Journal of Pharmacy and Alternative Medicine www.iiste.org
ISSN 2222-4807 (online) ISSN 2222-5668 (Paper) An International Peer-reviewed Journal
Vol.8, 2015

Treatment and Management of Acne

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Abstract
Due to increasing acne problem in females, we want to examine the safe use of cOCPs in the treatment of acne. Keeping in view the age of patients , safety and ease of use in appropriate patients in combination with more conventional acne therapies. This project will briefly address the physiologic rationale for the use of cOCPs in the treatment of acne. It will also review safety considerations and the adverse event profile for oral contraceptives will be presented. Finally, practical considerations for prescribing cOCPs will be discussed.
cOCPs: Combined Oral Contraceptive Pills
Keywords: Oral contraceptives, Acne, Treatment

1. Introduction

Acne is a problem for women in all age groups. It generally begins at adrenarche, between the ages of 8 and 10 years, and peaks around age 17. Studies have shown that 100% of females are affected sometime during their adolescent years. While often considered a side effect of puberty, adult acne is also fairly common, occurring in 5% to 12% of adult women. Surprisingly, it can continue to be a problem for some women even into their postmenopausal years. The psychosocial impact of acne is undeniable; adversely impacting the quality of life of those affected. Adults with severe acne have decreased employment rates compared to their unaffected peers. In addition to the psychological toll, acne can lead to permanent scarring and result in significant, life-long disfigurement.

Therefore, effective use of all available acne treatments is paramount to gaining control of this disorder and helping those affected. While excellent treatments are available, acne in females can pose a unique challenge for the treating physician. It is often recalcitrant to conventional acne therapies, including systemic antibiotics and even isotretinoin. Combined oral contraceptives and other hormonally targeted treatments can be effective in this group of patients and should be considered in the treatment plan for females with acne. Their use will be reviewed in this article.

Acne:

Acne, medically known as *Acne Vulgaris*, is a skin disease that involves the oil glands at the base of hair follicles. It commonly occurs during puberty when the sebaceous (oil) glands come to life - the glands are stimulated by male hormones produced by the adrenal glands of both males and females.

Acne is not dangerous, but can leave skin scars. Human skin has pores (tiny holes) which connect to oil glands located under the skin. The glands are connected to the pores via follicles - small canals. These glands produce Sebum, an oily liquid. The sebum carries dead skin cells through the follicles to the surface of the skin. A small hair grows through the follicle out of the skin. Pimples grow when these follicles get blocked, resulting in an accumulation of oil under the skin.

The word **acne** comes from the word *acme* meaning "the highest point", which comes from the Greek *akme* meaning "point" or "spot" - it was originally misspelt, with an 'n' rather than an 'm' in 1835.

In humans, pimples tend to appear on the face, back, chest, shoulders and neck.

Simply put - skin cells, sebum and hair can clump together into a plug, this plug gets infected with bacteria, resulting in a swelling. A pimple starts to develop when the plug begins to break down.

Scientists from the Washington University School of Medicine found that there are *good* and *bad* strains of bacteria which determine the severity and frequency of developing acne. They explained in the *Journal of Investigative Dermatology* (March 2013 issue) that not all acne bacteria trigger pimples - in fact, one strain they identified can actually help keep the skin pimple-free.

All acne lesions start out as a microcomedone.

1-There are two main types of acne

1. Non-inflammatory acne

Microcomedones can spontaneously become unplugged and heal or they become non-inflamed skin blemishes called comedones--either a whitehead or a blackhead.

- **Whitehead:** When the trapped sebum and bacteria stay below the skin surface, a *whitehead* is formed. Whiteheads may show up as tiny white spots or they may be so small that they are invisible to the naked eye.
- **Blackhead:** A *blackhead* occurs when the pore opens to the surface and the sebum, which contains the skin pigment melanin, oxidizes and turns a brown/black colour. It is not dirt and cannot be washed away. Blackheads can last for a long time because the contents very slowly drain to the surface.

2. Inflammatory acne

A blackhead or whitehead can release its contents to the surface and heal or the follicle wall can rupture and inflammatory acne can ensue. This rupture can be caused by random occurrence or by picking or touching the skin. This is why it is important to leave acne prone skin relatively untouched.

