or physical examination. However, using any methodology, reliable data on the prevalence of HS in the paediatric population are not available. It has been estimated that less than 2 % of HS cases debut before the age of 11 years, but 36 % of HS cases debut between the ages of 11 and 20 years [12].

As a consequence, evidence-based therapeutic recommendations are equally scarce. It may furthermore be speculated that the available literature is highly biased towards either more severe cases or unusual cases with publication potential [12–18]. This impression is reinforced by the published paediatric cases, which appear to display both a strong genetic predisposition as well as endocrine abnormalities that are rarely seen in the adult population.

HS in the paediatric population is of particular importance. For obvious reasons, HS can have a significant impact on patients' quality of life (QoL) [19–22]. Pain is an important symptom, and the frequent para-genital location of lesions undoubtedly contributes to the stigma of the disease [21, 23]. Little is known about the specific impact in children, but it is hypothesised that the importance of para-genital symptoms may be accentuated in puberty, where even more limited symptoms such as depigmentation may cause significant distress [24]. The possible long-term psychological risks have not been described in detail, but anxiety and depression are known to be common among adult patients [22], suggesting that the disease may have a profound effect on the life course of paediatric patients.

2 Therapeutic Options

Only a few specific randomised controlled trials of HS in adults are available. In the paediatric population, the best level of evidence appears to be small case series and expert opinion, although extrapolations of adult treatment recommendations appear to be reasonable, taking into account the general principles of paediatric medicine.

HS is a complex disease to treat and because of the often significant impact of the disease, direct patient involvement is strongly recommended [21].

2.1 Adjuvant Therapy

There is mounting evidence that weight loss may offer clinically significant relief of HS in obese adult patients [25–34]. Studies generally describe that HS patients have a higher average body mass index (BMI) [35, 36], and in the morbidly obese the prevalence appears to be approximately ten times higher than in the general population [30]. Disease severity as scored by the Sartorius score is influenced by BMI, and retrospective studies suggest that weight loss exceeding 15 % of BMI has a beneficial effect [30, 37].

Provided that paediatric HS patients are obese, weight loss should therefore be generally recommended, as it may also reduce some of the significant co-morbidity seen in HS patients.

Co-morbidities such as diabetes mellitus also appear associated with HS in a significant proportion of patients [38], and should be properly diagnosed in children in order to prevent later complications.

There is no evidence in the adult population of any beneficial effect of disinfectants such as chlorhexidine washes, nor does talcum or deodorant appear to play any significant role.

A large proportion of patients, however, have important clinical need for analgesic treatment. One study found a significant proportion of adult patients requiring opioids to cope with HS-related pain [36], suggesting a need to alleviate pain in children as well. No data exists for the paediatric population but pain should be treated using the usual pain management regimens for paediatrics. It should be noted that EMLA (lidocaine/prilocaine) cream is not recommended in HS because of the barrier deficiency, and the risk of methemoglobinaemia [39].

2.2 Topical Treatment

A small randomised controlled trial (RCT) of topical clindamycin lotion 10 mg/mL has been conducted in stage I or mild stage II HS [40]. Patients aged 18–59 years were treated with topical clindamycin 10 mg/mL lotion or placebo, and evaluated monthly for overall effect. Abscesses and nodules were counted, and patients' global assessment was noted.

A beneficial effect was described, and patients' assessments significantly favoured clindamycin ($p < 0.01$). Lesion counts indicated a significant effect on folliculitis, papules and pustules at 2 and 3 months, but only a very limited effect on deeper lesions such as nodules and abscesses [40].

Topical clindamycin is commonly used for the treatment of acne vulgaris even in children, and although formal studies of paediatric toxicity do not appear to have been carried out, systemic absorption appears negligible.

Topical clindamycin 10 mg/mL twice daily applied for 3 months therefore appears to be a possible therapy for milder cases of paediatric HS.

Topical resorcinol, while effective in adults in concentrations of 15 %, [41] is not advisable for use in children.

Several cases of resorcinol poisoning have led to the death of infants and young children, even in low concentrations [42].

2.3 Systemic Treatment

Systemic medical treatment is suitable for disease that cannot be adequately managed by topical treatment alone. Suitable medical treatment includes systemic antibiotics, although planktonic bacteria are rarely found In HS.

2.3.1 Antibiotics

The role of bacteria in HS is under discussion. Many different bacteria have been isolated from lesions, but most often routine swabs fail to identify pathogens even in fulminant lesions. Specific studies of bacteria in HS lesions have predominantly identified normal flora [43–45]. Current consensus therefore suggests it is not a classical infectious disease, but that bacteria play a role either in biofilms or as triggers of an inappropriate immune response.

In adults, there is an RCT comparing topical clindamycin 10 mg/mL twice daily with systemic tetracycline 500 mg twice daily; both treatments achieved a similar response rate of about 30 % (physician global assessment) and, while the study was not powered for equipotence, no significant difference between the two treatments was seen [46]. Systemic tetracycline is, however, not suitable for treatment before the age of 10 years [47], due to the risk of discolouration of the permanent teeth. It is speculated that the mechanism of action utilised when treating HS with tetracycline is not the bacteriostatic effect, but more likely the non-antibiotic effects of the drug, which may include immunomodulation and tissue breakdown [48–50].

