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CLINICAL REPORT

Bacteriology of Hidradenitis Suppurativa – Which Antibiotics are the Treatment of Choice?

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The bacterial superinfection in hidradenitis suppurativa (HS), although it does not initiate the disease itself, seems to be one of the major contributors to an inflammatory vicious circle. Antibiotic therapy is therefore commonly prescribed in HS. This study was undertaken to evaluate the prescription of systemic antibiotics in the light of bacteriological cultures and antibiograms. The study was conducted on a group of 69 patients with HS. The huge majority ($n = 62$) of the patients were treated with antibiotics. The antibiotics were prescribed 132 times and taken for a mean period of 9.9 ± 8.9 weeks. The most commonly used antibiotic was doxycycline (16.7%). The majority of the patients had a polymicrobial flora with up to 5 species, predominantly staphylococci and bacteria of intestinal flora. The highest effectiveness against isolates was observed for carbapanems, penicillins with β-lactamase inhibitors and fluoroquinolones – 8.5%, 11.9%, and 11.9% of resistant strains, respectively. In daily practice penicillins with β-lactamase inhibitors or fluoroquinolones could serve as first-line therapy of HS.
Key words: hidradenitis suppurativa; acne inversa; antibiotics; bacteria; treatment.

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Hidradenitis suppurativa (HS) is a recurrent, debilitating suppurative skin disease manifested by abscesses, fistulas and scarring with involvement of intertriginous regions. It is a common disease with an estimated prevalence of 1% and a female predominance (1). The aetiology is still not clear, but several factors seem to play a role such as genetics, smoking and obesity (2, 3). Recent findings have specified that the pathomechanism of HS is linked to follicular occlusion in combination with hyperkeratinisation, resulting in follicular dilatation and perifollicular inflammation, with bacterial infection as a secondary event (4, 5). The bacterial superinfection probably triggers a cascade of pathogen-associated molecular patterns (PAMPs), which leads to stimulation of inflammasomes. This stimulation promotes the maturation of potent pro-inflammatory cytokines (e.g. IL-1β) and induces further abundant cytokine dose-dependent migration of phagocytic cells, leading finally to cell pyroptosis, a highly inflammatory form of cell death resulting in excessive pus and scarring (6, 7). Therefore, bacterial involvement seems to be one of the major contributors responsible for the inflammatory vicious circle observed in HS.

The huge majority of therapeutic algorithms recommend antibiotics as a first line therapy in all severity stages of HS (8–10). However, the selection of antibacterial treatment seems to be done mainly accordingly to personal experience or even preference of the treating physician or popularity of given drug on the selected market in the selected timeframe, rather than with respect to literature data on microbiological cultures or effectiveness of antibiotics treatment, which are still scarce (11–14).

Therefore, our study was undertaken to evaluate the "trends" among dermatologists in prescribing systemic antibiotics in the light of bacteriological cultures and antibiograms.

PATIENTS AND METHODS

The study was conducted on a group of 69 HS patients (38 women, 31 men) aged 15–65 years (mean ± SD age 39.2 ± 11.89 years). The diagnosis of HS was made according to well-established clinical criteria (15). The disease duration was assessed as from 1.5 to 36 years (mean ± SD 10.06 ± 7.54 years). The clinical extent of disease severity was based on the 3-degree scale established by Hurley (Table I) (15). Among our subjects 17 patients (24.6%) were diagnosed as exhibiting first-degree disease severity, 37 subjects (53.6%) fulfilled the criteria for second-degree HS and 15 (21.8%) third-degree HS. The body mass index ranged from 19.49 to 52.03 kg/m^2 (mean ± SD 28.83 ± 5.96 kg/m^2), which qualified our patients as overweight or even obese. Active or ex-smoker rate was of 75.4% (pack-years: 3–72).

The patients' medical data were analysed to determine what kind of Pharmacological treatment (antibiotics) was prescribed and taken. If the same drug/antibiotic was for instance taken twice by the same subject, it was regarded as only once (Table I).