- **Papule:** A *papule* occurs when there is a break in the follicular wall. White blood cells rush in and the pore becomes inflamed.
- **Pustule:** A *pustule* forms several days later when white blood cells make their way to the surface of the skin. This is what people usually refer to as a "zit" or a "pimple"

A papule or pustule can completely collapse or explode, severely inflaming the surrounding skin and may engulf neighbouring follicles. These lesions are called cysts or nodules.

- *Cyst:* Sometimes a severe inflammatory reaction can result in very large pus filled lesions.
- *Nodule:* When a follicle breaks along the bottom, total collapse can occur, causing a large, inflamed bump that can be sore to the touch.

Urgent action

Although rare, deterioration in acne accompanied by a fever, arthralgia's, and myalgia's may indicate acne fulminant, an acute ulcerative acne with systemic symptoms that is usually treated with oral corticosteroids and isotretinoin.

1.1 Causes for Gout

Common causes

- Increased androgen production
- Overactivity/hyper responsiveness of sebaceous glands in response to androgens
- Colonization of *Propionibacterium acnes*, which metabolizes sebum to free fatty acid, leading to inflammatory lesions

Rare causes

Industrial exposure to halogenated hydrocarbons.

Serious causes

- Adrenal hyperplasia
- Polycystic ovarian syndrome

Contributory or predisposing factors

- Adolescence
- Hair greases or oil-based cosmetics
- Sports equipment such as helmet straps rubbing and occluding skin
- Medications with iodine (found in some cough medicines)
- Some prescription drugs: lithium, isoniazid, phenytoin, corticosteroids, anabolic steroids, and oral contraceptives with high androgenic activity
- Chemotherapeutic agents that act on epidermal growth factor receptors
- Excessive milk intake, especially skim milk, in teenagers.

1.2 Characteristics of the Disease

Examination in patients with acne vulgaris includes the following features:

- Comedonal acne: Presence of open and closed comedones but usually no inflammatory papules or nodules
- Mild acne: Presence of comedones and a few papulopustules
- Moderate acne: Presence of comedones, inflammatory papules, and pustules; a greater number of lesions are present than in milder inflammatory acne
- Nodulocystic acne: Presence of comedones, inflammatory lesions, and large nodules greater than 5 mm in diameter; scarring is often evident

Laboratory tests

Acne vulgaris is a clinical diagnosis. However, laboratory testing may be indicated in the following situations:

- Female patients with dysmenorrhea or hirsutism: Consider a hormonal evaluation with levels of total and/or free testosterone, dehydroepiandrosterone sulphate, luteinizing hormone, and follicle-stimulating hormone
- Cases refractory to treatment or when improvement is not maintained: Culture skin lesions to rule out gram-negative folliculitis

1.3 Treatment regime

Treatment of acne vulgaris should be directed toward the known pathogenic factors, including follicular hyper

proliferation, excess sebum, *P acnes*, and inflammation. The most appropriate treatment is based on the grade and severity of the acne.

Pharmacotherapy

The following medications are used in the treatment of *Propionibacterium* acne vulgaris:

- Retinoid-like agents (e.g. topical tretinoin, adapalene, tazarotene, isotretinoin)
- Antibiotics (e.g. tetracycline, minocycline, doxycycline, trimethoprim/sulfamethoxazole, clindamycin, topical clindamycin, topical erythromycin, daptomycin)
- Selective aldosterone antagonists (e.g. spironolactone)
- Estrogen/progestin combination oral contraceptive pills (e.g. ethinyl estradiol, drospirenone, and levomefolate; ethinyl estradiol and norethindrone; ethinyl estradiol and norgestimate; ethinyl estradiol and drospirenone)
- Acne products (e.g. erythromycin and benzoyl peroxide, clindamycin and tretinoin, clindamycin and benzoyl peroxide, azelaic acid, benzoyl peroxide)

When a topical or systemic antibiotic is used, it should be used in conjunction with benzoyl peroxide to reduce the emergence of resistance.

