ARTICLE

A survey of exposure to the use of Xiaflex for the treatment of Peyronie's disease among United States urology residency programs

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Xiaflex® (collagenase clostridium histolyticum) is a Food and Drug Administration-approved treatment for patients with Peyronie's disease. Despite its approval and implementation, there is concern that urologists in training are offered minimal exposure to its use. Thus, the purpose of this study was to evaluate the exposure of urology residents to Peyronie's disease and its management, particularly Xiaflex®. A Google Forms survey regarding the exposure of residents to Peyronie's disease and use of Xiaflex® was created and disseminated through email to urology programs. Overall, 47 institutional responses were received. At 45 institutions (95.7%), residents receive training in directly evaluating and caring for patients with Peyronie's disease. At 46 institutions (97.9%), residents receive training in observing and/or performing surgical procedures for Peyronie's disease. Residents at 31 institutions (66.0%) receive observational or procedural training for non-surgical management of Peyronie's disease, specifically Xiaflex®. Residents receive non-surgical training from an academic faculty who is fellowship trained in sexual medicine at 25 institutions and an academic faculty not trained in sexual medicine at six institutions. There exists a glaring disparity in residency exposure to Xiaflex®. Further research is warranted to elucidate how programs can provide residents with further exposure to the use of Xiaflex® in patients with Peyronie's disease.

IJIR: Your Sexual Medicine Journal (2024) 36:155–159; https://doi.org/10.1038/s41443-023-00781-7

INTRODUCTION

Peyronie's disease (PD) is a connective tissue disorder of the penis that causes pain on erection, curvature and/or deformity, palpable plaque(s), and erectile dysfunction. It can subsequently lead to adverse psychological effects such as depression and decreased feelings of masculinity, sexual confidence, and satisfaction [1, 2]. While the exact prevalence of PD is difficult to determine due to discrepancies between physician and patient-reported perceptions and varying study methodologies, recent self-report population surveys suggest a higher prevalence of probable PD of around 10%. PD may become even more common in urologic practice, given its association with cardiovascular and metabolic conditions such as diabetes [3, 4].

Collagenase clostridium histolyticum, or Xiaflex® (Endo International, United States), is a treatment option that targets and breaks down the penile plaques, reducing penile curvature [5–7]. Ultimately, it has received a moderate recommendation from the American Urological Association (AUA) in patients with stable PD with a penile curvature >30° and <90° with concomitant intact erectile function [8]. Xiaflex® is the most common intralesional therapy for PD in the United States, and its national use has increased significantly in recent years [9, 10]. However, only an estimated 15% of practicing urologists treat PD via procedural methods, such as intralesional injections [11].

Given its indication for use, urology trainees should have some familiarity with the use of Xiaflex® in the clinical setting. However, there appears to be a need for the further training of upcoming urologists on the administration of Xiaflex®-based intralesional injections, as the Accreditation Council for Graduate Medical Education (ACGME), the organization responsible for accrediting all graduate medical programs for physicians in the United States, has a minimum certification requirement that does not include exposure or training in this area. Thus, the goal of this study is to assess the access that urology residents across the United States have to training on the administration of intralesional injections, and if so whom they are being trained by, to either enforce the AGCME's current lack of a requirement for training or call for its addition in order to increase the familiarity and comfort of urology residents with administering intralesional injections for PD.

MATERIALS AND METHODS

We performed a cross-sectional survey study designed to be taken by residency program directors to understand the exposure to Xiaflex®

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Received: 16 July 2023 Revised: 28 September 2023 Accepted: 9 October 2023
Published online: 21 October 2023

training during urological residency. The study was reviewed and granted the status of non-human research by the Institutional Review Board at the University of Miami. To conduct our cross-sectional survey investigation, our team accessed a pre-existing registry of all 139 urological residency programs from the AUA website to use at the foundation of the database. Next, we collected the emails and phone numbers of all program directors. Our researchers used this registry to send individualized emails and follow-up communications to engage our respondents to partake in this identified and voluntary survey (Fig. 1). Respondents were asked about their demographics and three baseline questions followed by specific follow-up questions depending on their answers. Data analysis was performed using descriptive statistics in Excel. The data were organized by the respective sections of the AUA, and the results were reported as descriptive statistics.

