Is Intense pulsed light (IPL) an effective adjunctive therapy in Hidradenitis suppurativa – a retrospective study?

Är Intense pulsed light (IPL) en effektiv adjunktiv behandling vid Hidradenitis suppurativa – en retrospektiv studie?

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Abstract

Hidradenitis suppurativa (HS) is a chronic and recurrent inflammatory disease of the skin containing apocrine glands. It presents with nodules, painful abscesses, sometimes with purulent discharge, scar formation and fibrosis depending of the severity and stage. The most common sites affected are the apocrine-bearing areas such as the axillae and groin. Little is known about the pathogenesis of HS and the exact cause is widely debated. Follicular hyperkeratosis giving rise to follicular occlusion has been speculated to be the initial event. There is need for a wider array of treatment options since the condition is chronic and hard-to-treat in its nature. In this retrospective study we examined whether Intense pulsed light, IPL is an effective adjunctive treatment.

47 patients from the years of 2001-2012 that have been treated with IPL or CO2 were finally included in the study. The Sartorius score was measured at baseline, 24.7. After a mean of 3.53 treatments (median = 3) the Sartorius score was 5.64 points lower (CI 95%: -7.27;-4.00) Unfortunately, no significant lowering of the score was seen per treatment session and therefore it is impossible to draw any certain conclusions that the IPL or CO2-treatments caused the improvement.

One cannot draw any certain conclusion from this study, a larger study population or a different study design is needed. The need for future research regarding the efficacy of IPL is still huge given the fact that only one study in the subject has been published so far. It should desirable to offer the patients suffering from the disease a wider array of noninvasive treatment options and decreasing the use of antibiotics.

Populärvetenskaplig sammanfattning

Hidradenitis suppurativa (HS) är en kronisk och återkommande hudsjukdom som påverkar hudytor där apokrina körtlar återfinns. Den presenterar sig med alltifrån rodnad, bölder med varierande storlek, illaluktande varbildning till kraftig ärrbildning. De vanligaste lokalisationerna är armhålor, under brösten, ljumskar och kring genitalia.

Sjukdomen drabbar både män och kvinnor, där risken är tre gånger större att drabbas som kvinna, vanligtvis i åldern 15-45 år. Orsaken till sjukdomen är i stora drag fortfarande omdebatterad och okänd, men idag tror man att en tilltäppning av hårfollikeln som en följd av hyperkeratos är det första steget i sjukdomsutvecklingen. Man har även identifierat vissa riskfaktorer som både korrelerar med risken för insjuknande och svårighetsgrad. Dessa är exempelvis rökning, kvinnligt kön och övervikt.

Idag finns det en bred behandlingsarsenal mot HS såsom kirurgi, antibiotika, steroider och tömning av bölderna. Trots detta är sjukdomen fortfarande svårbehandlad och den orsakar patienterna ett stort lidande, både fysiskt och psykiskt. Nya behandlingsmetoder är önskvärt främst ur två aspekter. Dels för att eventuellt förbättra situationen för patienterna, men det är även önskvärt att kunna minska antibiotikaanvändningen och kirurgiska ingrepp hos dessa.

I denna studien undersöktes det om Intense Pulse light (IPL) är en effektiv tilläggsbehandling vid HS. IPL är en ljuskälla som strålas mot huden och kan, beroende på inställning, orsaka olika fysiologiska mekanismer. I den här studien användes IPL för hårborttagning, ärrförbättring och för att behandla aktiva bölder.

Studien var retrospektiv i sitt slag och totalt 47 patienter inkluderades. Dessa hade alla besökt Hudkliniken på SUS Malmö under åren 2002-2010 och blivit behandlade med IPL mot sin HS. Sjukdomens svårighetsgrad mättes med hjälp av Sartoriussystemet. Innan start av IPL-behandling låg den genomsnittliga poängen på 24.7, efter i genomsnitt 3.53 (median = 3) behandlingar hade patienternas poäng sjunkit med 5.64 poäng till 19.06. Denna minskning var statistiskt signifikant.

Däremot för att avgöra om minskningen berodde på ljusbehandlingen, och inte på andra faktorer så undersöktes det vidare hur förändringen i poäng/svårighetsgrad var per behandlingstillfälle. Här kunde man inte påvisa någon signifikant minskning från tillfälle till tillfälle.