Non-Pharmacotherapy

Diet therapy, such as a low-glycaemic diet and avoidance of "junk foods," has been suggested as a non-pharmacologic measure to manage acne vulgaris.

Procedures

Procedural treatments for acne vulgaris include the following:

- Manual extraction of comedones
- Intralesional steroid injections
- Superficial peels that use glycolic or salicylic acid

Medical Care

Treatment should be directed toward the known pathogenic factors involved in acne. These include follicular hyper proliferation, excess sebum, *P acnes,* and inflammation. The grade and severity of the acne help in determining which of the following treatments, alone or in combination, is most appropriate. When a topical or systemic antibiotic is used, it should be used in conjunction with benzoyl peroxide to reduce the emergence of resistance.

Treating mild acne

The majority of people who get acne will develop mild acne. This can usually be treated with OTC (over-the-counter) medications. OTC medications can be bought at a pharmacy without a doctor's prescription. They are usually applied to the skin - topical medicines.

Most acne OTC products may contain the following active ingredients:

- **Resorcinol** - helps break down blackheads and whiteheads. It is a crystalline phenol and comes from various resins. Resorcinol is also used for treating dandruff, eczema and psoriasis.
- **Benzoyl Peroxide** - kills bacteria and slows down your glands' production of oil. Benzoyl peroxide is a white crystalline peroxide used in bleaching (flour or oils or fats) and as a catalyst for free radical reactions. It works as a peeling agent, accelerating skin turnover and clearing pores, which in turn reduces the bacterial count in the affected area.
- **Salicylic Acid** - helps break down blackheads and whiteheads, also reduces shedding of cells which line the follicles of the oil glands, effective in treating inflammation and swelling. Salicylic acid is a white crystalline substance which is also used as a fungicide, or in making aspirin or dyes or perfumes. It causes the epidermis to shed skin more easily, prevents pores from becoming blocked while at the same time allowing room for new cells to grow. It is commonly added to shampoos used for treating dandruff.
- **Sulphur** - helps break down blackheads and whiteheads. Sulphur, in its native form, is a yellow crystalline solid. Sulphur has been used for centuries for treating acne, psoriasis and eczema. Scientists are not sure how sulphur works to help skin diseases. We do know that elemental sulphur does oxidize slowly to sulphurous acid which is a mild reducing and antibacterial agent.
- **Retin-A** - helps unplug blocked pores. Retin-A contains Tretinoin, an acid from of vitamin A, also known as all-trans retinoic acid (ATRA). Tretinoin is also used for the treatment of acute promyelocytic leukemia. Retin-A has been used widely to combat aging of the skin, it also acts as a chemical peel.
- **Azelaic Acid** - strengthens cells that line the follicles, stops oil eruptions, reduces bacteria growth. It is a saturated dicarboxylic acid found naturally in wheat, rye, and barley. Azelaic acid also mops up free radicals, which reduces inflammation. It is useful for patients with darker skin who have dark patches on their face (melasma), or whose acne spots leave persistent brown marks.

Treating more severe cases of acne

If your acne is more severe you should consider seeing a dermatologist - a skin specialist. The specialist may

prescribe a treatment that contains some of the active ingredients mentioned above, such as benzoyl peroxide, azelaic acid, as well as adabalene. Prescription medications for acne are presented in many forms, such as creams, lotions, etc. Your dermatologist will decide what is best for you.

You may be prescribed an oral or topical antibiotic. Antibiotics can combat the growth of bacteria and reduce inflammation. Most commonly Erythromycin and Tetracycline are prescribed as antibiotics for the treatment of acne.

