

# Diagnostic and Treatment Strategies of Dermatologists for Treating Morphea in Hungary

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**ABSTRACT** Localized scleroderma is an uncommon disease, only infrequently encountered by dermatologists in private practices or even in larger academic centers. Because of its rarity, current treatment guidelines are mostly based on low-level clinical evidence and expert opinions. The aim of this study was to evaluate treatment strategies to treat localized scleroderma. A questionnaire was developed and sent to dermatologists in Hungary. 101 returned questionnaires were eligible for evaluation. 87.12% of clinicians employed local steroids. Antibiotics were the most preferred systemic agents. Penicillin was used by 32.67% and doxycycline by 22.77% of dermatologists. Methotrexate was employed by only 6.93%. Borrelia serology was obtained by 80.19% of clinicians. More than half of practitioners performed extractable nuclear antigen (ENA) screening (53.46%). Most Hungarian dermatologists did not follow current treatment recommendations for morphea, a trend that likely holds true for other dermatology practices in the East-Central European region as well. Easily accessible, evidence-based guidelines are needed to improve patient care. Patients with localized scleroderma should be referred to specialized centers with more experience where high quality care can be ensured.

**KEY WORDS:** morphea, treatment approaches, survey

## INTRODUCTION

Morphea is an uncommon disease which leads to fibrosis of the dermis, subcutaneous fat, or both. Because of its rarity and due to the lack of universally used standardized clinical and histological scale to assess severity, evidence-based therapies are lacking (1). Treatment of morphea continues to be challenging, often leaving both the patients and the treating physicians unsatisfied. Treatments are mostly based on low-quality clinical evidence including non-randomized, uncontrolled clinical trials with only a limited number of patients. In Europe, infectious agents such as *Borrelia burgdorferi* are thought to be a pos-

sible contributor to the pathogenesis of morphea – in at least a subpopulation of patients – therefore antibiotics are often employed by dermatologists. Although convincing efficacy data are lacking, topical corticosteroids are also frequently used to target the inflammatory aspect of the disease. Extensive forms of localized scleroderma are also commonly treated with various forms of light therapy, which have been shown to inhibit several key steps of fibrosis.

The aim of this study was to evaluate the diagnostic and therapeutic decisions of dermatologists in this challenging disease in Hungary and to compare our

findings with the currently available recommendations.

## METHODS

Based on the mailing list of the Hungarian Dermatology Society, 800 questionnaires were sent out to dermatologists working both in outpatient and inpatient settings in Hungary. The questionnaire included questions concerning treatment and management of localized scleroderma.

Treatment-specific questions were the following: use of topical agents (topical steroids class 1-2 and 3-4, topical calcineurin inhibitors, emollients, other agents), use of light therapy (psoralen and ultraviolet A (PUVA), narrowband ultraviolet B (nbUVB), others), use of systemic antibiotics (doxycycline, clarithromycin, azithromycin, penicillin, others), use of systemic immunosuppressive and immunomodulatory drugs (systemic steroids, methotrexate, cyclosporine, cyclophosphamide, azathioprine, mycophenolate mofetil, tumor necrosis factor (TNF)-alpha inhibitors, rituximab, etc.). Furthermore, practitioners were also requested to rank their therapeutic choices into lines of therapy (first line, second line, third line).

Investigation-specific questions were as follows: dermatologists were asked to provide a list of frequently ordered diagnostic tests such as histology, autoimmune serology, post infectious serology especially for *Borrelia burgdorferi*, *Mycoplasma pneumoniae* and cytomegalovirus, search for infectious foci, search for sexually transmitted infections (STI), etc. Dermatologists had to indicate how often they used these tests (often, rarely, or never). Dermatologists were asked how they determine the efficacy of treatment (photo documentation, palpation, severity scales such as body surface area (BSA), or a localized scleroderma cutaneous assessment tool (LoSCAT) as well as patient satisfaction, etc.). Furthermore, clinicians were asked what factors influence their intent to treat (presence of a concurrent infection, extent of disease) and if they use only antibiotics or only immunosuppressive drugs in the systemic treatment of morphea.

Clinicians were also asked to estimate how many patients with morphea they treat each year and if they have an additional board-certification (allergology and clinical immunology, etc.) besides dermatology. Lastly, practitioners were also requested to provide the setting where they practice dermatology (university department, hospital, private practice, etc.).

## Statistical analysis

We used descriptive statistics. The statistical anal-

ysis and graphic illustration of the results were performed using Microsoft® Excel® 2015 for Windows®.

## RESULTS

### Occupational data

An average of 6.75 patients with morphea were seen by dermatologists per year. 14.85% of the practicing dermatologists decided to refer patients with morphea to larger clinical centers.

15.84% of the participants worked at a university department, 18.81% at a hospital with inpatient dermatology, and the majority, 45.54%, in a private medical office.

11.88% of the specialists held dual board certification in dermatology and allergy and clinical immunology.

