Toward evidence-based practice in acne: Consensus of an Asian Working Group

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ABSTRACT

Acne vulgaris is common throughout the world and often perceived by both patients and clinicians as an inconsequential disease of adolescence. In reality, however, acne is a chronic medical disease that lasts for years and causes a considerable impact on quality of life. Many patients with acne experience emotional problems due to their disease, which can lead to reduced social interactions and even a lower likelihood of employment. Little has been written specifically about acne in Asian patients in the English-language medical published work. A group of acne experts from nine Asian countries and the USA met to review and discuss acne care within the Asia-Pacific region, focusing on evidence-based medicine. This group developed a care algorithm using results of clinical trials as well as knowledge of practice patterns.

Key words: acne, Asian skin, management, oral antibiotics, topical retinoids.

INTRODUCTION

Acne vulgaris is a chronic inflammatory disease of the pilosebaceous unit.1 It has a variety of manifestations, ranging from a few comedones to severe nodulocystic disease. While acne is often perceived as an inconsequential disease of adolescence, a majority of patients experience their disease chronically for years and it has a negative impact on quality of life. Patients with acne may experience emotional problems due to their disease, which can lead to reduced social interactions and even a lower likelihood of employment.

Little has been written specifically about acne in Asian patients in the English-language medical published work. Several national conferences in Asian
countries have produced independent treatment guidelines but no group has previously fully reviewed, compared and contrasted acne care within the Asia-Pacific region. A group of acne experts from 10 countries (Hong Kong, India, Japan, Korea, Malaysia, the Philippines, Singapore, Taiwan, Thailand and the USA) gathered in 2005 and 2006 to discuss current Asian practices in acne treatment and the available evidence supporting practice. In 2008, a dermatologist from Australia joined the group and provided information about management of acne in that country. At the first meeting, practice patterns from different countries were presented and the diversities and similarities were explored. At the second meeting, the goal was to assess, adopt and promote best practices and guidelines developed from evidence-based medicine measures such as those proposed by the Global Alliance to Improve Outcomes in Acne.1 This group of Asian dermatologists with a special interest in acne vulgaris was an offshoot of the Global Alliance, and included four members of the worldwide Global Alliance group. The result was the following recommendations for the treatment of acne in Asian patients. The population of individuals of Asian descent is increasing in most areas of the world, including the USA; for this reason, we believe that publishing recommendations for managing Asian patients with acne can be helpful to dermatologists throughout the world.

MEDICAL PERSPECTIVES ON ACNE

Acne treatment in Asia may come from a number of different types of providers, ranging from physicians (dermatologists or primary care physicians) to beauticians. In many Asian countries, the proportion of dermatologists to the overall population is very low (Table 1); therefore, most patients with acne are not managed by dermatologists. Although other providers may give effective care, they are not always fully informed of the impact of acne or the availability of effective therapies, and could benefit from guidance from dermatologists.

Several factors complicate acne treatment in Asia. The most universal is probably the wide availability of over-the-counter (OTC) medications, cosmeceuticals and generics. In addition, there are a variety of unproven and unorthodox treatments, which are often used by beauticians and other non-health-care personnel. In India, for example, the market for OTC acne medications is an order of magnitude larger than that for prescription acne medications and homeopathy is commonly used. Many acne patients try multiple OTC medications before seeking medical care and some patients continue using them while receiving care, thereby possibly affecting diagnosis, therapy, and outcomes. In addition, many Asian countries have ethnically mixed populations which may have different needs, preferences and reactions to therapy. Finally, the health-care environment for acne management varies from country to country, with significant differences in the acceptance, availability and insurance support for acne treatment modalities. For instance, in Japan, health insurance covers acne treatment including topical retinoids, whereas acne is not covered by medical insurance in Korea. As will be discussed, these differences can have considerable impact on clinical practice.

Several Asian countries have well-established dermatological societies and national acne groups. These include Malaysia, the Philippines, Korea, Taiwan, Japan and Thailand. Most of these countries have developed national guidelines for acne care. Some other countries have formed national acne boards, while still other countries have dermatological societies but often lack a recognized acne subgroup. Our group recommends that the training curricula on acne should be enhanced to achieve better treatment outcomes in acne.

