Analyzing Patient Effectiveness Ratings to Stratify Pachyonychia Congenita Treatments

Albert G. Wu, MS[1]; Shari R. Lipner, MD PhD[2]

1 New York Medical College ● 2 Department of Dermatology, Weill Cornell Medicine

Background and Purpose

Pachyonychia congenita (PC) is an autosomal dominant disorder due to keratin gene mutations. It is characterized by a constellation of findings, including palmoplantar keratoderma, debilitating neuropathic pain, onychodystrophy, follicular hyperkeratosis (FHK), and PC-induced cysts 1. Since standardized treatments are lacking2, lifelong morbidities are often managed with lifestyle modifications and pain control. Our objectives were to compare the efficacy of therapeutic options used by PC patients for keratodermas, FHK, and PC-induced cysts.

Objective:

- To evaluate patient experiences and ratings of treatment effectiveness on quality of life.

Methods

Design: The most recent International PC Research Registry patient survey data consisting of 120 responses to a questionnaire from 2012-2020. Patients were asked to assess for the presence of keratodermas, FHK, and PC-induced cysts, as well as, and quality of life (QoL) impact, treatments used and efficacy (evaluated with Likert scale).

Setting: The survey data was collected as part of a multinational, initiative and comprises a representative sample of the population with PC.

Participants: Participants (survey respondents) were included in the study based on questionnaire responses and a genetic confirmation of having a PC subtype.

Main Outcomes and Measures: The main outcome measurements for the data were average patient rating and use of the treatment.

Acknowledgements

We are grateful to the Pachyonychia Congenita Project for the data and support on the project. We are indebted to all the patients with PC who participated in the IPCRR.

Results

One-hundred thirteen (94%) patients reported having keratodermas, with 95 (84%) affirming “always” or “often” having limited QoL due to pain, and 76 (67%) seeking treatment to lessen pain. Mean efficacy was 2.52 across all treatments, with filing/grinding and orthotics the most commonly used and effective treatments, and topical retinoids and steroids being least effective (p<0.01) (Table 1). Although 40-50% of patients reported using antifungals, salicylic acid, urea cream, and antibiotics, these treatments were rated as significantly less effective.

FHK was reported by 62 (51.6%) surveyed patients. The most effective and widely used management methods were clipping and moisturizers (p=0.01). Almost half of patients (30, 47%) with FHK never sought treatment (Table 1). Cysts were reported by 49 (42%), with 12 (24%) never seeking treatment. Surgical excision and incision and drainage were the most effective and widely used therapies for cysts (p<0.01) (Table 1).

Table 1: Pachyonychia Congenita Treatment Efficacy, Usage, and Reasons Seeking Treatment for Keratodermas, Follicular Hyperkeratosis, and Cysts

	Treatments	Efficacy (/5)	%Used	Reason Seeking Treatment	Count	%
Keratodermas	Filing/grinding	3.79	0.95	Lessen Pain	76	0.67
	Pain meds	3.01	0.65	Walking difficulty	77	0.68
	Orthotics	2.96	0.72	Infection	30	0.27
	Surgery	2.68	0.34	Never sought treatment	23	0.20
	Custom Orthotics	2.6	0.49	Difficulty using hands	15	0.13
	Vaseline	2.54	0.5			
	Moisturizer	2.53	0.79			
	Keratolytic	2.18	0.25			
	Topical antibiotics	2.11	0.57			
	Urea cream	2.07	0.5			
	Oral retinoid	2.06	0.3			
	Botox	1.92	0.11			
	Salicylic acid	1.85	0.42			
	Topical antifungal	1.68	0.42			
	Topical retinoid	1.29	0.15			
	Oral steroids	1.27	0.13			
	Topical steroids	1.07	0.12			
	Avg Efficacy, Std Dev	2.52, 1.29				
Follicular Hyperkeratosis	Clipping	2.82	0.34	Never sought treatment	30	0.47
	Moisturizer	2.43	0.55	FHK is annoying	19	0.30
	Antibiotics	2.12	0.27	FHK is painful	15	0.23
	Vaseline	2.06	0.25	FHK changes (red, swollen, draining, other)	12	0.19
	Salicylic acid	1.57	0.11			
	Urea	1.5	0.16			
	Keratolytics	1.29	0.11			
	Avg Efficacy, Std Dev	2.20, 1.24				
Cysts	Surgical removal	4.3	0.51	Cyst Location	27	0.55
	Incision & drainage	4.0	0.49	Cyst Condition	24	0.49
	Pain medications	2.4	0.33	Cyst Size	21	0.43
	Antibiotic ointment	2.2	0.41	Cyst Number	15	0.31
	Topical steroids	1.6	0.20	Never Sought Treatment	12	0.25
	Injected steroids	1.5	0.16			
	Oral retinoids	1.4	0.20			
	Topical retinoids	1.3	0.20			
	Oral steroids	1.3	0.16			
	Avg Efficacy, Std Dev	2.62, 1.65				