Alltså kan man inte dra några säkra slutsatser från den här studien. Det är möjligt att IPL hjälper men vi fick det inte bekräftat. Fler studier med mer avancerad studiedesign och mer information från patientjournalerna behövs för att kunna få den styrka i undersökningen som önskas.

Introduction

Hidradenitis suppurativa (HS) is a chronic and recurrent inflammatory disease of the skin containing apocrine glands. It presents with nodules, painful abscesses, sometimes with purulent discharge, scar formation and fibrosis depending of the severity and stage. The most common sites affected are the apocrine-bearing areas such as the axillae and groin. Other common sites affected are the sub-mammary and infra-mammary folds, buttocks, and perianal and perineal areas. The inguino-femoral site is the most common area involved both among men and women. The buttocks and perianal area are more common sites among men compared with women, while patients with mammary involvement are more likely among women. However, the patients can have multiple lesions at multiple sites varying over time.[1]

Classification and pathogenesis

Little is known about the pathogenesis of HS and the exact cause is widely debated. Follicular hyperkeratosis giving rise to follicular occlusion has been speculated to be the initial event. This can lead to secondary apocrine stasis and follicular rupturing leading to inflammation and subsequent infection.[2] The events leading to the characteristic scaring formation is speculated to be exacerbated by the sinus tracts formed during the course of disease.[3] The fact that the lesions often are symmetrical distributed supports the idea that it is a systemic disease rather than local. [1]

Table 1. Description of the Hurley stages

Hurley stages	
Stage	**Definition**
I	Abscess formation without sinus tracts and cicatrization
II	Recurrent abscesses with tract formation and cicatrization.
III	Diffuse involvement or interconnected tracts and abscesses across the entire anatomical region.

The disease can clinically be characterized into three stages depending on the severity, also called Hurley stages (I-III). See table 1. At Hurley stage I, there are acute primary lesions, often deep-seated nodules that can progress to abscesses. The primary nodules often resolve spontaneously with a mean duration of 7 days, while abscesses often

require surgical intervention. [4] In stage II, sinus tracts and fibrosis are ultimately formed in some patients. The underlying mechanisms are the chronicity and recurrence of the condition where nodules and abscesses are formed at the same sites multiple times. At this second stage, the affected skin is often colonized by gram-negative bacterias causing a foul odor and social stigmatizing. Finally, the third Hurley stage is described by the characteristics of stage I and II plus hypertrophic scar formation. These scar formations can both be very painful for the patient and obstruct movement, i.e. arm abduction in cases with severe axillary scar formation. According to an epidemiological study by Canoui-Poitrine *et al*, about two thirds of the patients are classified as Hurley stage I and 3.9 percent were in stage III. [1]

Another system for staging HS, called the Sartorius staging system (see textbox 1), has been developed by Sartorius and colleagues.[5] This staging system is more sophisticated than Hurley's and is therefore more suitable for clinical trials. The points are accumulated to provide both a local and global score, where a higher score means more severe disease. Sartorius has been shown to have a low interobserver variability.[6]

Textbox 1. Sartorius score.

1 Anatomical region involved. 3 points per region.

2 Number of lesions. Points per lesion. Fistulas 4 points. Nodules 2 points. Scars and others 1 point.

3 The longest distance between two lesions in each region. 0-5 cm, 2 points. 5-10 cm, 4 points. > 10 cm, 8 points.

4 Are all lesions separated by normal skin? In each region, yes 0 points/no 6 points.

Epidemiology

HS is a disease with a one-year prevalence of 1%, and it is more common among women with a female-male ratio of 3.3:1. [1] The onset is typical insidious in the second or third decade of life, prepubertal onset is rare because of the fact that the apocrine glands normally aren't active until puberty.[7] Because of the appearance of the disease, it is often misdiagnosed and common differential diagnoses are carbuncles, common abscesses and cysts, such as epidermoid cysts.