PATIENT’S PERSPECTIVES ON ACNE

Although attitudes towards acne vary widely among different Asian countries, a common theme is that acne is not viewed as a treatable medical condition.
Instead, the public perceives acne to be a normal part of growing up, has a low awareness of the availability of effective therapies and does not recognize the possibility of significant long-term consequences from acne. The after-effects of acne, such as post-inflammatory hyperpigmentation (PIH) and scarring, are prominent issues. In the Asian population, PIH is more common than in fair-skinned individuals and a greater concern. Some patients do not seek treatment because they believe that acne is a natural part of growing up; but in many patients, acne does not resolve with time.2

In addition, attitudes toward acne are heavily influenced by advertising and the media (with the exception of India, where this is not the case). Information from these sources can be unreliable or misleading. Even when patients know about effective medical acne treatments, they tend to have unrealistic expectations regarding the speed of onset and time to improvement and these are likely to adversely affect adherence. In addition, patients may be fearful of adverse effects from prescription medications.

RECOMMENDATIONS FOR ACNE MANAGEMENT

Acne management practices in different Asian countries vary somewhat amongst each other and from standard Western practice. The guidelines and recommendations put forth by the Global Alliance to Improve Outcomes in Acne in 2003 (Fig. 1)1 are a good representation of currently available, evidence-based acne management, are largely evidence-based, and are considered appropriate for Asian countries as well as Western countries.

The Global Alliance guideline recommends using combinations of agents to target most of the four pathophysiological features of acne (abnormal

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Figure 1. Acne treatment algorithm. Alt., alternatives; BPO, benzoyl peroxide. (Reproduced with permission from the original publishing company.)
keratinocyte differentiation and proliferation, *Propionibacterium acnes* proliferation, and inflammation, and excess sebum production. Topical retinoids inhibit the formation of acne precursor lesions, the microcomedo, and are recommended for all but the most severe cases of acne. Mild, non-inflammatory acne can be treated with topical retinoids alone. If both comedonal and inflammatory lesions are present, topical retinoids should be used in combination with antimicrobial agents. Combination therapy not only targets multiple pathophysiological processes, but also has been shown to provide faster and more complete lesion clearance than monotherapy. Topical antimicrobial agents, including benzoyl peroxide (BPO) and antibiotic-BPO combination products, are recommended for mild-to-moderate disease and oral agents for moderate-to-severe disease. Because of concerns about bacterial resistance, the Global Alliance and European acne experts have created guidelines for the use of oral antibiotics in acne.1,3

The preferred oral antibiotic agents include tetracyclines such as lymecycline, minocycline and doxycycline, or, if these agents are not tolerated, macrolides may be used. Oral antibiotics should always be used in combination with a topical retinoid. Monotherapy should be avoided and the duration of treatment should be limited to 12 weeks whenever possible. BPO should be added to the regimen if antibiotic therapy continues for more than 8–12 weeks. Hormonal therapy, including anti-androgen agents, is also an option for women with moderate-to-severe acne; the effectiveness of hormonal therapy can be further enhanced by use in combination with a topical retinoid with or without an antimicrobial agent. Oral isotretinoin, which targets all of the factors involved in acne pathogenesis, is the mainstay of therapy for severe acne. However, it must be used cautiously because of the potential for adverse effects, especially in women of childbearing age. In addition to these core pharmaceutical interventions, counseling to educate patients on proper skin care and set realistic expectations for therapy is important.1

The Asian group’s recommendations for treatment of acne in Asian patients are only slightly different from those of the Global Alliance. For mild acne, the group recommends topical retinoids, with antimicrobials added if inflammatory lesions are present. More aggressive therapy should be considered for patients with a family history of severe acne or other risk factors. For moderate acne, the first-line therapy for papulopustular presentations is combination therapy including a topical retinoid, a topical antibiotic and/or BPO, while the first-line therapy for nodular presentations includes oral antibiotics in combination with topical retinoids and BPO. For either type of presentation, the recommended second-line therapy for patients who do not respond or cannot tolerate the first-line therapy is oral isotretinoin. For female patients, hormonal therapy in combination with topical retinoids and either BPO (preferred) or topical antibiotics is a third option. For severe acne, oral isotretinoin is the first-line therapy. The dose should be individualized based on the patient’s response, but a minimum cumulative dose of 120–150 mg/kg bodyweight should be given to reduce the likelihood of relapse. Additional topical and oral treatments should be added as needed. Second-line therapies include high-dose oral antibiotics or (for women) hormonal therapy with topical retinoids or BPO as needed.