	Keratodermas	Follicular Hyperkeratosis	Cysts
Tier 1	Filing/Grinding, Pain Medications, Vaseline, Moisturizers, Orthotics	Clipping, Moisturizers	Surgical Removal, Incision & Drainage
Tier 2	Custom Orthotics, Surgery	Antibiotics, Vaseline	Pain Medications, Antibiotic ointment
Tier 3	Keratolytics, Antibiotics, Urea cream, Oral Retinoids, Botox injection	Salicylic Acid, Urea	Topical, intralesional, or injected steroids, oral retinoids
Tier 4	Salicylic Acid, Topical Antifungals, Topical retinoid, Oral & Topical Steroids	Keratolytics	Topical retinoids, Oral Steroids

Discussion

A wide range of treatments are used to manage keratodermas, FHK, and PC-induced cysts, varying significantly in efficacy. Symptoms in PC patients are often challenging to treat. With the exception of cyst excision and drainage, treatments averaged below “Effective” (Likert scale). Combinations of medical and surgical therapies are often selected based on specific manifestations and severity3, but there remain no established treatment options for PC. Due to the rarity of the disease and limited data on treatment4, patient-sourced experiences are invaluable for guiding therapy. For example, since antifungals/antibiotics have poorer patient-reported efficacy for keratoderma, filing/grinding or orthotics may be considered first. Therapies with efficacies below one standard deviation from average (steroids) should not be considered first line. Our study allows for generation of a treatment hierarchy tiered by patient rated efficacy (Table 2). We recommend proceeding in a stepwise fashion, adding one therapy at a time until symptom relief is achieved.

Limitations include survey biases since some patients used multiple treatments and rated them subjectively. While sample size is small, it is representative, including >10% of the entire recorded PC population with mutation frequencies roughly matching population statistics5.

Conclusion

A diagnosis of PC often means a lifelong patient-physician relationship to anticipate, manage, and treat associated symptoms. Therapeutic approaches should be strategic and individualized. We hope our study provides physicians and PC patients with guidance when considering treatment options.

References

1. Samuelov L, Sarig O, Adir N, Pavlovsky M, Smith FJ, Schwartz J, Hansen CD, Sprecher E. Identification of clinically useful predictive genetic variants in pachyonychia congenita. Clin Exp Dermatol. 2021 Jan 23. doi: 10.1111/ced.14569. Epub ahead of print. PMID: 33486795.
2. Wu, A. G., & Lipner, S. R. (2021). Distinctions in the Management, Patient Impact, and Clinical Profiles of Pachyonychia Congenita Subtypes. Skin Appendage Disorders, 7(3), 194–202. https://doi.org/10.1159/000513340
3. Daroach M, Dogra S, Bhattacharjee R, Tp A, Smith F, Mahajan R. Pachyonychia congenita responding favorably to a combination of surgical and medical therapies. Dermatol Ther. 2019 Sep;32(5):e13045. doi: 10.1111/dth.13045. Epub 2019 Aug 16. PMID: 31364784.
4. Frommherz L, Has C. Successful treatment of Pachyonychia congenita with Rosuvastatin. J Eur Acad Dermatol Venereol. 2020 Sep;34(9):e480-e482. doi: 10.1111/jdv.16393. Epub 2020 May 27. PMID: 32236980.
5. PC Data. (n.d.). Retrieved April 13, 2021, from https://www.pachyonychia.org/pc-data/