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Side Effects and Efficacy of Isotretinoin in College Students

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SIDE EFFECTS AND EFFICACY OF ISOTRETINOIN IN COLLEGE STUDENTS

A Capstone Experience/Thesis Project Presented in Partial Fulfillment

of the Requirements for the Degree Bachelor of Science

with Mahurin Honors College Graduate Distinction

at Western Kentucky University

By

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*****

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ABSTRACT

Isotretinoin, also known by the trade name Accutane, is an oral medication used in the treatment of acne. Isotretinoin can be used to treat acne with varying levels of severity. The age of patients that may take isotretinoin also ranges depending on severity and on the opinion of the patient's dermatologist. Isotretinon is a serious drug that has many side effects that range from slight discomfort such as dry lips to a serious side effect of elevated liver enzymes. Treatment is determined by need. Benefits and risks to the patient are also weighed. The purpose of this article was to compare side effects of the medication based on survey reports from the student body of a university in the Midwest. The acne severity of each respondent was recorded and compared with the satisfaction following a full course of treatment.

I dedicate this thesis to my fiancé, Tory Bowling, who inspires me everyday to follow and work hard for my dreams. I also dedicate this to my parents, Kimberly and Charles Smith, who encouraged me to pursue a career in nursing. Lastly, I also dedicate this work to my fellow nursing students for their hard work during their schooling to prepare to provide care for their future patients.

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VITA

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CHAPTER ONE

Acne vulgaris is a serious disease that can have serious consequences for the person who has the condition. Acne can occur on the face, chest, back, and among other locations on the body. Its pathogenesis is complex and has many factors. Ahmad (2015), states acne involves abnormal keratinization, hormonal dysfunction and immune hypersensitivity. This condition can range from mild, moderate, or severe. Acne can be debilitating to the person who is struggling with it. Acne can occur at any age, but it is seen more often in adolescents. According to Marron, Tomas-Aragones, and Boira (2013), acne is prevalent in up to 80% of the adolescent population. This occurrence could be explained by the production of androgens during puberty.

Acne affects the pilosebaceous unit (PSU) of the skin. During puberty, the cells that line the central canal of the PSU are stimulated by hormones (especially androgens). The cells are activated and proceed to proliferate. This causes a "backup" when the proliferated cells cannot exit the infundibulum of the PSU. Sebum also backups, while hair growth continues. This leads to pressure within the units which decreases the oxygen availability to cells within the unit. With these conditions and the nutrients provided by the sebum, bacteria are able to multiply rapidly. When white blood cells begin to attack the pathogens in the unit, the formation of erythematous pustules form (Lynn, Umari, Dunnick, & Dellavale, 2016).

Acne is treated in a variety of ways. These range from topical creams, face washes, and oral antibiotics/medications. The traditional treatment regimen initially begins with topical agents. If these do not work the next steps are short-term anti-inflammatory medications, antibiotics, hormonal treatments for females, then isotretinoin (Rademaker, 2010). The ultimate goal of treatment is to rid the patient of acne. However, for many patients there are a few goals with treatment. Some of these goals include the prevention of scars forming, limiting the number and the intensity of lesion outbreaks, reducing the duration of outbreaks and the disease, and minimizing the negative psychosocial affects (Marron et al., 2013).

As stated above, isotretinoin is considered when other forms of treatment have failed. Isotretinoin is a serious medication that is not for mild acne. It was originally the first drug created for the purpose of modifying the disease, rather than simply controlling symptoms (Rademaker, 2010). According to Kaymak et al. (2009), isotretinoin is an oral retinoid that has "great efficacy against severe, recalcitrant, nodulocystic acne". The drug was first synthesized in 1955 and was approved for treating severe nodulocystic acne in the United States in 1976 (Brzezinski, Borowska, Chiriac, & Smigielski, 2017). Isotretinoin is used with acne that has not been responsive to other forms of treatment.