In adults, several case series involving a total of 187 [51–54] patients have described the beneficial effect of combination therapy using clindamycin and rifampicin systemically. Although no RCT has been conducted, the results of the published case series are very consistent and support the use of the combination. None of the published series include any paediatric patients, but both drugs are used in children to treat other infections, suggesting that this may be a viable approach to paediatric HS as well. It is speculated that the underlying therapeutic mechanism may again be directed against the inflammatory response, or possibly in the case of rifampicin against bacteria anchored in a biofilm [55–57].

It should be remembered that superinfection may occur with *Staphylococcus aureus,* causing acute suppurating flares and positive cultures. In these cases, specific anti-staphylococcal therapy is indicated.

2.3.2 Endocrine

Much speculation has been provided over the possible endocrine influence on HS as suggested by the female preponderance (3:1 female:male ratio) [1]. Although cases of HS associated with premature adrenarche in children and the use of oral contraceptives have been linked to the onset of HS [12, 58–65], more systematic reviews of the endocrine status of women with HS have proved inconclusive. An early trial suggested that the efficacy of oestrogen-based oral contraceptives was similar to that of combined oestrogen and cyproterone acetate [62].

Early-onset HS may occur in the absence of endocrine abnormalities or androgen excess in prepubertal children, but it is advisable to perform an endocrinological examination of sex hormones in children presenting with HS [12, 59] (see Table 1).

Cases implying the efficacy of finasteride in paediatric patients have been published, suggesting that antiandrogen therapy may be useful in recalcitrant cases irrespective of hormone levels [16].

2.3.3 Immunosuppressants

Immunosuppression is also a viable strategy in the treatment of HS. Paediatric data are lacking, but in other contexts, such as psoriasis or arthritis, children are treated over longer periods with immunosuppressants, suggesting that extrapolation of adult treatment regimens is possible.

Looking at the adult literature, RCTs are available to suggest the beneficial effect of tumour necrosis factor-alpha (TNFα) antibodies in the treatment of HS. Two RCTs describe the use of adalimumab in adult patients with HS. In 2011, Miller et al. [66] published the results of an initial investigator-initiated RCT studying the effects of

Table 1 Endocrine work-up for premature adrenarche

Physical examination
Tanner stage
Imaging
Bone age
Endocrine workup
Androstenedione (nmol/L)
Dehydroepiandrosterone sulphate (μmol/L)
Testosterone (nmol/L)
Sex-hormone-binding globulin (nmol/L)
Free androgen index
Luteinising hormone day 4
Follicle-stimulating hormone day 4 (IU/L)
Oestradiol day 4 (pmol/L)
17-Hydroxyprogesterone

adalimumab in a standard adult dosage (21 patients, loading dose 80 mg, thereafter 40 mg every other week [eow] vs placebo) in a simple double-blinded randomised controlled two-arm design for 3 months, followed by a 3-month period without any treatment. While the study failed to achieve the primary endpoint of a significant reduction of disease severity, as described by the Sartorius score after 3 months of treatment, this was reached after 6 weeks of treatment, and the secondary goal of significant improvement of QoL was achieved. Recurrence during follow-up corroborated a beneficial effect of the treatment as a suppressive therapy. Subsequently, a larger three-arm RCT was conducted (154 patients, loading dose 160 mg, 80 mg week 1, thereafter 40 mg every week vs loading dose 80 mg, thereafter 40 mg eow vs placebo). The primary end-point (physician's global assessment score of clear, minimal or mild with at least a 2-grade improvement relative to baseline score, at week 16) was achieved in 17.6 % of patients in the every-week treatment group. Secondary endpoints of improved QoL were also met in the every-week treatment group [36].

Earlier, Grant et al. [67] published an RCT of infliximab (33 patients, infliximab 5 mg/kg at week 0, 2 and 8 vs placebo). Although the study failed its predefined primary goal, it showed that significantly more patients in the active group had a 25–50 % reduction in the HS Severity Index score, along with significant positive effects on QoL, visual analogue scale (VAS) score, erythrocyte sedimentation rate, and C-reactive protein.

These RCTs were conducted on the basis of numerous previous case series suggesting a beneficial effect. In aggregate, they suggest that TNFα antibodies may be indicated in the treatment of HS. Again, no specific paediatric data are available and whilst these drugs have been used in children, age-specific modifications of the treatment regimens should be done as appropriate.

An RCT of TNFα blockage using the fusion protein etanercept failed to show superior effect compared with placebo, in spite of numerous earlier case reports describing beneficial outcomes of the treatment [68].

In our experience, flares of the disease can be treated over the short term with oral corticosteroids.

2.3.4 Retinoids

Isotretinoin has been proven ineffective in managing HS in adults. In a retrospective study by Boer and van Gemert, 11 of 68 (16.2 %) patients achieved a maintained clearing of lesions during a mean follow-up of 46 weeks [69]. In a study by Soria et al. [70], 88 adult patients treated with isotretinoin reported that 14 (16.1 %) experienced an improvement while 67 (77.0 %) experienced no change and six patients (6.9 %) experienced a worsening of the condition. These studies suggest that isotretinoin is an ineffective treatment for HS.

