doi:10.36849/JDD.2303

BRIEF COMMUNICATION

Journal of Drugs in Dermatology

Self-Reported Long-Term Side Effects of Isotretinoin: A Case Series

T. Roxana Ghadimi BS, Michael J. Martinez BS, Evan A. Rieder MD

The Ronald O. Perelman Department of Dermatology, New York University Grossman School of Medicine, New York, NY

INTRODUCTION

Isotretinoin is considered the gold standard treatment for severe nodulocystic acne, though it has been the subject of controversy in the media for concerns related to adverse psychiatric effects. In 2005, the FDA issued a black box warning for suicide, depression, aggression, and psychosis.[1] However, repeated high quality studies have found no association between isotretinoin and psychiatric disorders.[2]

Isotretinoin's side effect profile is well-documented and includes xeroderma, teratogenicity, psychiatric, gastrointestinal, and neurological symptoms.[3] There has been little evidence demonstrating long-term side effects beyond effects on acne and sebum production. Nevertheless, long-term side effects associated with isotretinoin are discussed on social media platforms, such as the Facebook page "Accutane Survivors, Roaccutane, Isotretinoin Injuries & Side Effects" which contains approximately 12,000 members.

The YouTube channel, Life After Accutane, contains seven video interviews about long-term side effects attributed to isotretinoin. The seven interviews were independently and qualitatively analyzed by two authors to identify self-reported short-term and long-term side effects attributed to isotretinoin therapy. Consensus discussion led to the organization of reported symptoms and common themes according to thematic analysis research protocols.[4]

Table 1 contains important interviewee demographics and treatment course features. Table 2 contains self-reported short- and long-term side effects.

Six interviewees stopped taking isotretinoin before the end of their treatment course due to various side effects, most commonly psychiatric symptoms (4/7). For all interviewees, symptoms that led to medication termination were reported to persist after stopping isotretinoin. Every interviewee also reported at least one novel symptom which began only after stopping the medication, including joint pain, irritable bowel syndrome (IBS), and visual disturbances.

TABLE 1.

Interviewee Demographics and Treatment Course

Video	Gender	Age at start of isotretinoin therapy	Years since stopping isotretinoin at time of interview	Isotretinoin Dose	Early termination of treatment
1	Male	15 y/o	13 years	60 mg/day x 5 months	At 5 months due to mental side effects
2	Male	15 y/o	19 years	40 - 60 mg/day x 6 months	At 6 months due to mental side effects (behavior and mood)
3	Male	27 y/o	1.5 years	20 mg/day x 2 months	At 2 months due to neurological / psychiatric symptoms (stroke-like experience)
4	Female	23 y/o	6 years	10 mg/day x 6 wks, then 20 mg/day x (at least) 1 months	Due to worsened mood and hair loss
5	Male	18 y/o	5 years	40-80 mg/day x 5 months	At 5 months due to skin clearing and side effects
6	Female	19 y/o	8 years (since 2nd course)	1st course: 40-60 mg/day x 6 months 2nd course: 80-150 mg/day x 7 months	No
7	Male	18 y/o	2 years	40 – 80 mg/day x 5 months	At 5 months due to GI side effects

TABLE 2.

Self-Reported Side Effects by Body System

Body System	Listed as short-term side effect	No. of patients reporting short-term side effects (%)	No. of patients reporting persistent side effects (%)
Dermatologic symptoms	Yes	7 (100)	6 (85.71)
Gastrointestinal symptoms	Yes	4 (57.14)	6 (85.71)
Ocular symptoms	Yes	4 (57.14)	6 (85.71)
Neurological symptoms	Yes	3 (42.86)	4 (57.14)
Musculoskeletal symptoms	Yes	3 (42.86)	4 (57.14)
Psychiatric symptoms	Yes	7 (100)	7 (100)
Sexual dysfunction	No	3 (42.86)	4 (57.14)
Immune system symptoms	No	0 (0)	1 (14.29)

Reported long-term symptoms that either persisted after stopping isotretinoin or started after stopping isotretinoin included dermatologic symptoms (6/7) (dry skin and hair), psychiatric symptoms (7/7) (depression and anxiety), gastrointestinal symptoms (6/7) (IBS and constipation), ocular symptoms (6/7) (dry eyes and visual disturbances), neurologic symptoms (4/7) (brain fog and fatigue), musculoskeletal symptoms (4/7) (joint pain and myalgias), and sexual dysfunction (4/7). Psychiatric symptoms were the most common long-term complaint. Two individuals reported admission into a psychiatric facility after early termination of an isotretinoin course.

It is uncertain how symptoms experienced by interviewees years later could be attributed to isotretinoin, as its elimination half-life is about 20 hours.[5] Age is a confounding factor to consider, as individuals commonly experience onset of both acne and multiple common psychiatric disorders during adolescence and early adulthood. Though there is insufficient information to posit any diagnoses, all interviewees had symptoms concerning somatic symptom disorder.

This is the first evidence of self-reported long-term, remote side effects to isotretinoin, including sexual, neuropsychiatric, and gastrointestinal dysfunction. With growing social media discussion and interest in skin care and disease, dermatologists must be aware of these individuals. Further research on the validity of self-reported long-term side effects will allow both physicians and patients to better understand individual vulnerabilities to isotretinoin.

DISCLOSURES

The authors have no conflicts of interest to declare. The article has no funding source.

IRB approval status: Not applicable – IRB Exempt.

REFERENCES

1. Isotretinoin capsule information. FDA. Available at: https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/isotretinoin-capsule-information. Accessed December 20, 2021.
2. Singer S, Tkachenko E, Sharma P, et al. Psychiatric adverse events in patients taking isotretinoin as reported in a food and drug administration database from 1997 to 2017. *JAMA Dermatol.* 2019 Oct;155(10):1162-1166. doi: 10.1001/jamadermatol.2019.1416.
3. Accutane [package insert]. Nutley, NJ: Roche Laboratories Inc; 2000.
4. Thomas J, Harden A. Methods for the thematic synthesis of qualitative research in systematic reviews. *BMC Med Res Methodol.* 2008;8:45. doi:10.1186/1471-2288-8-45.
5. Wiegand UW, Chou RC. Pharmacokinetics of oral isotretinoin. *J Am Acad Dermatol.* 1998;39(2):S8-12. doi: 10.1016/s0190-9622(98)70438-4.

AUTHOR CORRESPONDENCE

T. Roxana Ghadimi BS
E-mail:..... Roxana.Ghadimi@nyulangone.org