This medication is unique in comparisons to other drugs because it affects all of the major known etiologies of acne mechanisms. These include: sebum production, comedogenics, *Propionibacterium* acne colonization of ductal and skin surface, and monocyte chemotaxis-induced inflammation (Ahmad, 2015). Marron et al. (2013), states that isotretinoin reduces sebum production by 90%.

Though originally used solely in cases of severe acne cases, treatment has begun in moderate-severe cases that have responded poorly to other forms of treatment. It is not recommended for children under twelve years old unless significant clinical indications. All patients—male and female, must enroll in the National Registry "iPLEDGE". Isotretinoin is a category X teratogen, meaning it causes severe birth defects in unborn children. Because of this, it is imperative that pregnancies do not occur while taking this drug. Acne is a growing problem for young adults. This is leading dermatologists to prescribe the drug to increasing number of adults past the age of 25, because adults with persisting acne past the age of 30 are likely to have acne for an additional ten years (Layton, 2009).

Literature Review

Isotretinoin is an effective drug that has a significant number of adverse effects. Most adverse effects are found to be dose dependent (Rademaker, 2010). The larger the dose, the more severe the adverse effects will be for the patient. The most common side effects of isotretinoin deal with dry mucous membranes and dry skin. Specifically, mucocutaneous side effects are dose dependent (Layton, 2009). Dry lips were found in 100% of patients that partook in the research conducted by Brzezinski et al. (2017). Cheilitis (dry and cracking lips) was the most reported adverse effect in the research conducted by Rademaker (2010), where 78% of 1653 participants experienced cheilitis. Twelve percent of these experienced eczema. In another study conducted using 50 participants, 98% of participants experienced cheilitis and 84% developed xerosis (Rao, Bhat, Nandakishore, Dandakeri, Martis, & Kamath, 2014). Further, Ahmed (2015), included 52 patients in his study and 46 of these patients experienced dry lips, 20

experienced dry skin, and 12 experienced eczema. Isotretinoin can also present a hazard to the liver. In a study by Ahmad (2015), the researcher found a significant rise in alanine transaminase (ALT) and aspartate aminotransferase (AST) when compared to levels before the start of treatment with isotretinoin. Brzezinski et al. (2017), found there was an increase in liver enzymes after treatment in 2.09% of participants.

Headaches and gastrointestinal (GI) upset were less common than dry lips and cheilitis but still prevalent. Headaches occurred in 16.87% and GI upset occurred in 0.19% of participants and in Brzezinski et al.'s (2016), study. In Rademaker's (2010), study of 1653 participants, 0.7% of patients experienced headaches and 0.3% experienced GI upset. Out of Ahmad's 52 patients, only one of them experienced headaches and five of them experienced GI upset (Ahmad, 2015).

One serious adverse effect of isotretinoin is the occurrence of depression and suicidal ideation. There has been controversy about this claim, as many researchers question whether the depression came from the drug itself, or the acne and psychosocial effects of the condition (Rademaker, 2010). Kaymak et al. (2009), state in their article that in one study isotretinoin did not increase depressive and anxiety symptoms in adolescents and young adults. However, in their own research study they found that the use of isotretinoin alleviated depressive symptoms. In another study that included 346 participants, findings suggested that isotretinoin helped relieve depression and anxiety symptoms in patients and that isotretinoin is not a risk factor for depression (Marron et al., 2013). In a study with 1653 participants, there were 13 patients that reported mood change (7.1%) but none of the patients reported suicidal ideation or attempted suicide

(Rademaker, 2010). Depression was also not reported or noticed in the study conducted by Ahmad (2015).