**INFLUENCE OF ASIAN SKIN TYPES**

Several clinically significant differences between Asian skin and Caucasian skin contribute to the variations between Asian practice and the Global Alliance recommendations. Asian skin is more prone to PIH than Caucasian skin, as are other dark skin types.4 Although several studies have shown that topical retinoids are effective in treating acne in Asian patient populations,5–7 there is a perception that topical retinoids appear to cause more irritation among Asian patients than among Caucasians. A few studies support the idea that the tolerability of topical retinoids varies for different skin types. Unpublished data from a split-face study comparing the tolerability of adapalene to tretinoin found considerable differences between Asian races, with tolerability highest for Chinese, intermediate for Malays and lowest for Indians. There were no significant differences in colorimetry or total epidermal water loss (Dr Chee Leok Goh, unpubl. data, 2007). Japanese studies on adapalene gel found that approximately 80% of Japanese patients experienced mild adverse effects (AE) during the first month, compared to 20–30% in trials involving Caucasians. However, it should be noted that side-effects in Japanese patients diminished or
resolved within 2–3 weeks of the initiation of therapy, and caused only one discontinuation among 100 patients in one study. Similarly, four out of 444 patients of the adapalene gel 0.1% group dropped out in the other clinical trial. A study of photodamaged skin in Japanese patients concluded that tretinoin caused a higher than anticipated level of irritation among Japanese compared to that reported in Caucasians. Quantitative testing found no significant differences between Indians, Malays and Chinese. These variations may be partly due to facial skin care routines, which may make certain groups more sensitive to topical medications.

Additional studies that evaluate the efficacy, safety and tolerability of acne therapies in Asian patients and compare acne therapies in Asian patients with therapy in other races are needed to investigate and confirm these impressions and to better define the optimal approaches to treating Asian patients.

**SCARRING AND PIH**

The prevention or management of facial scarring and PIH is an important objective of acne therapy. This is especially true in Asia because of the cultural importance of maintaining smooth, unscarred facial skin and because of the increased risk of PIH in Asian skin. In an ideal situation, patients would prevent scarring by using effective acne therapies early. However, because of the wide availability and acceptance of cosmeceuticals and other non-medical approaches to acne care, many patients experience noticeable PIH or scarring, and management of these problems is a considerable part of dermatological practice.

Post-inflammatory hyperpigmentation, due either to acne or to acne treatments such as ablative laser therapy, may have a substantial psychological impact on Asian patients. Although lesions may resolve over time (≥1 years), additional therapy can speed resolution. Therapies to treat PIH commonly used in Asia include topical hydroquinone, and/or retinoid monotherapy or in combination with corticosteroids, and non-ablative skin rejuvenation procedures such as intense pulsed light (IPL). Pulsed dye lasers (PDL) may be used to treat post-acne erythema. Recently, a stable formulation of hydroquinone 4%, tretinoin 0.05% and fluocinolone acetonide 0.01% was introduced. This combination offers several advantages: hydroquinone inhibits melanin synthesis, while tretinoin decreases hyperpigmentation, enhances the epidermal penetration of hydroquinone, and increases collagen production, blocking the potential of the steroid to cause atrophy. Finally, fluocinolone acetonide, a relatively mild, low-potency topical steroid counters the irritant effects of tretinoin and hydroquinone on the stratum corneum and inhibits melanin synthesis.

Established scars, of which atrophied scars are the most common, present a more difficult treatment challenge. Asian practices in scar management include the full range of therapies: topical agents, chemical peels, microdermabrasion, surgery, IPL treatment and lasers. Topical agents, especially retinoids, are generally used in combination with one or more procedures. Treatment may be difficult and require multiple sessions and therapeutic approaches, with the treatment approach dependent on the anatomy and pathophysiology of the scar. Chemical peels provide subtle and slow improvement and are used frequently for minor scarring. Laser therapies predominate in treating more severe scars. Only a few studies have investigated laser therapy for scar treatment in Asians. Jeong et al. found that erbium:yttrium–aluminum–garnet (Er:YAG) lasers provided a good response but were associated with PIH and erythema in most patients. Therapy with a non-ablative 1450-nm laser caused minimal, gradual clinical improvement. Overall, some laser therapies appear to have benefit but more study is needed to determine optimal approaches. However, they may cause hyperpigmentation and erythema, especially in Asians.