- **Treating a cyst with interlesional corticosteroid injection**
- If an acne cyst becomes severely inflamed there is a high risk of rupturing. A rupturing acne cyst can often result in scarring. The specialist may inject a diluted corticosteroid to treat the inflamed cyst and to prevent scarring. The injection will lower the inflammation and speed up healing. The cyst will "melt" within a few days.
- **Isotretinoin**
- This is a strong oral retinoid, used for the treatment of severe cystic acne, as well as severe acne that has not responded to other medications and treatments.
- **Oral antibiotics**
- Oral antibiotics are frequently prescribed for patients with severe acne and some patients with moderate acne too. The aim of such oral antibiotics is to lower the population of *Propionibacterium acnes (P. acnes)*, a bacterium commonly found on the skin, which will multiply rapidly in blocked follicles. The dosage will be initially high, and then as the acne reduces so will the dosage. Antibiotics are not taken for more than six months. As time passes the *P. acnes* can become resistant to the antibiotic and another antibiotic is needed. Some American studies have indicated that it is better to use oral broad-spectrum antibiotics.
- **Oral contraceptives**
- The majority of women with acne find that taking certain oral contraceptives clears it up. Oral contraceptives suppress the overactive gland and are commonly used as long-term treatments for acne in women. If the woman has a blood-clotting disorder, smokes, has a history of migraines, or is over 35, she should not take this medication without checking with a gynaecologist first.
- **Topical antimicrobials** (topical = applied to the skin or mucus membranes)
- As with oral antibiotics, the aim of topical antimicrobials for the treatment of acne is to reduce *P. acnes* populations. Topical antimicrobials are used for patients with moderate to severe acne. Examples may be clindamycin, erythromycin, and sodium sulfacetamide
- The dermatologist may prescribe a topical retinoid. Topical retinoids are a derivative of Vitamin A and are very popular for the treatment of acne. They unclog the pores and prevent whiteheads and blackheads from developing. Examples of topical retinoids prescribed in the USA are adapalene, tazarotene, and tretinoin.

What can make acne worse?

- **Menstrual cycle** - Girls and women with acne tend to get it worse one or two weeks before their menstrual period arrives. This is probably due to hormonal changes that take place. Some people say they eat more chocolate during this time and wonder whether there may be a connection. However, experts believe the worsening acne is not due to chocolate, but rather to hormonal changes.
- **Anxiety and stress** - mental stress can affect your levels of some hormones, such as cortisol and adrenaline, which in turn can make acne worse. Again, stress can make some people binge-eat. Experts believe the culprits are most likely the hormone levels, rather than the binge-eating.
- **Hot and humid climates** - when it is hot and humid we sweat more. This can make the acne worse.
- **Oil based makeups** - moisturizing creams, lubricating lotions, and all makeup that contain oil can speed up the blocking of your pores.
- **Greasy hair** - some hair products are very greasy and might have the same effect as oil based makeup. Hair products with cocoa butter or coconut butter are examples.

Squeezing the pimples - if you try to squeeze pimples your acne is more likely to get worse, plus your skin scarring.

2. Materials & Method

2.1 Method:

We performed a survey with designed questionnaire for physicians and patients

2.2 Study Design:

The core data was collected from different hospitals of Punjab majorly

- DHQ Hospital Sheikhupura
- Jinnah Hospital Lahore
- Sheikh Zaid Hospital Lahore
- National Hospital & Medical Center, DHA Lahore

- Aziz Bhatti Shaheed DHQ Teaching Hospital Gujrat

The selected hospitals were among the major hospitals of Punjab where majority of patients rush. The study was conducted on 100 patients, few of them were in the OPD or in the emergency and few were from close relatives and friends.

Patients of age groups 10-64 year are included in the study.

100 case reports were collected that include patient profile, patient medical history, lab diagnosis, medication given and pharmacist management.

HOSPITALS	NUMBER OF CASE REPORT
DHQ SHEIKHUPURA	25
JINNAH HOSPITAL, LAHORE	15
NATIONAL HOSPITAL & MEDICAL CENTER DHA, LAHORE (Pvt)	15
SHEIKH ZAID HOSPITAL, LAHORE	20
AZIZ BHATTI SHAHEED DHQ TEACHING HOSPITAL GUJRAT	25

SETTINGS:

There was no discrimination about the race and age. The patients along with their relatives were interviewed in order to gather the information.

3. Literature Review

How Do Oral Contraceptives Work:

cOCPs include an estrogen component, usually ethinyl estradiol, and a progestin component which will vary. Estrogens are known to decrease sebum production. They are hypothesized to accomplish this in several ways, both locally at the level of the sebaceous gland, and systemically. First, they may directly oppose androgens at the local level and regulate genes involved in sebum production and sebaceous gland growth. Second, they provide negative feedback on the pituitary/hypothalamus. That is, they inhibit the anterior pituitary's production of luteinizing hormone (LH) and follicle-stimulating hormone (FSH), thus decreasing ovarian production of the androgen, testosterone. Third, estrogen administration increases sex hormone binding globulin, which binds serum testosterone, decreasing the amount of free testosterone available to bind with the androgen receptor.