Isotretinoin is a serious medication that can cause a multitude of side effects ranging in severity. Despite this, overall, it is an effective medication in treating acne vulgaris. In Ahmad's study, 54 patients (93%) showed improvement of their acne and 44 patients (75.9%) showed 100% acne clearance at the end of treatment (Ahmad, 2015). Compared with traditional medication treatment for acne such as adapalene and benzoyl peroxide, isotretinoin treatment can achieve acne blemish reductions of 80 to 90% over a 20-week course treatment (Penna, Meckfessel, & Preston, 2014). According to Layton (2009), patients who receive oral isotretinoin will be free from acne in four to six months. Isotretinoin is now treating a different population of patients than originally intended, including younger adults. However, when looking at older patients, such as young adults above the age of 25, these results are not as efficient. Layton (2009), says that patients in this subgroup may need small, intermittent-dose therapy because they relapse more quickly. Rao et al. (2014), stated three months of treatment with isotretinoin (20 mg/day) was effective in treating moderate to severe acne vulgaris. Ninety percent of patients received "very good" results, and relapse occurred in 4% of patients over a six-month period. Isotretinoin not only treated the disease of acne vulgaris, but it also improved patients' quality of life (Yesilova, Bez, Ari, & Turan, 2012). In another study of 3,525 patients, there was a recurrence of acne in the period of six months to one year in 1.67% (59 patients) (Brzezinski et al., 2016). There was a significant reduction in the negative impact of acne on quality of life, measured with the Dermatology Life Quality Index and

the Health Survey-Form-36, with a significant decrease of scores using the Hospital Anxiety and Depression Scale (Marron et al., 2013).

CHAPTER TWO

Methodology

A literature review was conducted to determine the most common side effects and adverse events associated with the use of isotretinoin in the treatment of acne. Attention was also given to the efficacy of treatment and whether the majority of patients were satisfied with their treatment program. A copy of survey questions is provided below.

1. What is your age?
2. What is your race/ethnicity?
3. What is your gender?
4. At what age did you complete Accutane/isotretinoin treatment?
5. Please indicate the severity of your acne.
6. Were you previously treated with any of the following treatment options?
    a. Benzoyl peroxide, antibiotics, salicylic acid, other
7. If other, please write what your previous treatment was.
8. If female, were you enrolled in "iPLEDGE"?
9. Please check any of the following side effects you experienced while taking Accutane/isotretinoin?
    a. Dry lips, cracking lips, eczema, xerosis/dry skin, altered liver enzymes, headaches, gastrointestinal upset, depressive thoughs, increase in anxiety, mood changes, emotional mood swings, other
10. How long did you receive treatment with Accutane/isotretinoin?
11. How long did you experience an improvement in your acne?
12. Were you satisfied with the outcome of your treatment with Accutane/isotretinoin?

Figure 1. Survey Questions

Following the literature review, a survey was created using Qualtrics software. This survey consisted of 12 questions. The survey sought to find the most common side effects and satisfaction of survey participants. The survey also addressed other questions such as the duration of treatment, the duration of an acne free state, demographic information, among others.

The research survey was disseminated to all students, approximately 18,000 students (WKU Office of Institutional Research, 2019), currently attending a university

in the Midwest. The survey was sent out via mass email distribution to all student email accounts on July 6, 2020. A second email was sent to student email accounts during the week of August 21st, and a third and final email was sent out two weeks later. The email included a word document of informed consent and an email link to the survey on Qualtric's website. There were a total of 169 responses to the survey with the majority of responses submitted between first and second email.

The survey was closed September 13, 2020 and no further responses were collected. Results were counted and collected by hand, then checked for accuracy using Qualtrics' system of analyzing. Results will be further discussed.

CHAPTER THREE

Results

There were a total of 169 responses to the survey. Particpants were asked to identify gender, race/ethnicity, and age range. Results are located in the table below.

Age			Race/Ethnicity			Gender		
	18-20	99		White/Caucasian	150		Male	46
	21-23	43		Black/African American	12		Female	122
	24-26	8		Hispanic or Latino	2		Prefer not to answer	1
	27-29	2		Asian or Pacific Islander	2			
	30 or greater	17		Other	1			
				Prefer not to answer	2			

Table 1: Demographic Survey Results

Participants were asked a variety of questions about their specific acne and Isotretinoin treatments. The age range of isotretinoin completion varied from ages 11 to greater than 20. Forty-one participants were 11-15 years, 100 were ages 16-20, and the remaining 23 were 20 years or greater. Five participants did not respond to this question.