RESULTS

In total, 47 responses to the Google Forms survey were received from urology residency programs, eliciting a response rate of approximately 34%. The most responses were received from programs in New York ($n = 7$), Illinois ($n = 6$), and Texas ($n = 5$), respectively (Fig. 2). Responses were obtained from all AUA sections: North Central ($n = 11$), New York ($n = 8$), Western ($n = 7$), South Central ($n = 6$), Southeastern ($n = 6$), Mid-Atlantic ($n = 4$), New England ($n = 4$), and Northeastern ($n = 1$) (Fig. 3).

Overall, 45 of the 47 institutions (95.7%) provide direct training in evaluating and caring for patients with PD (Fig. 4). Out of those 45 institutions, residents at 36 institutions (80.0%) receive this direct training from an academic faculty who is fellowship trained in sexual medicine and 8 institutions (17.8%) receive it from an academic faculty who is not fellowship trained in sexual medicine (Fig. 5). When responses were stratified by AUA section, it was found that residents receive training in directly evaluating and caring for PD at all 4 Mid-Atlantic programs (100%), all 4 New England programs (100%), 7 out of 8 New York programs (87.5%), the 1 Northeastern program (100%),

1. Do your residents receive training in directly evaluating and caring for patients with Peyronie's Disease?
    a. If you said yes to the previous question, which best describes who is teaching your residents?
2. Do your residents receive training in observing and/or performing surgical procedures for the treatment of Peyronie's Disease (plication, grafting, penile implants)
    a. If you said yes to the previous question, which best describes who is teaching your residents?
3. Do your residents receive training in observing and/or providing non-surgical options for managing Peyronie's Disease, specifically Xiaflex®?
    a. If you said yes to the previous question, which best describes who is teaching your residents?

Fig. 1 Survey Questions. Survey Questions Distributed to Urology residency programs.