Risk factors and comorbidity

Studies have shown a strong correlation between smoking, obesity, family history of HS and incidence of HS. There is also a correlation between a higher body mass index (BMI) and the severity of the disease. Furthermore, smoking patients experience a more severe course of the disease than non-smoking patients.[8] The exact etiological mechanisms behind these findings remain unclear. Lately, recent studies has proposed an involvement of the tumour-

necrosis-factor α (TNF-α) and earlier investigations have reported associations with Crohn's disease. This has led to the idea that HS is an immunological disorder to some extent.[9] [10] It is debated whether there are some hormonal influences on the pathogenesis. There is a female overrepresentation and an association with oral contraceptive use has been reported but studies have failed to show direct biological evidence for the hypothesis.[11] [12]

For the individuals suffering from HS, the condition has a considerable impact on the quality of life. A study of a Polish population from Matusiak et al. showed that HS had no effect at all on quality of life in only 1.9 percent of the patients with active HS, while 59.2 % of the study population expressed "very large" or "extremely large" effect on everyday life. At the same time, the disease caused absence from work among 58.1 % of the patients.[13] Another study showed that HS has a larger impact on life than for example alopecia or moderate psoriasis.[14]

Treatment

The treatment of HS varies depending on stage and severity and there are no existing guidelines today and much of the chosen treatments are based on clinical experience.[15] Overall, treatment is usually not successful and has a high level of dissatisfaction. Among patients in the first Hurley stage, topical antibiotic has shown to be effective with the addition of oral antibiotic in more severe cases. Another choice of therapy that is widely used by dermatologists is the injection of glucocorticoids in nodules. Furthermore, anti-androgens and isoretinoin are also often used as therapy, but isoretinoin has failed to show efficacy in studies.[16] The idea that HS is partly or fully an immunological disorder has led to case reports and small population studies studying the effect of immunosuppressive agents such as interleukin-pathways-inhibitors with varying results.[17] [18] In more severe cases the condition often requires surgery, such as incision of abscesses, localized excision and sometimes even skin transplantation.

Recently, the use of laser and radiation therapy has been adopted for treatment in HS even though the research still is limited. For example, Lapins et al showed that only 12% of the patients treated with carbon dioxide laser developed new lesions at the treated site with a mean follow-up 34.5 months.[19] Highton et al suggests in a study with 18 participants that intensed pulsed light (IPL) might be effective against HS, showing significant improvement in

the treated areas.[20] Furthermore, a study from Strauss et al. showed no improvement in treating four patients with photodynamic therapy.[21]

IPL-devices emit a polychromatic high-frequency pulsed light as opposite to laser devices that emits a monochromatic light. The wavelength, pulse duration and frequency can be determined which gives the opportunity to be very selective regarding thermal damage comparing to lasers. The conditions treated with IPL vary from hair removal, skin rejuvenation, vascular lesions, acne vulgaris, and pigmented lesions while it also shows anti-bacterial effects.[22] Our hypothesis is that depilation with IPL can be a relief for patients with HS because of the follicular and apocrine origin, together with the possible anti-bacterial effects. Based on all this, we aim to examine whether IPL is an effective adjunctive therapy for patients with HS and can reduce the use of surgery, antibiotic use, CO2-surgery and improve the quality of life in the patients.

Material and methods

IPL has been used as an adjunctive therapy in the treatment of HS at the Skåne University Hospital in Malmö, Sweden. In this retrospective study we investigated the medical records of all patients admitted to the Dermatology department with confirmed HS between the years 2001-2012, a total of 286 patients (226 females, 60 males). The diagnoses were confirmed by the treating physicians based on clinical presentation and recorded in the medical records. All participating patients gave their consent that their medical records could be used for research purposes in the future. The exclusion criteria were one, or no treatment with IPL or lack of photographs with decent quality in the medical records making it impossible to score the patient. A total of 47 patients were finally included in the study. 31 of the patients were treated with IPL, 16 patients were treated with both IPL and CO2-laser. Scores were given according to the Sartorius staging system based on high resolution photographs, in some cases with the additional information given by the text records. In cases were not all affected areas were treated with IPL, a local score for the regions treated were calculated. Reasons for not treating areas with IPL were for example; patients that didn't shaved the affected regions or their desires not to be treated. Other variables such as smoking status, number of years with the condition, overweight, earlier local and system therapies used were also obtained from the records.