Severity of acne prior to treatment with isotretinoin was also assessed. Participants were asked to indicate the severity as mild, moderate, or severe. They also had the option to choose “I do not know.” Twenty-three rated acne as mild, 92 rated acne as moderate, 51 rated acne as severe, and three responded that they did not know the severity.

As there are a variety of acne treatments typically taken before treatment with isotretinoin, participants were asked if they were treated with any of the following acne medications: benzoyl peroxide, antibiotics, salicylic acid or other. There was similar use of benzoyl peroxide (34.57%), antibiotics (27.71%), and salicylic acid (29.14%) according to participant reporting. Out of the participants, 8.57% reported using "other treatments". A table has been provided below of the most common other treatment modalities.

Birth Control	3
Home Remedies/Herbal Remedies	4
Face Washes	7
Adapalene	1
Retinols	2
Proactive Treatment System	2
Differin Gel	1
Antibiotics	3

Table 2: Other Acne Treatment Modalities

The program iPledge is a very important means to prevent patient pregnancy during isotretinoin treatment. Female patients were asked if they were enrolled in this program during treatment. This question has potential and evident reporting problems because males were not given an answer choice to opt out of the question. There were 138 respondents, indicating that males answered this question as well as female. The survey indicated that 100 people responded "yes", 26 responded "no", and 12 responded "I do not know."

Assessing the most common side effects of isotretinoin medication was one of the purposes of this study. Eleven possible side effect choices were given for respondents to check, with the option of "other" as well. Participants were not given the ability to write

in other side effects if applicable. A table is included below showing the distribution of side effects reported by participants.

Dry Lips	145	Cracking Lips	117
Eczema	26	Xerosis/Dry Skin	113
Altered Liver Enzymes (ALT and AST)	8	Headaches	47
Gastrointestinal upset	27	Depressive Thoughts	35
Increase in Anxiety	42	Mood Changes	52
Emotional Mood Swings	42	Other	34

Table 3: Side Effects of Isotretinoin

Participants were also asked to report their isotretinoin treatment length. Twenty-five (15.24%) participants reported a treatment of five months. Ninety-one (55.49%) participants reported a treatment of six months. Forty-eight (29.27%) participants reported a treatment lasting greater than six months. There were a total of five people who did not respond to this question.

The next survey questions addressed the other important aspect of the study which were satisfaction and efficiacy of treatment. Participants were asked to report how long they experienced an improvement in their acne. Improvement was subjective based on each participant's experience and opinion of themselves. Forty-four (26.83%) reported skin improvement for six months. Thirty-one (18.90%) reported a one year improvement time. Eighty-two (50.00%) reported an improvement of longer than two years. Seven (4.27%) reported no improvement and five participants did not respond to this question. Participants were then asked about their satisfaction with a "yes" or "no" choice. There was also a choice of "I prefer not to answer" given. Eighty percent (132) of participants reported that they were satisfied with their treatment with isotretinoin, while 17.58% (29)

reported they were not satisfied with their treatment. Four participants chose “prefer not to answer”, and four people did not respond to the question.

Discussion

Acne is a common problem that occurs in most people (Ayer & Burrows, 2006). Acne can cause problems in adolescents and up into adulthood. Because of this, most healthcare professionals will treat patients suffering from this condition. Some patients may be in the middle of a treatment that is not working, some patients may be in the middle of a course of isotretinoin, and some may have never been given medical advice on the treatment of their acne. It is the healthcare professional’s duty to recognize and assess these patients. We must assess their knowledge of acne vulgaris and if they know the array of treatments available to them. As nurses, we are given the opportunity to have in-depth conversations with our patients. We are able to get to know them and build rapport. This allows us to provide the best care to our patients and ensure they are living their highest quality of lives.