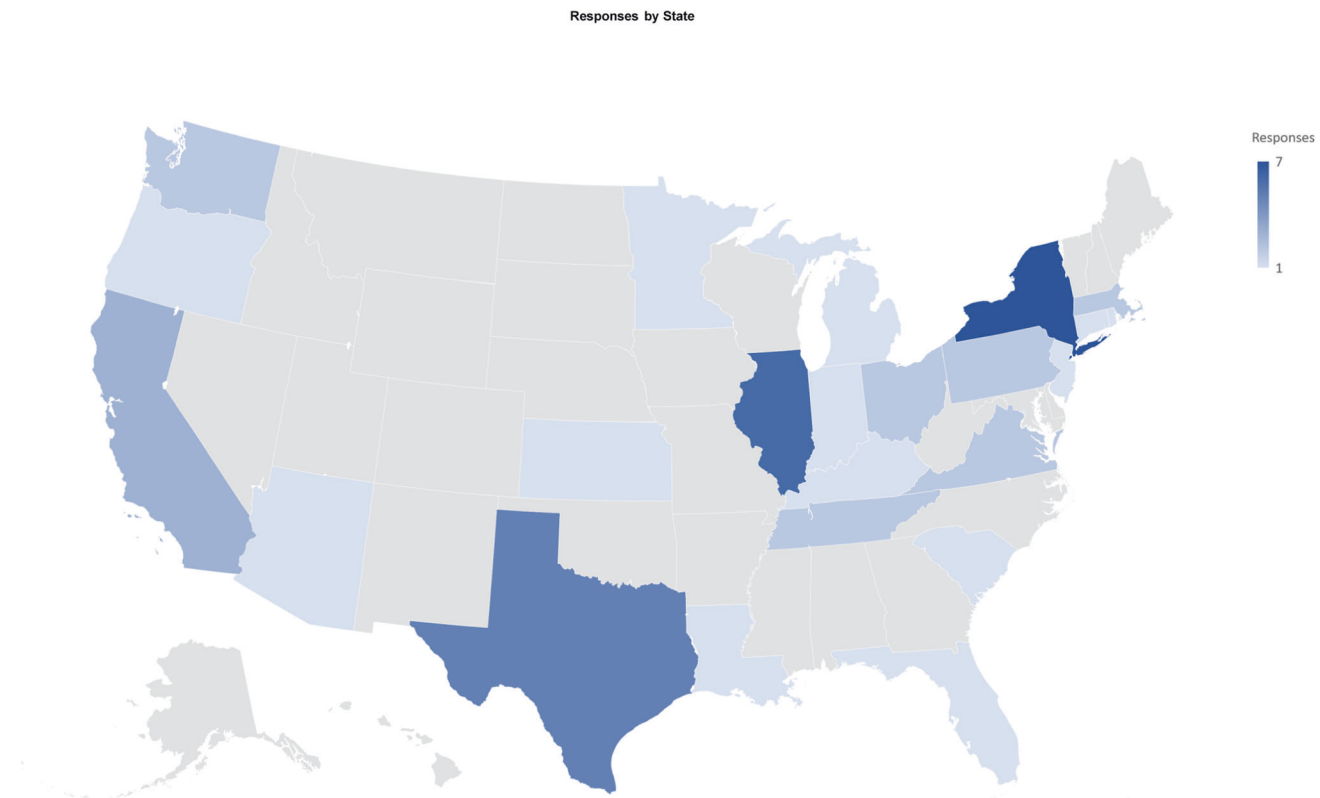

Fig. 2 State Distribution of Xiaflex® Responses. Illustration detailing the varying degree of Xiaflex® exposure to residents by state.

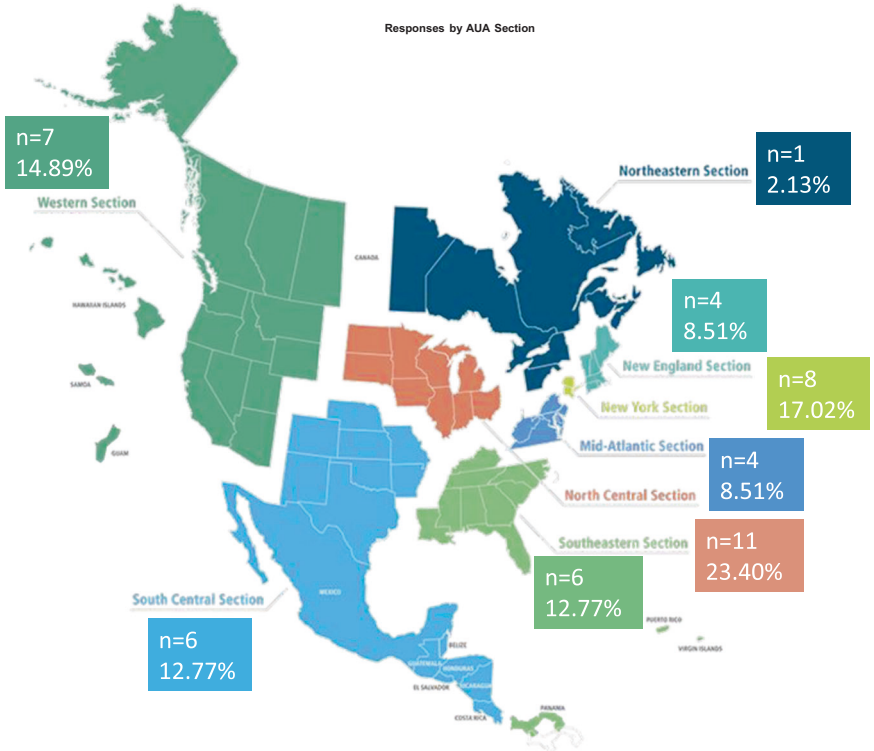

Fig. 3 AUA section distribution of Xiaflex® survey responses. Varied exposure of residency programs to Xiaflex based on AUA section.

