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Accutane: An Update for Dermatology Nurses

Diana M. Hanno

This article updates and reinforces for dermatology nurses the necessity of understanding Accutane as well as the need for precautions and education to the female patient who meets the criteria for the use of Accutane.

Diana M. Hanno, BS, RN, is Head Nurse of the Dermatology Department at the Gundersen Clinic in LaCrosse, WI.

To each subspecialty of medicine there has been a drug developed that has opened new doors to patient care: (a) surgery — the development of local anesthetic; (b) OB-GYN — birth control pills; and (c) endocrinology — insulin. The list goes on and on. For the patient suffering from severe cystic acne, the breakthrough for the dermatologist was isotretinoin, or Accutane.

Pathogenesis of Acne

To understand how effective a drug Accutane (isotretinoin/Roche) is, one must first understand the pathogenesis of acne. Acne can be classified by its severity and treated accordingly. It usually has its onset in adolescence and is associated with the endogenous hormone production. This leads to an increase in the size of the sebaceous gland and the sebum production. At this point the triglycerides in the sebum, upon contact with the normal cutaneous organisms, break down to form free fatty acids. The fatty acids produce both inflammation around the gland and may also produce a build-up or thickening of the stratum corneum in the gland duct. The thickening of the stratum corneum produces a follicular plugging, obstructing the flow of sebum. The obstructed poral opening causes a build-up of pressure behind the plug as sebum continues to be produced, and comedonal acne occurs.

Organisms within the comedone continue breakdown of the triglycerides to fatty acids, and as pressure continues to build the eventual rupture of the gland lining occurs with leaking of the fatty acids into the surrounding tissue, producing inflammation.

Each individual responds to acne in a different way, and the key to this is within the individual's sebaceous glands. Some individuals never have acne, or their acne is so minimal it goes unnoticed. Others have a range from comedonal to inflammatory papulopustular acne. The above types of acne are usually self-limiting, and with medical intervention clear with the use of topical preparations and oral antibiotic therapy.

Severe cystic acne, nodulocystic acne, and acne conglobata are disfiguring conditions seen more commonly in young men. It commonly involves the trunk, shoulders and face, and tends to become a chronic, unremitting condition. The breakthrough for acne patients and the dermatologist came with the studies to control this disfiguring condition.

Vitamin A and its effect upon keratinization was used in the 1920s for treatment of diseases of the skin due to the production of

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abnormal keratinization. In 1973, topical Retin-A (vitamin A acid) was first marketed by Johnson & Johnson for its action on keratinization and comedonal acne. In 1976, Doctors Peck, Olsen, and Yoder began studies on 13-cis-retinoic acid, a synthetic isomer of naturally occurring all-transretinoic acid (a vitamin A derivative) in the United States. Controlled double blind studies on nodulocystic acne with the use of 13-cis-retinoic acid were done at the University of Iowa by Doctors Farrell and Strauss in 1980. Their findings concurred with Doctor Peck's study that 13-cis-retinoic acid improved cystic acne and reduced sebaceous gland activity during the treatment, but their findings showed sebum production returned to normal following discontinuation of treatment while the acne continued to show improvement, leading them to postulate that oral retinoids controlled acne by correction of abnormal patterns of follicular keratinization.

Introduction of Accutane

In September, 1982, Accutane was released on the market by Roche Laboratories as Accutane (isotretinoin/Roche). It was known and documented by Peck et al (1979) that retinoids are teratogens, a major side effect for women. Farrell et al (1980) documented other side effects with effects on the mucous membrane, skin, and the central nervous system. Side effects the patient needs to be concerned about are headaches, nausea, vomiting, and blurred vision, along with changes in mood. The medication can cause severe stomach pain, diarrhea, and some rectal bleeding. For the skin and mucous membrane, there is a feeling of dryness of the eyes, extreme dryness of the skin, and there can be the possibility of yellowing of both the skin and eyes and/or dark urine. The protocols for the use of Accutane were presented by Roche to be used in patients with severe cystic acne who were unresponsive to conventional therapy.

The most important contraindication is the teratogenicity of the drug. Because of this, extreme caution and good education must be given to the woman of childbearing age who meets the criteria for being placed on Accutane. Women of childbearing age should not be given Accutane unless two reliable forms of contraception are used simultaneously, "and they should be fully counseled on the potential risk to the fetus should they become pregnant while undergoing treatment, (PDR, 1982)" and contraception should be continued for 1 month following the discontinuation of the treatment. Abstinence is considered an acceptable form of prevention of pregnancy, but the woman of childbearing age must be again counseled on the strict adherence to abstinence during this time frame of Accutane therapy, and not to take the chance of an unprotected sexual relationship for the welfare of the fetus that might result from this relationship.

Guidelines for Usage and Side Effects

Today, Accutane has made a dramatic difference in our severe cystic acne patients both physically and psychologically. It is the drug of choice for these patients, but before the physician prescribes the medication, the patient must fall within the guidelines for usage. Nurses must be well informed about Accutane — its merits, its side effects and, most importantly, its protocol when used in women of childbearing age.