Results

The mean age of the study population was 34.4 years (median 31.0 years) and the self-proclaimed mean duration of the condition was 10.1 years. All the characteristics are described in table 2. The most common sites affected were the axillae, affecting 62% of the patients, and the groins affecting 53 % of the patients. The frequency of HS in different localisations is shown in table 3. The energy used in the IPL treatments were 3.5-21.5 Joule with pulse duration of 2-55 milliseconds.

Table 2. The characteristics of the study population (n = 47)

Characteristics	Frequency	Percent
Age (years)		
-Mean	34.4	
-Median	31.0	
Gender (n)		
-Female	38	80.9
-Male	9	19.1
Years with the disease (mean)	10.1	
Overweight (n)		
-Yes	20	42.6
-No	2	4.3
-N/A	25	53.1
Smoking status (n)		
-Current or former smoker	13	27.6
-Never	2	4.3
-N/A	32	68.1
Earlier local treatment (n)		
-Surgery	12	25.5
-N/A	35	74.5
Earlier systemic treatment (n)		
-Antibiotics	33	70.2
-Roaccutan	2	4.3
-N/A	12	25.5

Table 3. The frequency of HS in different anatomical regions among the study population (n = 47)

Anatomical region	Frequency (%)
Axillae	29 (61.7)
Groin	25 (53.2)
Breasts	6 (12.8)
Gluteal	2 (4.3)
Abdominal	1 (2.1)
Genitals	11 (23.4)

The patients received 1-10 treatments, mean IPL-treatments = 3.04, mean CO2-treatments = 0.49, median = 3 treatments. The mean Sartorius baseline score was 24.7. Using Wilcoxon's

signed rank test, the Sartorius score was 5.64 points lower after the treatments, (CI 95% -7.27;-4.00). Furthermore, linear regression was used to estimate the change in Sartorius score per IPL-treatment and per CO2-treatment, one session of IPL changed the Sartorius score – 0.28 points (CI 95% -1.05;0.49) and one session of CO2 changed the Sartorius score – 1.19 points (CI 95% -2.84-0.47).

Discussion

The patients had a lower Sartorius score after the course of treatment, but no significant effects of the single treatment occasions were seen among the patients, therefore it is impossible to conclude that the IPL or CO2-treatment caused the improvement seen in the patients. This does not mean that IPL or CO2 are useless against HS but one cannot draw any certain conclusions from this material. One possible explanation is that the patients are more likely to be photographed after clear improvement of the condition or that the cyclical nature of the disease caused the differences in Sartorius score. This means that maybe the Sartorius score obtained are biased. Therefore, an analysis calculating the differences in the score per treatment were a much more reliable tool for investigating whether the improvement was caused by the IPL or CO2-treatments. Unfortunately, this numbers were not significant. Another aspect of this is that the documentation procedure of the records should be improved. This is especially of great importance when newer and non-evaluated treatments are used.

The female-male-ratio among the original 286 patients was 3.77-to-1 which correlates well to earlier epidemiological studies.[1] There are some limitations to this study. Due to its retrospective nature, one cannot avoid a large number of patients falling off as a consequence of inadequate information in the records such as lack of detailed photographs and inadequate written information. Still, it is difficult to obtain a large study population prospectively when a rare disease is about to be investigated. The result of this is a less than desired study population. On other hand, the only published study so far that has investigated IPL as a treatment for HS only conducted 18 patients as compared with 47 in this study.[20] Unfortunately, another consequence of running retrospective studies based on medical records is the lack of information regarding different outcomes. The only possible

outcome variable in these cases was the Sartorius score. One weakness is that the lack of sufficient number of photographs. A possible bias occurs when photographs are taken arbitrarily and when, during the course, different physicians choose to document the condition. It would have been desirable to test for other variables such as patient satisfactory, the amount of antibiotics used by the patients before and after and the need of future surgery for example. Nevertheless, the Sartorius score has shown to correlate well with disease burden such as pain intensity, numbers of days with pain and suppuration. [1] Given the fact that there were a large number of patients that could not be scored according to the Sartorius score, this study design might have been too ambitious. If the Hurley stage classification were used instead, more patients would have been included and therefore the power of the study would have been increased.