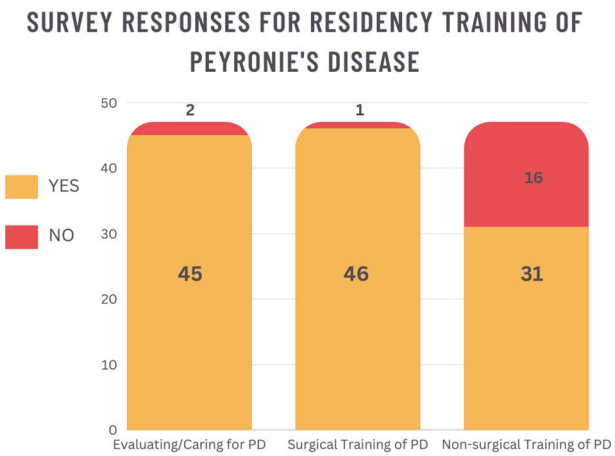

Fig. 4 Residency exposure to the treatment of Peyronie's Disease. Bar graph illustrating residency exposure to the evaluation, medical and surgical management of Peyronie's Disease.

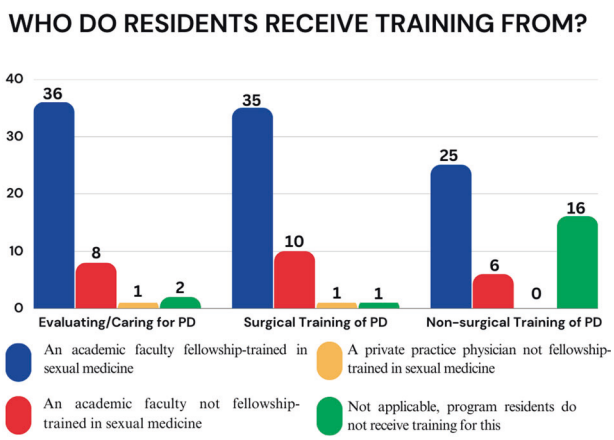

Fig. 5 Who do residents receive training from? Bar graph describing the positions of those training urology residents in the evaluation and management of Peyronie's Disease.

all 11 North Central programs (100%), all 6 South Central programs (100%), all 6 Southeastern programs (100%), and 6 out of 7 Western programs (85.7%).

Residents at 46 programs (97.9%) receive direct training in observing and/or performing surgical procedures for the treatment of PD (i.e., plication, grafting, and penile implants). Within this cohort, 35 programs (76.1%) have an academic faculty who is fellowship trained in sexual medicine teaching the residents about surgical procedures, and 10 programs (21.7%) have an academic faculty who is not fellowship trained in sexual medicine. When stratified based on AUA section, a large majority of residents received training in performing surgical procedures for PD, with all AUA sections reporting residency exposure except for 1 of 8 New York programs.

Glaringly, despite the fact that approximately 96% of residents received training in the evaluation and caring for patients with PD and the notion that Xiaflex® represents the sole FDA-approved medical management for PD, residents at only 31 programs (66.0%) reported receiving training in observing or providing Xiaflex® for the management of PD. Of those 31 programs, 25 programs (80.6%) have an academic faculty who is fellowship trained in sexual medicine teaching and 6 programs (19.4%) have an academic faculty who is not fellowship trained in sexual medicine teaching. When categorizing based on AUA section: 3 out of 4 Mid-Atlantic programs (75.0%), 3 out of 4 New England programs (75.0%), 2 out of 8 New York programs (25.0%), the 1 Northeastern program (100%), all 11 North Central programs (100%), 5 out of 6 South Central programs (83.3%), 5 out of 6 Southeastern programs (83.3%), and 3 out of 6 Western programs (50.0%) reported residency to the use of Xiaflex®.

DISCUSSION

Xiaflex® remains a viable medical therapy for the management of PD. However, given the recommendation for its use and the importance of urologists treating PD to be familiar with the treatment, it remains to be seen whether urology residents gain exposure to Xiaflex® use during residency education. The results of this study demonstrate that a considerable proportion of Urology residents do not receive formal teaching in using Xiaflex® and shed light on a potential gap in urology residency training with respect to the management of PD.