**KEY VARIATIONS AMONG ASIAN COUNTRIES**

**Australia**

Australia’s population of 20 million is serviced by 350 dermatologists. The majority of acne patients are managed by their general practitioners who act as gatekeepers and may then refer cases onto a specialist. There is an increasing trend for treatment by cosmetic means and the Australasian College of Dermatologists tries to encourage patients to seek medical help. Topical and oral treatments are widely used often as combination therapy. Oral isotretinoin can
only be prescribed by a specialist dermatologist and is reserved for nodulocystic acne. The Australian website www.allaboutacne.com has been very successful in educating patients.

**Hong Kong**

In Hong Kong, steroid-induced acne, excoriated acne and post-pubertal acne are common. Hong Kong’s population of approximately 7 million individuals receive medical care from approximately 11 000 physicians, of whom only 60 are diplomate dermatologists. Because of the low ratio of dermatologists to patients, acne is usually managed by primary care physicians or beauticians. Systemic agents are the most commonly used prescription medication, comprising 61% of the market. Oral isotretinoin accounts for approximately half of systemic therapy, with oral antibiotics and oral contraceptives accounting for approximately one-quarter each. Use of oral antibiotics is limited by the high prevalence of antibiotic phobia. Among topical agents, antibiotics are used in 46% of cases, followed by retinoids in 30% of cases, then BPO in 9%. Combination topical therapy is used in only 4% of patients. Prescription drugs are readily available at the pharmacy, without physician consultation.

**India**

In India, a wide variety of generic products are available (e.g. there are 17 different generic forms of adapalene). Regulation of the market is lax, and agents such as steroids and isotretinoin are widely used OTC due to their low cost and easy availability. There is currently no accepted standard of care for acne; the approach to therapy is highly dependent on the individual physician’s training and clinical experience. Medical treatment typically relies on topical and oral antibiotics and topical steroids. Topical retinoid use is relatively uncommon due to a widespread fear of skin irritation based on early experiences with tretinoin. In contrast, oral isotretinoin is used frequently for all grades and types of acne, often with low-dose or pulsed/intermittent dosing schedules.

Several special considerations are relevant to acne treatment in India, including steroid acne, fungal infections and cutaneous hypoandrogenism. Steroid acne and steroid-modified acne are common because of the widespread use of OTC steroid preparations. Both may distort the clinical presentation and cause hypersensitivity to topical medications. Acne patients in India have a high incidence of fungal infections (by the way, seborrheic dermatitis of the scalp has been identified in >75% of acne patients), and topical antifungal agents are frequently included in acne treatments. Acne treatment programs also often include anti-androgen agents for women with signs and symptoms consistent with hyperandrogenism. Acne scars, particularly atrophic scars, are common.

**Japan**

The Japanese Dermatological Association has developed guidelines for acne management. Rates of acne scarring have decreased in Japan, probably because patients are encouraged to manage acne early. Until 2007, treatment options for acne have been limited to OTC products, topical antibiotics, oral antibiotics and chemical peeling. However, the clinical trial of adapalene had been completed and adapalene was launched in 2008. This development is now changing the practice of acne management in Japan. Launching of other drugs such as BPO in the recent future will make considerable effect on acne treatment in Japan within the next few years.

**Korea**

In Korea, acne is one of the major diseases seen in outpatient dermatology clinics. Korea has an active dermatology society with a recognized acne subgroup, the Korean Society for Acne Research (KSA). The KSA holds annual meetings and has finished in a national epidemiological survey of acne. KSA is establishing Korean acne treatment guideline. Oral isotretinoin is currently used to manage mild, moderate and severe acne; in addition, there is a perception that the response to topical retinoids is slower among Asian patients than among Caucasians. Scarring is common, with multiple scars in many patients. Treatment is usually done on a case-by-case basis, taking care to avoid hyperpigmentation. Laser and light-based therapy are popular for acne scar as well as active acne lesions.