It should be noted that all the patients included in this study received concomitant treatment during the course of the IPL treatments, mostly well-established regimes such as steroids (such as azelic acid cream), hydro peroxide cream and systemic antibiotics a few weeks after the CO2-treatment, therefore IPL was tested as an adjunctive therapy or as option to surgery. On the other hand, it should be mentioned that a very large amount of these patients have received these treatments before with little or no effect. Over the last years, most patients have not needed antibiotics after and in conjunction with CO2- and IPL-treatments. Based on this, the results neither support our rejects our hypothesis that IPL is an effective adjunctive therapy for the patients. A larger study population or a different study design is required. Other variables that can possibly change the course of the disease are smoking and overweight. As mentioned before, these variables are associated with the severity of the disease and it is possible that weight reduction or smoking cessation in some patients has been left out in the records affecting the outcomes, even though most patients were recommended to lose weight and stop smoking, but very few succeeded or even tried to follow this recommendations.

Why IPL?

Compared to other treatment options, IPL offer a wide range of advantages. First of all, it is noninvasive and relatively safe for the patients with a low frequency of therapy sequelae and discomfort. Furthermore, the hair removal causes the patients to stop their shaving, which we know is not good for their HS. IPL also open up closed HS in the submamillary

folds, an area that is hard-to-treat- with CO2-laser. The most common side effects are hypo- or hyperpigmentation, erythema, pain, blistering, atrophy and scarring. Of the 45 patients included in this study, none of them voluntarily discontinued IPL-treatment because of side effects. Depending on the indication and IPL settings, the rate of side effects and discomfort varies. A study by Moreno-Arias et al. investigated the incidence of side effects after 3-9 treatments, comparable to our study, and found that erythema was only seen in 6.1% of the patients after 72 hours, and only 2% experienced transient hyperpigmentation that lasted more than 16 weeks. In the same study, pain was described as mild among 87.8% of the patients.[23] Furthermore, Troilius et al. presented an efficient method in a study of 10 patients treated for hair removal with IPL with no discomfort or pain in none of the patients. This is the very same method that has widely been used among our study population.[24] Another positive aspect of IPL treatment is that it is easily manageable and patients can be treated by trained nurses, which is economically advantageous compared to surgery and CO2-laser. Some patients are keen to avoid surgery for different reasons. Depending on localization, surgical scars can cause great discomfort and surgery increases the risk of infection and recovery time needed. With the use of IPL, this is most often avoided. IPL also have the ability to soften the conglomerates of scarred tissue, reducing the pain and tension produced by these scars.

The exact molecular mechanism behind the possible improvement seen in the patients remains unknown. Therefore, future biological studies investigating the exact mechanisms are required. However, earlier studies have shown that IPL used in skin rejuvenation, alters the gene expression in different genes responsible for the inflammatory response[25]. Most of the patients in this study received IPL treatment both with acne- and hair removal-settings. This means that there were subject to both hair removal and acne treatment. One possible mechanism is that the removal of the hair opens up the follicular occlusion, which is the first step of the disease, and aids draining thus preventing abscess formation. At the same time, the acne settings used facilitates the healing of already formed abscesses. Furthermore, one can speculate whether the hair itself acts as a foreign body, facilitating the inflammatory response.

Future treatments

Based on the possible molecular mechanism and etiology, several other treatment options that have been investigated recently is the used of immunosuppressive agents. The results so far are inconclusive. Gulliver et al. reported in a short report that the use of ustekinumab, an interleukin 12/23 pathway-inhibitor, is a potential therapeutic option in some patients.[26] Another case report by Sharon et al. have shown promising results in a patient, with little or no respond to antibiotics, treated with infliximab, thus blocking TNF-a.[27]

Conclusion

HS is a hard-to-treat condition with several treatment options. Despite this, some patients fail to respond to the given therapy options. A wider array of potential options is therefore desirable. Our hope was to examine if IPL could be an effective adjunctive treatment that lowered the Sartorius score and disease burden. In other words, increasing the quality of life, decreasing the use of antibiotics and the need of traditional surgery such as excisions, incisions and skin transplantation. The argument for this is that the Sartorius score correlates well with the severity and need for these interventions. Unfortunately, no conclusions can be draw from this study. A longer and more detailed and structural follow-up procedure is required but it was practically difficult given the relatively small number of participants and limited follow-up time.