Currently, the AGCME does not require exposure to intralesional injection therapy for PD during training. While the ACGME minimum certification requirement does call for 10 cases for male incontinence/penile reconstructive (including penile prosthesis and artificial urinary sphincter) procedures, there is no additional requirement for exposure, much less training, in administering intralesional injections.

The results of the survey revealed that while almost all programs (96%) provided specific education on the evaluation and treatment of PD, only approximately 66% of residents received some degree of training on the usage of Xiaflex®. Interestingly, almost 20% of these programs provide training on intralesional injections by way of faculty not fellowship trained in sexual medicine. Near a third of residency programs then do not yet provide training on intralesional injections as part of their curricula, a number that is surprisingly high given the seeming growing demand for Xiaflex® as a treatment across the country.

Since its approval in 2013, there has been an increase in studies on Xiaflex® as well as its trends in use, to where it now sits as the most common intralesional therapy and subsequently represents the most common means of treatment for PD [9, 10]. From 2014 to 2017, there was a 230% increase in the number of Xiaflex® vials distributed by the pharmaceutical company Endo Pharmaceutical [9]. However, while the percentage of PD patients who receive treatment has shown a steady rise, only around 15.4% of practicing urologists are treating it via procedural methods, such as intralesional injections, based on a review of the American Board of Urology case logs [11].

It is intriguing to observe such limited exposure to Xiaflex® during residency training, particularly considering the 2015 American AUA Guidelines on PD, which recommended it as a first-line therapy with a Moderate Recommendation Grade B evidence level for reducing penile curvature in stable PD [8]. This recommendation strength represents the highest level of endorsement among all treatments for PD. There are several potential explanations as to why this gap in residency training exists. First, programs may not be performing Xiaflex® administration in large volumes or may face resource constraints in providing Xiaflex® to their patient population, thus limiting resident exposure to its use; however, nearly all programs reported providing direct training in evaluating and caring for patients with PD. Interestingly, with respect to program characteristics, each of the programs where residents reported no exposure to Xiaflex® during training is affiliated with a large university hospital or system. Second, programs may not have an Andrologist or Men's Health specialist on staff, further limiting the number of providers employing Xiaflex® in their practice. A potential strategy to bridge this gap may include program and resident collaboration with other Andrologists or Men's Health specialists who may be offering Xiaflex® in their clinical practice. Finally, given the other case-log duties a resident must fulfill during training, there may not be much focus given to learning and administering Xiaflex® as it does not represent a trackable item for surgical case logs. Similar work has been carried out in the realm of microsurgery training amongst Urology trainees, where only 78% of programs offer residents training in microsurgery [12].

The study has limitations in terms of the ambiguity surrounding the diverse academic faculty backgrounds and the response count from ACGME-accredited urology residency programs. There may be recall bias associated with having program directors recall whether residents are exposed to Xiaflex®. It is also difficult to assess the value that residents place upon their Xiaflex® training as it is unknown what proportion of residents go on to use Xiaflex® in their practice, which may represent an area for future investigation. However, despite these limitations, we are encouraged by our survey response rate and to our knowledge, the present study represents the first study to shed light on current resident exposure to Xiaflex® for the treatment of PD.

CONCLUSION

Xiaflex® has emerged as a gold standard for non-surgical management of PD. Despite its widespread use and indication, a considerable proportion of Urology residents are not exposed to delivering Xiaflex® in clinical practice. To our knowledge, we present the first study evaluating resident exposure to Xiaflex® in the treatment of PD. We believe it is important for United States residency programs to ensure that their trainees are educated on the use of this treatment option. A broader incorporation of training of Xiaflex® among urology residents may increase the number of providers who are comfortable and competent with providing this level of care to a potentially vulnerable patient population. Further research is warranted to better elucidate why this training gap exists.

DATA AVAILABILITY

All data generated or analyzed during this study are included in this published article.

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AUTHOR CONTRIBUTIONS

JL, KS, RVR, FR, AB, PR, NK, TM, and RR prepared the manuscript and figures. All authors approved the submitted manuscript.

COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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