Before Accutane is prescribed, preliminary lab work is done consisting of a CBC and baseline liver function studies and a 12-hour fasting study for cholesterol and triglycerides. These base lipid studies are repeated 1 month after treatment. If hypertriglyceridemia occurs, these lab studies should be repeated at intervals; or, if markedly elevated, Accutane therapy is discontinued. It is essential to continue laboratory monitoring of the blood lipids until normal readings are again present. Nurses should counsel patients to not drink any alcoholic beverages 36 hours prior to the fasting lab work as this could produce a false high reading. For a woman, the laboratory workup includes a serum pregnancy test preceded by being on contraceptives 1 month prior to treatment. Only after a negative serum pregnancy test within 2 weeks prior to the beginning of Accutane can the treatment be started. It should be taken on the second or third day of the next menstrual cycle.

As the nurse, once patients are placed on Accutane, be sure they understand the side effects and have a list of appropriate topical preparations your dermatologist recommends, and that they understand how to use them. Encourage the patient to call with questions or if any central nervous system (CNS) symptoms such as headaches occur.

Preparations used for the side effects of the skin and mucous membrane will differ according to the preference and location. The important point is helping the patient to stay comfortable. For the dry, chapped lips, the patient can use Blistex or plain white petrolatum. The white petrolatum also will relieve the dryness within the nasal septum and help reduce nosebleeds, which are a possible side effect. For the dryness of the skin generally, a moisturizer can be used; one that is noncomedogonic is preferred. The dryness of the eyes that frequently occurs can be relieved with the use of artificial tears.

As with Retin-A, sun sensitivity to vitamin A is an important factor for the patient to understand. The use of good sun protection must be stressed; lifestyle, time of year, and location will dictate proper usage and the level of sun protective factor to be used. The best rule to fol-

how is to apply a sunscreen each morning to exposed skin. For the person in Wisconsin in the dead of winter, this means the face. If that same person travels to Hawaii for vacation, it means applying total body. A sunscreen with a sun protective factor (SPF) of 15 or greater should be used, even if the individual has a skin type of III or greater.

CNS symptoms need to be reported to the dermatologist at once. Unusual changes your patient should be aware of are insomnia, fatigue, headaches, and double vision, or decreased night vision. Depression has been reported, and this tends to be seen more in the adolescent patient. Parents or adults need to understand the possibility of Accutane-induced depression and not brush it off as age related or stress induced.

Because of fatigue and the possibility of musculoskeletal symptoms, we caution our patients not to begin strenuous athletic activities while on Accutane. If they are already on exercise programs or are involved in athletics, they need not discontinue this activity, but should be instructed to warm up slowly.

Accutane is our miracle drug, the only cure for severe nodulocystic acne. Early in 1989, Accutane underwent investigation by the Food and Drug Administration (FDA) because of the number of Accutane exposed pregnancies and the report of birth defects.

On Thursday, May 12, 1988, the *New York Times* printed an article on Accutane, and in this article accused Hoffman-LaRoche, the FDA, and dermatologists as being "careless . . . for failing to minimize its side effects." Prior to this article, the American Academy of Dermatology had formed a special task force to draw up guidelines for the usage of Accutane in females of childbearing age. Along with this, the then President of the American Academy of Dermatology, Doctor G. Thomas Jansen, wrote a letter to all dermatologists concerning the FDA Dermatology Drug Advisory Committee, and Doctor Jansen also testified before this committee. The importance of avoiding pregnancy while on Accutane was again emphasized by the Academy of Dermatology, and Hoffman-LaRoche produced an extensive pregnancy prevention and education kit to be used by the physician in prescribing Accutane to females in the childbearing age.

Doctor Robert Stern (1989), in his article in the *New England Journal of Medicine*, summarized the estimated number of birth defects to be 48 known to the FDA by 1986. The FDA has approved the new changes in packaging, labeling by the manufacturer, and the education program. As stated, these changes are aimed at proper education of the patient and control of the medication to prevent pregnancy while on Accutane.

Hoffman-LaRoche's new kit makes the program easier (but time consuming) for the physician as all materials and steps are within this unit. It provides for the woman a free contraceptive counseling session with a gynecologist. This again reinforces the need for birth control measures while on the drug. The last step is a patient information/consent form.

Nursing Interventions

Nursing plays an important role here in helping the woman, teenager and parent to fully understand the necessity of these measures and the need for the female on Accutane to follow them. Our role then is to reinforce compliance. For the adult, birth control measures should be easier to adhere to, as opposed to the adolescent whose experimentation in sex is spontaneous, unplanned, and frequently unprotected.

The parent/adolescent relationship also plays a big part. An adolescent patient with cystic acne may fulfill all the criteria for the use of Accutane except that she is sexually active, without proper contraceptive measures. Often the parent will not be aware of the sexual activity or may be denying the activity. It is important to stress to both parents and daughter the need to avoid pregnancy, and initial discussion should take place with both parties present. It may be necessary to speak to the patient separately, but openness of communication is important here. If the patient is sexually active, two means of contraception must be used and must be in use at least 1 month before starting Accutane. Abstinence that is sustained is, of course, adequate; however, again, it must be emphasized to the teenager the necessity of not having any unprotected sexual relationship during this period of time.

Just one birth defect is too many, and the only one who can prevent this from happening is the patient. We can educate and we must document that we have done so, but we cannot give 24-hour surveillance. The monthly serum pregnancy test and the office visit is our time to reinforce education and give support.

It was estimated that by the end of 1987, over 800,000 people had received Accutane; approximately 40% of these were women. If birth defects continue, we may be faced with the withdrawal from the market of this valuable drug. This would be detrimental for our patients, as this drug is without equal in the therapy of patients with disfiguring cystic acne. □

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