101 questionnaires were completed and returned to us.

### Topical therapy

Class 3-4 topical steroids were used most frequently by dermatologist and were noted as first-line topical therapy (37.95%). Class 1-2 steroids were prescribed by 26.27% as the first-line treatment. Dermatologists began to treat morphea with a topical calcineurin inhibitor in 7.29% respondents. Emollients were recommended in 28.46% of the cases. Others agents included vitamin D3 analogues alone or in combination with bethamethasone valerate, urea, or ichthyol (Figure 1).

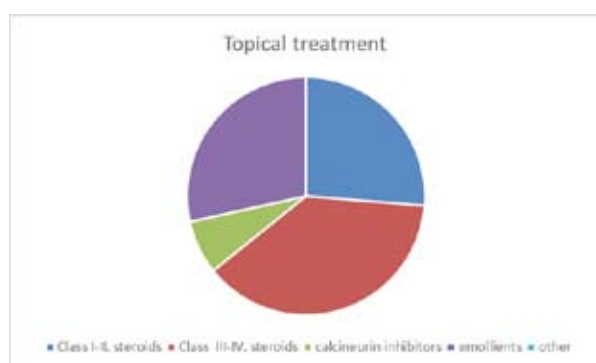


Figure 1. Use of topical treatment (first line).

### Light therapy

PUVA was employed as a 2<sup>nd</sup> line treatment in 20.79% of the cases. nbUVB was ordered as a 1<sup>st</sup> line light therapy by 9.90% of respondents. Some dermatologists recommended bath PUVA, cream PUVA, and UVA treatment alone.

### Use of antibiotics

Antibiotics were widely used by dermatologists in the treatment of morphea. More than half of the practitioners used antibiotics as a first-line treatment (Figure 2). One third of dermatologists prescribed penicillin (32.67%). The second most frequently prescribed antibiotic was doxycycline with 22.77%. Other antibiotics such as macrolides were used less frequently (4.95%).

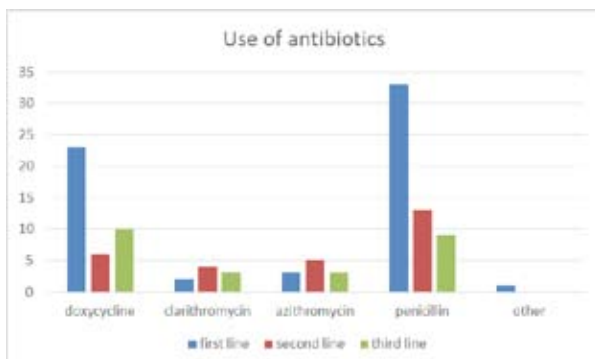


Figure 2. Use of systemic antibiotics (1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup> line).

### Use of immunosuppressive and immunomodulatory drugs

Immunosuppressive drugs were rarely prescribed (Figure 3). Systemic steroids were used as a first choice in 21.78% of respondents and relatively common as a 3<sup>rd</sup> line therapy with 13.86% frequency. Methotrexate was used as a 1<sup>st</sup> line systemic agent only in 6.93% and more frequently as a 2<sup>nd</sup> line treatment by 12.87% of respondents. Cyclosporine was mentioned as a 3<sup>rd</sup> line agent. Other immunosuppressive drugs were used sporadically.

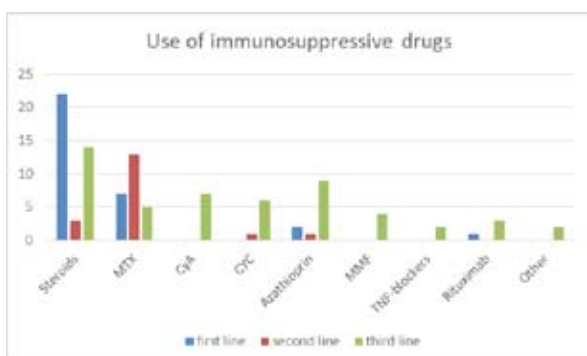


Figure 3. Use of immunosuppressive drugs (1<sup>st</sup> 2<sup>nd</sup> 3<sup>rd</sup> line).

### Treatment decision

91.08% of dermatologists noted that the extent of the disease is an important factor when choosing treatment modality (91.08%). 71.28% answered that their treatment choice depended on whether a

concurrent infection was identified. 30.69% of practitioners chose only antibiotics as systemic agents. Only 4.95% exclusively used immunosuppressive drugs if a systemic therapy was required (Figure 4).

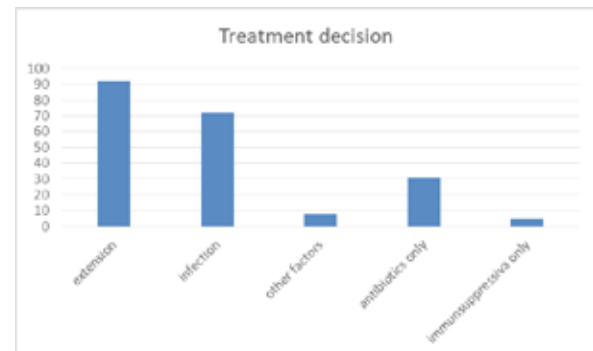


Figure 4. Factors influencing therapeutic decision.