Acitretin may be more effective but has only been examined in small studies. Matusiak et al. [71] found that 8 of 17 (47 %) adult patients reported more than 50 % reduction in the HS severity index (HSSI). This study, however, was an open-label study with a 47 % dropout rate due to lack of effect and/or intolerable adverse effects.

In a carefully documented long-term follow-up study of 12 adult patients receiving acitretin for HS by Boer and Nazary [72], all 12 patients experienced remission and a decrease in the maximum pain of nodules and abscesses on a VAS scale. In this study, half of the patients would not undergo a second treatment with acitretin due to adverse effects.

Retinoids are, however, unlikely to be used as a first-line therapy in paediatric HS. While the efficacy of acitretin is promising, the rate of adverse effects is high. Indeed, the potential for closure of the epiphysis due to long-term treatment with any retinoid [73] should prompt physicians to explore other avenues of treatment before trying retinoids. If acitretin is chosen, it is important to remember the teratogenic effect of the drug and its metabolites for the older paediatric population as women should be advised to avoid pregnancy for up to 3 years after discontinuation of the drug [74].

2.4 Surgery

Whenever significant scarring has occurred in HS, surgery is the only potentially curative option left. Numerous surgical techniques have been described for the treatment of HS, ranging from the minimally invasive 'de-roofing' to extensive excisions radically removing all HS-prone skin [1, 75–77]. CO_2 laser therapy is also an option with low recurrence rates [78–81], and it is considered safe for use in a paediatric population [82]. Lancing is only possible if a soft and fluctuating abscess is present, which is uncommon. Incision and drainage (attempts) of painful nodules and inflamed sinus tracts should, as a rule, be avoided as it is generally not effective and only adds to the scarring process.

In a paediatric population, the threshold for surgery may differ from that in adults. Even minor procedures such as de-roofing require local anaesthesia, and while much can be achieved by preceding intradermal injections with topical anaesthetics, using thin gauge needles, slow injection, distraction and local anaesthetic without added adrenaline, children often do not take well to local anaesthesia.

The general surgical principles of HS treatment are that excisions need to be radical, and it has been suggested that open healing may be of benefit to the cure rates. If direct closure is used, an RCT indicates that the use of gentamycin sponges in the surgical wounds may be of benefit to the

recurrence rates [83]. Therefore, if children with HS are in need of surgery, this may be a prudent precaution, provided the paediatric dosing regimens of gentamycin are considered.

2.5 Miscellaneous Therapies

In adults, a range of drugs have been used to treat HS, including dapsone, cyclosporine, metformin and zinc, among others [84–87]. Data are not available for children and evidence is often limited to small open case series, limiting the strength of the evidence.

A single case suggests that injections with botulinum toxin may have alleviated HS for 6 months in a 7-year-old girl [14]. However, the role of botulinum toxin is not yet defined in the treatment of HS, and evidence is limited to a few cases [14, 88, 89]. The underlying mechanism is not well defined, and awaits independent confirmation. Application appears possible using topical anaesthetics and nitrous oxide sedation.

For the cooperative child with pubic or axillary hair, light-based epilation may also be a possible, safe therapy. Trials have described the benefits of neodymium-doped yttrium aluminium garnet (Nd:YAG) lasers as well as intense pulsed light therapy in adults [90–92]. Obviously, paediatric HS patients in Tanner stage I are unlikely to benefit from a hair-directed therapy.

3 Conclusion

HS is a troublesome disease for most patients. Early recognition and treatment is therefore of the utmost importance in the paediatric population, in order to minimise the life-course effects of this disease.

HS is a rare and poorly described disease in children. Reliable data on prevalence and incidence are not available. No therapeutic trials have been published in paediatric HS, and any treatment recommendations are therefore based on case reports and extrapolation of therapies tested in adult patients. This review has therefore focused on the treatments with the best evidence. Other treatments taken from the range of adult treatments tried and described may be relevant. See Table 2 for recommendations.

Paediatric patients with HS should be examined for possible endocrine co-morbidities (premature adrenarche or diabetes). If they are obese they should receive help and encouragement to achieve weight loss, and any pain should be treated. Medical therapy of lesions may be topical (clindamycin 10 mg/mL lotion twice daily for 3 months) or systemic. Systemic therapy requires appropriate paediatric dosing but may include antibiotics (clindamycin and rifampicin), antiandrogens (finasteride), immunosuppressants (corticosteroids, TNFα blockers). Patients may experience superinfections, which need to be identified and appropriately treated with antistaphylococcal drugs systemically.

For scarred lesions, surgery may be necessary. The scope of surgery is dependent on the patient's ability to cooperate but may include de-roofing and excisions. Incision and drainage is generally not recommended.

Table 2 Medical therapy suggested for paediatric cases of hidradenitis suppurativa

First line
Topical clindamycin
Second line
Add: oral rifampicin and clindamycin
Add: finasteride
Third line
TNFα inhibitors
Corticosteroids

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