Figures

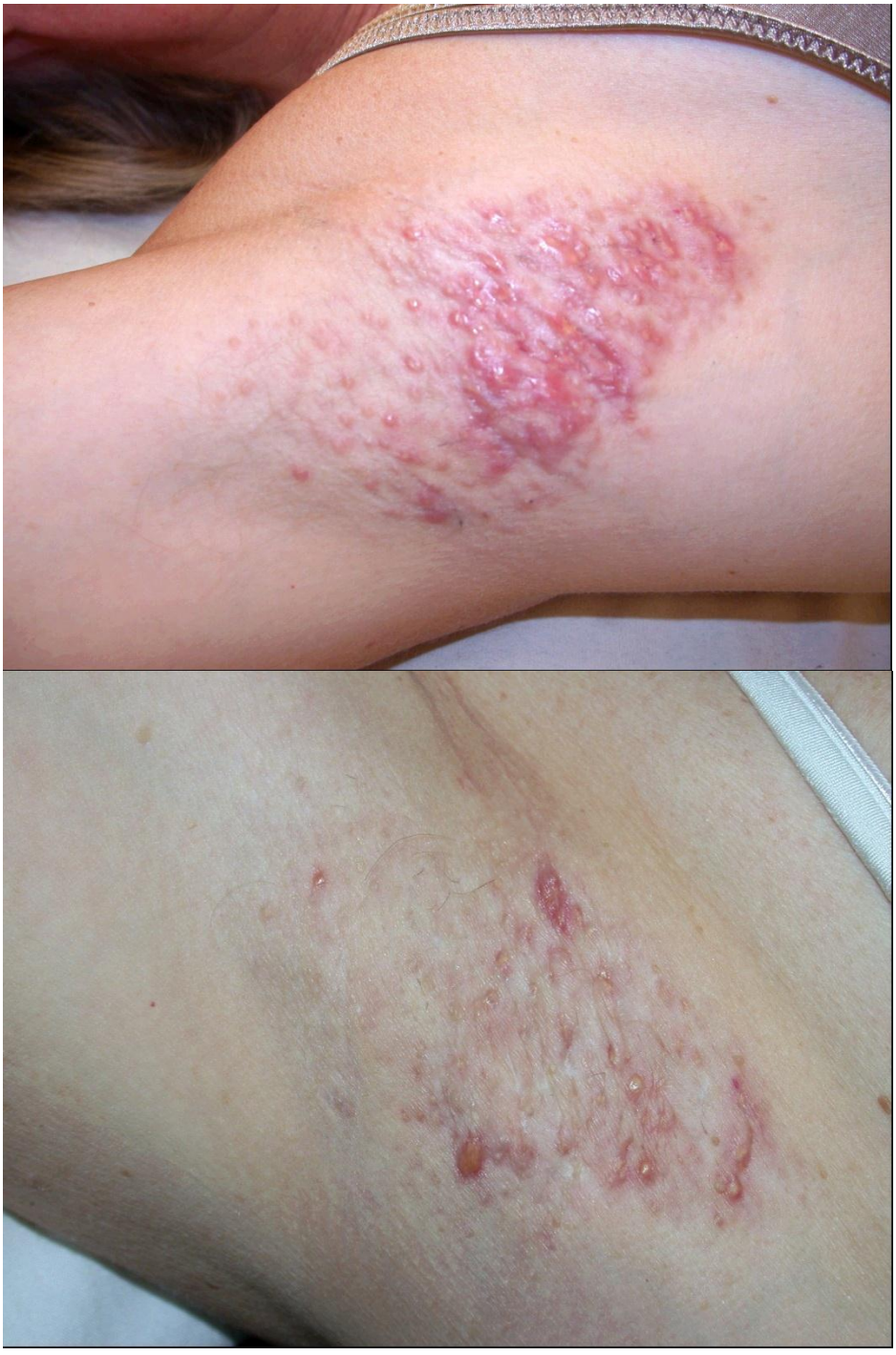

Figure 1. The appearance of HS in a 45-year old woman before and after three treatments with IPL.

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