### Controlling treatment efficacy

28.71% of the polled dermatologists reported employing photo documentation. 88.81% noted they palpate the plaques for signs of softening. 54.45% calculated BSA and 6.93% used LoSCAT to monitor disease progression.

### Diagnostic tools and procedures

About half of dermatologists relied on histopathology to diagnose morphea (50.49%). Search for infectious foci was also commonly recommended (57.42%). *Borrelia burgdorferi* serology was obtained by 80.19% respondents. Search for autoantibodies was recommended by 53.46% percent of physicians. Diagnostic tests for sexually transmitted infections were used in 10.89% of responses (Figure 5).

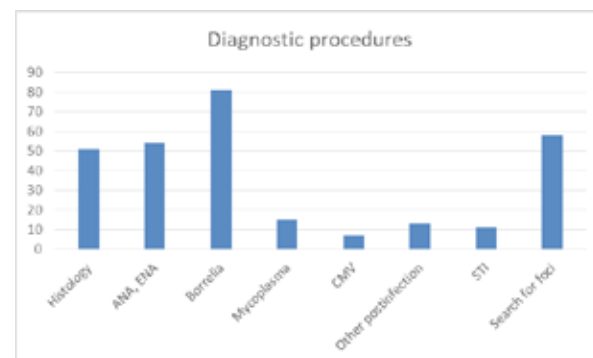


Figure 5. Diagnostic tools and procedures.

### DISCUSSION

Little is known about how patients with morphea are treated by dermatologists in East-Central Europe, including Hungary. In our survey, we found that dermatologists prefer antibiotics in the systemic

treatment of morphea. More than half of surveyed dermatologists chose penicillin or doxycycline if a systemic treatment was needed. The use of immunosuppressive drugs was surprisingly low. Methotrexate (MTX) was ordered as a first line treatment by only 6.93% of dermatologists. Systemic steroids were also used more frequently (21.78%). These results show that most of the dermatologists in Hungary do not follow the current international recommendations.

Similar to the therapeutic strategies detailed above, our diagnostic approaches also seem to differ from current regional guidelines. *Borrelia* serology is almost routinely ordered (80.19%) by clinicians, even though this test is only recommended if there is a high degree of clinical suspicion to suggest *Borrelia burgdorferi* infection. More than half of practitioners perform ENA screening (53.46%). The actual guidelines recommend this procedure only if another autoimmune disease is clinically suspected (1).

An official Hungarian morphea guideline does not exist. The European Dermatology Forum recently published the current S1-Guideline on the Diagnosis and Treatment of Sclerosing Diseases of the Skin (1). This work recommends the use of systemic steroids and MTX. The use of antibiotics is no longer recommended. In the United States, a detailed continuing medical education paper discussed the treatment of morphea. The authors concluded that the best evidence indicates the combination of steroids and MTX as well as UVA1 phototherapy for the treatment of severe morphea (2). Antibiotics are not mentioned in this paper either.

In North America, one web-based survey investigated the treatment regimens used by pediatric rheumatologists to treat morphea in children. Most pediatric rheumatologists used a combination of MTX and corticosteroids. Topical medications were used only in limited forms (3).

A cohort trial on morphea in adults and children revealed a large variation in treatment in the United States. Treatment strategies depended partially on the diagnosing specialty. While rheumatologists preferred systemic immunosuppressive drugs, dermatologists primarily prescribed local therapy and phototherapy. Topical steroids were prescribed by 40.72% dermatologist for morphea, and phototherapy is used by 16.29%. Antibiotics as well as antimalarials were used by 7.17% of dermatologists and approximately twice as often by rheumatologists (14.12%) (4).

A national survey of 155 clinicians in the United Kingdom revealed that all respondents recommend topical therapy (very potent and potent topical steroids, vitamin D analogues, calcineurin inhibitors).

PUVA was employed by 38%. Methotrexate was used alone by 25% of clinicians and by 37% in combination with steroids (5).

## CONCLUSION

The low prevalence of morphea provides limited opportunities for most dermatologists to gain sufficient experience in treating this condition. According to our results, dermatologists only see 6.75 patients with morphea per year on average, and hence most have only limited experience in treating this patient population. In light of these numbers, it is somewhat surprising that only a fraction of dermatologists (14.85%) decided to refer patients with morphea to a larger university department. A better approach may be to identify clinical centers with specialists who have more experience in treating morphea and to consistently refer patients to these departments. This may facilitate the training of future specialists with expertise in treating localized scleroderma and may also provide enough patients to design larger clinical trials, advancing the field of translational morphea research and ultimately benefiting this unique patient population.

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