Bacteriological sampling

For specimen collection, the site was first scrubbed and disinfected with Skinsept® Pur (Ecolab sp. z o.o, Cracow, Poland). Specimens were obtained from the abscesses during surgical treatment or from fistulas after pressure of skin lesions. The pus was collected by a sterile swab that was dipped in the pus and transferred to transport medium AMIES (code 300287, Deltalab S.L., Rubí, Spain), and then inoculated within 1–2 h of

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Table I. *Patient characteristics and prior therapies*

Variable	Value
Gender (female/male), *n*	38/31
Age, years, mean ± SD (range)	39.2 ± 11.89 (15–65)
Age at HS onset, years, mean ± SD (range)	29.22 ± 10.48 (13–58)
HS duration, years mean ± SD (range)	10.06 ± 7.54 (1.5–36)
Hurley stage (I/II/III), *n*	17/37/15
BMI, kg/cm^2, mean ± SD (range)	28.83 ± 5.96 (19.49–52.03)
Smoker (yes[a]/no), *n*	52/17 (pack years, 3–72)
Pharmacological treatment (yes/no), *n*	68/1
Antibiotics, *n*	62
Retinoids, *n*	26
Antiandrogens, *n*	7
Oral glucocorticoids, *n*	4
Autologous vaccine, *n*	3
UV-light therapy, *n*	2
Inosine pranobex, *n*	2
Sulfones (dapsone), *n*	2
Zinc gluconate, *n*	1
X-ray therapy, *n*	1
Topical treatment, *n*	67

[a]including former smokers.

collection. Swabs from the surface of the skin were not allowed and excluded from further analysis.

Microbiological procedures

The specimens were processed according to standard microbiological procedures. The plates were incubated under aerobic and anaerobic conditions. After incubation, all types of colonies were counted, and then isolated into distinct cultures. All isolates were identified according to colony morphology, Gram reaction, and biochemical tests. Antibiograms were done for all collections with regard to the cultured strains (except for one sterile swab). For instance, if methicillin-resistant *Staphylococcus aureus* (MRSA) was isolated, disks with β-lactams were not applied. The same situation was for *Enterococcus faecalis* HLAR, which are resistant to high concentrations of aminoglycosides, etc (16, 17). The results for vancomycin and linezolid were not taken into account, as these antibiotics are reserved for the treatment of recalcitrant infections, and should not be used routinely.

Statistical analysis

Statistical analysis was performed using the Student's *t*-test or Pearson's chi-squared test, where applicable. Descriptive statistics were applied to the majority of all analysed variables. $p < 0.05$ was considered statistically significant.

RESULTS

The Pharmacological treatment was applied to the 68 patients. One patient was treated only surgically. The huge majority of the patients, 62 subjects, were treated with antibiotics, which constitutes approximately 90% of all patients treated conventionally. The second and third most frequently used treatments were retinoids and antiandrogens – 38.2% and 10.3%, respectively (see Table I).

The antibiotics were prescribed 132 times and taken for a mean period of 9.86 ± 8.91 weeks, which makes almost 2 antibiotics for each of the treated subject. The most common antibiotic was doxycycline (16.7%) followed by amoxycyllin with clavulanic acid (11.4%), clindamycin (7.6%), tetracycline (7.6%) and ciprofloxacin (7.6%). The rest of antimicrobials are listed in Table II.

The bacterial sampling was performed in 28 out of the 68 patients and antibiograms were conducted among 27 HS subjects (as one sterile swab was collected), which constitute 39.7% of all the patients. The majority of the patients had more than one isolate – mean ± SD 2.1 ± 1.4 per collection (range 1–5 isolates). Among these patients, the most common cultured pathogen was Gram positive coccal bacterium *S. epidermidis* (22.0%), – a component of the normal flora of the skin. Other common cultures were the following: *Proteus mirabilis* (13.6%), *S. aureus* (13.6%), and *Enterococcus faecalis* (11.9%). The remaining microorganisms together with their frequencies are listed in Table III. No significant difference between the distribution of particular bacterial strains was observed with regard to the place of sampling. However, *S. aureus* was more frequently isolated from the axilla (6 vs. 2; $p = 0.12$) and bacteria of the human intestinal flora (incl. *Escherichia coli*, *Klebsiella* sp., *Proteus mirabilis*, *Enterococcus faecalis*, *Pantoea agglomerans*) were slightly more commonly isolated from the perianal region (12 vs. 8; $p = 0.58$).