How to start oral contraceptives

cOCPs may be started in three different ways (Table 1).They may be started on the first day of the patient's menstrual period, within 24 hours of the period commencing. This is known as "First Day Start" method. The theoretical advantage to this method is that there is no need for backup contraception. Despite this, however, many practitioners still instruct their patients to use backup contraception for the first week. In the "Sunday Start" method, the first pill is taken on the Sunday following the first day of the last menstrual period.

Backup contraception should be used for the first week if itis started between days 1 and 5 of menses. If Sunday falls beyond day 5, backup contraception should be used for the entire first month. In the "Quick Start" method, cOCPs may be started at any time during the menstrual cycle. This has been shown to increase compliance. In this method, a urine pregnancy test is drawn in the office and, if negative, the patient may begin taking the cOCPs immediately. Some practitioners have their patients take their first pill in the office to increase compliance. Patients should use a backup form of contraception for the first month when using the "Quick Start" method. Fear of undiagnosed pregnancy is a barrier to physician prescription of cOCPs. Physicians may delay pill initiation until the patient's next period if they have engaged in unprotected intercourse, in fear of teratogenicity. Although cOCPs carry a pregnancy category rating X, according to current literature, exposure to oral contraceptives during early pregnancy is not teratogenic or dangerous to pregnancy. There is no association between genital and nongenital malformations and the use of low dose oral contraceptives during early pregnancy. If pregnancy does occur in a patient using the "Quick Start" method, the pregnancy is easily diagnosed after the patient does not experience withdrawal bleeding during the placebo cycle of her oral contraceptive pack.

Table 1: Starting oral contraceptives

	First day start	**Sunday start**	**Quick start**
When to take 1st pill	Started on first day of pregnancy	Started on first Sunday after the onset of menses	Started anytime during the menstrual cycle after a negative urine pregnancy test
Back-up contraception	Back-up contraception not needed but advocated by some for the first week	If Sunday falls on days 1–5 of menses: back-up contraception advocated for the first week If Sunday falls on days 6–7 of menses: back-up contraception needed for the first month	Back-up contraception needed for the first month
Advantages	Less chance of pregnancy occurring during first month	Easier pill administration- most packets of pills labelled with day of the week	Better patient compliance
Disadvantages	Poorer patient compliance	Poorer patient compliance	Possibility of pregnancy occurring during first month, despite negative initial testing

Spotting/breakthrough bleeding and how to manage:

Spotting and breakthrough bleeding may be a problem for women started on oral contraceptives. Spotting is defined as bleeding not requiring sanitary protection while breakthrough bleeding requires the use of a tampon or menstrual pad. Up to 20% of women stop using oral contraceptives secondary to this side effect.45 Spotting and breakthrough bleeding are common in the first 3 to 4 months after starting oral contraceptives and patients should be counselled regarding this side effect. After this period, it tends to cease.

SAFETY:

Our objective is to examine the use of oral contraceptives in acne patients. There are several important safety concerns and interactions to consider when starting a patient on oral contraceptives. More serious adverse events may occur in certain patients and should thus be avoided in those at risk (Table 2)

Table: 2

Smokers greater than 35 years old	Morbid obesity
Undiagnosed abnormal uterine bleeding	Estrogen dependent neoplasms, breast cancer, endometrial cancer, hepatic adenomas and carcinomas
Pregnancy and lactation	History of jaundice in pregnancy or with prior OCP use
Thromboembolic disease	Hypersensitivity
Hypercoagulable state	Migraine headaches after age 35 or before age 35 with focal neurologic deficits/aura
Cardiovascular disease including poorly controlled hypertension, angina, complicated valvular disease	Diabetes with evidence of nephropathy, retinopathy, neuropathy, vascular disease or >20 years duration
Hypertriglyceridemia	Severe cirrhosis