As discussed in the literature review, patients with acne are at increased risk for depression and anxiety (Kaymak, Tanner, E., & Taner, Y., 2009). Nurses need to recognize this and understand the implications of untreated depression and anxiety. Because adolescents and children are at greater risk for depression due to acne, we need to be hyperaware for signs that is occurring. Proper education is required as patients near their adolescent years. Patients and family members need to be educated on the development of acne, and the first steps of treatment. Patients are the most affected by their condition. Their feelings towards themselves and how they look should be assessed. If the patient is unconcerned with their acne, then this will affect the aggressiveness of

their treatment options. This is because the patient may not want to experience increasing side effects with stronger acne medications.

The majority of participants in this study were treated with other modalities as well as isotretinoin. It was a given consensus that isotretinoin was a last resort medication for the majority of participants. Healthcare professionals may learn from this result that patients who continue to require treatment changes for their acne may not be benefitting from these treatments. We must recognize that patients may continue to deal with acne and the development of scarring from acne if more aggressive treatment is not introduced. While isotretinoin is becoming more well known for the general public, there is a high possibility that our patients may not know this is an option for them. Educating about isotretinoin and its use in acne treatment may be needed.

Once patients are educated on isotretinoin, benefits and risks are then measured with the patient. This is typically done with the patient's dermatologist, physician, physician's assistant, or nurse practitioner depending on the facility. Because of the risk for depression, anxiety, and suicidal thoughts, the patient's psychological health history will be assessed as well. A history of suicidal tendencies may be a contraindication for treatment. Once the patient and the healthcare provider have decided isotretinoin is the best treatment option, this patient will begin on a treatment plan that could prove to be difficult to complete. Close monitoring, education, and nurse involvement is necessary for successful completion of the treatment plan.

The vast majority of participants in this study reported side effects while taking the medication. Dry lips, cracked lips, and dry skin were the most common side effects. These effects, while they might seem harmless and like a simple inconvenience, can

greatly affect compliance with treatment. The patient needs to be educated on the fact that these side effects are highly likely. There are ways to manage these symptoms, such as use of prescribed anti-inflammatory creams and over-the-counter lotions and lip balms. These may seem like harmless side effects, but when left untreated, these can lead to great discomfort of the patient. If the lips and skin are scratched open, bacteria may be able to enter the broken skin and cause infection.

Depression, anxiety, and mood changes were assessed in this research survey. Based on the results, these side effects were experienced by a minority of participants. However, because of the numbers and studies conducted in the past, depression, anxiety, and mood changes are still significant and should be assessed in all patients taking isotretinoin. Changes should be tracked, and healthcare providers should be notified immediately if patients begin to feel more depressed or anxious than their baseline. Another serious complication of isotretinoin therapy is elevated liver enzymes (Ahmad, 2015). In my study, only eight participants reported elevated liver enzymes. Though this number is small, elevated liver enzymes could indicate liver dysfunction. This requires prompt recognition and intervention due to the importance of the liver organ.

The last important discussion point is the iPledge Program. This program as discussed in the literature review section was begun in order to educate patients about the urgency of not female patients not becoming pregnant while taking isotretinoin. This program is supposed to be a requirement of female patients, however only 100 of 169 patients reported they were enrolled. According to the survey question regarding gender, 122 patients were female. There is a potential that this survey question could produce skewed results because male participants were not given an opportunity to opt out of this

question. This is evidenced by 31 participants not responding to the question. Regardless of this number, 22 females either responded with a “no”, “I do not know”, or no response. Due to the level of teratogenity of isotretinoin, it is imperative that all females are given adequate education about prevention of pregnancy. iPledge is an excellent way to do this, and it is alarming that 22 females did not know about iPledge or were not properly educated on it.

As in other studies conducted on isotretinoin, satisfaction with treatment occurred with the majority of participants, with most participants maintaining an acne-free state for greater than two years. While results vary because acne vulgaris is very individualized, isotretinoin remains a satisfactory choice in the treatment of acne.

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