The isolated strains in our study were mainly resistant to monobactams (74.6%), tetracyclines (64.4%), macrolides (57.6%), trimethoprim/sulfamethoxazole (54.2%), and lincosamides (50.8%). Therefore, the use of all antibiotics listed above was commonly ineffective in eradication of given microbes. The highest effectiveness against isolates was observed for carbapanems,

Table II. *The list of antimicrobials used in the treatment of studied population with hidradenitis suppurativa*

Antibiotic	Used, *n* (%)
Doxycycline	22 (16.67)
Amoxicillin + clavulanic acid	15 (11.36)
Ciprofloxacin	10 (7.58)
Clindamycin	10 (7.58)
Tetracycline	10 (7.58)
Gentamicin	9 (6.82)
Metronidazole	9 (6.82)
Co-trimoxazole	8 (6.06)
Lincomycin	7 (5.30)
Cefuroxime	7 (5.30)
Azithromycin	4 (3.03)
Lymecycline	3 (2.27)
Clarithromycin	3 (2.27)
Ampicillin	2 (1.52)
Amoxicillin	2 (1.52)
Spiramycin	2 (1.52)
Ceftriaxone	2 (1.52)
Erythromycin	1 (0.76)
Cefaclor	1 (0.76)
Roxithromycin	1 (0.76)
Oxacillin	1 (0.76)
Pefloxacin	1 (0.76)
Vancomycin	1 (0.76)
Rifampicin	1 (0.76)
Total	132 (100.00)

Table III. *Bacteria isolated from 28 hidradenitis suppurativa patients with regard of number of isolates, their frequency and localisation*

Species	Isolates, *n* (%)	Axilla/Perineum[a]
Staphylococcus epidermidis	13 (22.03)	5/8
Proteus mirabilis	8 (13.56)	4/4
Staphylococcus aureus	8 (13.56)	6/2
Enterococcus faecalis	7 (11.86)	4/3
Escherichia coli	3 (5.08)	0/3
Streptococcus agalactiae	3 (5.08)	2/1
Streptococcus group C	3 (5.08)	1/2
Acinetobacter baumannii	2 (3.39)	0/2
Corynebacterium sp.	2 (3.39)	2/0
Propionibacterium acnes	2 (3.39)	1/1
Streptococcus bovis	2 (3.39)	2/0
Pseudomonas aeruginosa	1 (1.69)	0/1
Klebsiella sp.	1 (1.69)	0/1
Finegoldia magna	1 (1.69)	0/1
Streptococcus constellatus	1 (1.69)	0/1
Staphylococcus lugdunensis	1 (1.69)	0/1
Pantoea agglomerans	1 (1.69)	0/1
Total	59 (100.00)	27/32

[a]Groins, anus and buttocks.

penicillins with β-lactamase inhibitors and fluoroquinolones – 8.5%, 11.9%, and 11.9% of resistant strains, respectively. The rest of the evaluated antibiotics together with resistance rate were as follow: semisyntetic penicillins (22%), cephalosporins (I–IV) (40.7–28.8%) and aminoglycosides (40.7%).

DISCUSSION

The results of our study highlight the variety of bacteria isolated from patients with HS lesions. All but one patient was found to have positive cultures, which is in concordance with previous study by Sartorius et al. (18). Our findings show that the bacterial cultures were positive for various microorganisms and the majority of the patients had a polymicrobial flora with up to 5 species, thus confirming data from other studies (18–20). As in previous studies (18, 19, 21), the high numbers of coagulase-negative staphylococci (CNS) were isolated in HS patients (almost every fourth subject). This raises the question whether these isolates indeed play a pathogenic role in the development of chronic inflammation or whether they are just bystanders. Answering this query, it should be highlighted, that most CNS infections have a slow, subacute evolution – resembling the course of HS inflammation (18, 22).