Hormonal changes lead to the most common side effects. Nausea, breast tenderness, headache, and bloating Are attributed to the estrogen component of the cOCP. Fatigue, irritability, weight gain, acne, oily skin, increased low-density lipoprotein level (LDL) and breast tenderness are attributed to the progestin component of the cOCP. Decreased libido is also attributed to low progesterone levels. Menstrual irregularity can also occur. As the levels of estrogen in cOCPs have decreased, the incidence of unscheduled bleeding and spotting has increased. If estrogen levels are too low, hypo menorrhea and early cycle breakthrough bleeding can occur. If progesterone levels are low, late cycle breakthrough bleeding results. Knowledge of these effects can help the clinician choose the right cOCP for their patient and troubleshoot any problems with ongoing cOCP therapy.

AGE:
When the effectivness of oral contraceptives are assessed in different age groups of females, it was found that they are equally effective in all age groups of females except those who are pregnant.

AGE GROUP	NUMBER OF PATIENT
10-24	6
25-34	27
35-44	36
45-54	21
55-64	4
Unknown	6

4: Discussion
Worldwide every second person is suffering from Acne vulgaris, it is due secretion of sebaceous glands in the skin. Earlier antibiotics and retinoid were considered as the only therapy for acne. Now a day cOCPs are considered safe for the treatment of acne as it decrease the secretion of sebaceous glands.

Treatment Plan:

FIRST LINE OF THERAPY:
- ANITIBIOTICS
  - Azithromycin
  - Doxycycline
  - Clindamycin

SECOND LINE OF THERAPY:
- RETINOIDS
  - Isotretinoin

THIRD LINE OF THERAPY:
- ORAL CONTRACEPTIVES
  - Ethinyl estradiol
  - Levonorgesterol

5: Result
Several combined oral contraceptive preparations have proven to be effective and safe in the treatment for acne in women when used appropriately. All of those approved foruse in acne, and many others, have near equal efficacy in decreasing total acne lesion counts, with a greater effect on inflammatory acne. Their use should regularly0 be considered in female patients with acne, especially those not responding to first line treatments, namely topical therapies and oral antibiotics. Careful screening and selection of patients is important to minimize risk. In addition, a working knowledge of the individual combined oral contraceptive formulations can help the prescriber to select the best medication for their patient and help with troubleshooting when problems arise. With this knowledge, any physician who regularly treats acne can safely include cOCPs in their therapeutic armamentarium.

References
1. Burton J, Cunliffe W, Stafford I, et al. The prevalence of acne vulgaris in adolescence. *Br J Dermatol*. 1971;85(2):119–126.
2. Mallon E, Newton J, Klassen A, et al. Quality of life in acne: a comparison With general medical conditions using generic questionnaires. *Br J Dermatol*. 1999; 140(4):672–676.
3. Cunliffe W. Acne and unemployment. *Br J Dermatol*. 1986; 115:386.
4. Kim J, Ochoa M, Krutzik S, et al. Activation of toll-like receptor 2 in acne triggers inflammatory cytokine responses. *J Immunol*. 2002; 169(3):1535–1541.
5. Liu P, Krutzik S, Kim J, et al. Cutting edge: all-trans retinoic acid down-regulates TLR2 expression and function. *J Immunol*.2005;174(5):2467–2470.
6. Cunliffe W, Forster R. Androgen control of the pilosebaceous duct? *Br J Dermatol*. 1987; 116:449.
7. Looking bill D, Abram's B, Ellis C, et al. Inocoterone and acne. *Arch Dermatol*. 1992; 128:1197–1200.
8. Thiboutot D, Knaggs H, Gilliland K, et al. Activity of type 1 5 reductase in the follicular infrainfundibulum compared with the epidermis. *Br J Dermatol*. 1997; 136:166–171.
9. Pochi P, Strauss J. Sebaceous gland response in man to the administration of testosterone, D4-androstenedione, and dehydroisoandrostenedione. *J Invest Dermatol*. 1969; 52:32–36.
10. Rony H, Zakon S. Effect of androgen on the sebaceous glands of human skin. *Arch Dermatol Syph*. 1943;48:601–604.