In concordance with the studies of majority of other authors (19–21), *S. aureus* was the second most common isolate obtained. Moreover, patients with *S. aureus* strains were found to have a shorter duration of the disease (mean 6.8 vs. 15.8 years; $p = 0.03$), which is in agreement with the findings of Jemec et al. (21). Previously it was suggested that *S. aureus* may play a role in the pathogenesis of HS (especially in the early phases of this disease), causing anatomical changes in the hair follicles units by inflammation and necrosis (21). Moreover, such high prevalence of *S. aureus* may be linked to the smoking, as nicotine favours the growth and colonisation of this pathogen (23). Consequently, HS patients are, like smokers in general, heavily colonised with this pathogen (noteworthy, all of our subjects with *S.aureus* isolates were indeed heavy smokers).

The second largest group of bacteria in addition to staphylococcal species were strains of the intestinal flora, including *E. coli*, *Klebsiella* sp., *P. mirabilis*, *E. faecalis*, *P. agglomerans*, which were isolated (20 isolates [33.9%]) slightly more often from perineum. Such frequent occurrence of abovelisted strains was not previously observed by other researchers. On the other hand, the number of anaerobic strains was of slightly lower percentage (18–20).

With regard to our findings and the literature data (24), bacteria seem to play an important role in the development of HS. The majority of review articles, or consensuses point out the antibiotics as first-line therapy, although rarely specify when (active/maintenance treatment) or which one to use (9). The literature data regarding usage of antibiotics in the treatment of HS are limited. To the best of our knowledge, there is only one small randomised controlled trial comparing topical clindamycin 0.1% with tetracycline (46 patients) (13), 4 studies on combination of rifampicin with clindamycin encompassing 187 patients (11, 12, 25, 26) and one on rifampin-moxifloxacin-metronidazole combination (28 patients) (14). Therefore, in most cases (if at all), it is recently recommended to either use a combination of rifampicin with clindamycin, or tetracyclines (as an alternative) (8).

In the light of our findings, both clindamycin and tetracyclin do not appear to be especially effective for the elimination of the cultured pathogens. The percentage of resistant pathogens to lincosamides and tetracyclines was of significant relevance – 50.8% and 64.4%, repectively. Therefore, it is likely that in a combination of rifampicin with clindamycin, the former antibiotics (particularly effective in inhibiting the growth of staphylococci) plays the pivotal role in the treatment. Clindamycin can however be recommended because of its activity against anaerobics, which, although present in minority in our material, seem to play an important role in the development of the disease (18–20).

With regard to our results, tetracyclines seem to be almost completely useless, especially in exacerbated disease. However, this group of drugs may play a role in the long-term therapy, because of their anti-inflammatory properties (27).

In our opinion, it seems reasonable to consider to use wide spectrum antibiotic, i.e. penicillin + β-lactamase inhibitor (e.g. amoxicillin + clavulanic acid) or fluoroquinolones as an initial therapy of HS as it had only 11.9% resistant isolates. Noteworthy, majority of the most commonly prescribed antimicrobials (i.e. tetracy-

clines and lincosamides – see Table II) were ineffective against cultured isolates.

To summarise, bacterial infection undoubtedly plays an important role in HS. This superinfection has a number of unique features, including absence of lymph node involvement and chronicity (24, 28). A polymicrobial flora is involved, which consists mainly of 3 groups: staphylococci (*S. aureus* among patients with disease of shorter duration and CNS), bacteria of intestinal flora (*Enterococci* and *Enterobacteriaceae*) and anaerobes. The first-line treatment are still antibiotics and the management of HS is usually long-term, with a frequent need for maintenance therapy.

Therefore, with respect to the previous literature data and our findings, we suggest the use of amoxicillin with clavulanic acid (interchangeably with fluoroquinolones) as a first step therapy. The carbapenems seem to be even more effective, however parenteral administration will undoubtedly restrict their usage in daily routine practice. As a second step, the use of a combination of clindamycin and rifampicin seems to be a good choice, and finally, a third step may be implemented with the combination of rifampin-moxifloxacin-metronidazole (eventually preceded by ceftriaxone). The maintenance, long-term therapy could be carried out with help of tetracyclines (or macrolides), with regard to their anti-inflammatory properties.

The authors declare no conflict of interest.

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