**Malaysia**

One key factor in acne management in Malaysia is the diversity of the population, which includes several distinct ethnic groups (Malays, Chinese, Indians and others). These groups have different perceptions of
acne and have different sociocultural practices when it comes to the initial approach to acne treatment. The bulk of medical treatment for acne in Malaysia is by the general or family practitioners. This is because dermatological services are still in short supply, with the dermatologist to population ratio of 1:250 000.

Patients in Malaysia very often resort to non-medical treatment of their acne as first-line management. Non-medical treatment is popular and attractive as a result of the very intense marketing and promotional activities done on a commercial basis. Many patients and their families are unaware that acne is a treatable medical disease.

Medical treatment, especially systemic treatments like oral isotretinoin, are usually not the first choice of patients due to misperceptions about side-effects and costs. As for oral isotretinoin therapy, the general prescription pattern in Malaysia is for many physicians to tailor doses in the lower end of the standard recommended regimen (i.e. ≤0.5 mg/kg) based on patients’ tolerance and cost (Dr Steven K. W. Chow, pers. comm., 2005). Oral isotretinoin, which was first available in Malaysia in 1999, is strictly supervised and can only be prescribed by authorized physicians and dermatologists trained and registered in the usage of the medication.

As for other modalities of medical treatment for acne out of the dermatologist’s office, it is usually provided by family or general practitioners who manage the majority of patients with mild-to-moderate acne.

The Philippines
Dermatology is an active specialty in the Philippines, and acne treatment is an important subspecialty. There is an active and organized acne board, which has developed a consensus guideline for acne management. Both pharmaceutical and surgical therapies are popular and widely used. A survey found that 58–73% of Filipino dermatologists regarded acne surgery as a good therapeutic option depending on the severity and type of acne. Atrophic scarring is common and is usually treated with a combination of surgical and laser therapies.

Singapore
Topical retinoids and BPO are widely used, and are recommended as first choice therapies for non-inflammatory and topical antibiotics in combination with BPO or retinoids for mild-to-moderate inflammatory acne. Low-dose oral isotretinoin therapy is popular among the general practitioners. Oral antibiotics are usually prescribed for inflammatory acne and oral isotretinoin for nodulocystic acne. For most patients, the primary concern with regard to acne is the possibility of scarring. Management of scarring typically focuses on treatment using laser therapy. Other therapies for scars include chemical peels, scar revision (subcision) and intralesional steroid injections for keloidal scars.

Taiwan
Topical retinoids in combination with BPO or a topical antibiotic are the standard of care for mild-to-moderate acne and for maintenance therapy. Use of topical medications has been increasing, in part because of the introduction of adapalene. For moderate-to-severe acne, oral antibiotics, hormonal therapies or chemical peels may also be added. Oral isotretinoin is generally reserved for severe nodulocystic acne and use of systemic agents is limited by patient fears.

Thailand
Acne of significant severity is a common problem in Thailand. Acne treatment by cosmeticians in aesthetic boutiques has been popular in recent years; however, recent lawsuits may slow this trend. The Dermatological Society of Thailand has developed two acne treatment algorithms, one intended for dermatologists and one for non-dermatologists. Acne management relies primarily on topical therapy for mild acne and combinations of topical and oral agents for moderate and severe acne. Topical retinoids are a key component of therapy and are used in treating at least 70% of patients. Low-dose isotretinoin use is relatively common, often in mild acne as well as more severe forms. Non-pharmaceutical treatments including acne surgery, laser and IPL therapy, and chemical peels are increasing in popularity.

CONCLUSIONS
Acne is a treatable, medical disease. Compared to Western countries, the approaches to acne management in Asian countries are more varied. In most of the Asian countries surveyed, patients often view acne as a natural consequence of adolescence that...
is a cosmetic issue rather than a disease. As a result, patients frequently ignore their acne, self treat or seek treatment from beauticians. Use of OTC acne management products and cosmeceuticals is common throughout Asia. This non-medical care is usually driven by advertising, personal experience and cultural factors instead of evidence, and is commonly ineffective or harmful. When patients do seek medical care, it is often late in the course of the disease. Thus, acne frequently has adverse consequences including scarring, pigmentation problems and psychological sequelae. To prevent this, patients and physicians need to be better informed about acne, the availability of effective therapies and the importance of early management.

Most Asian dermatologists with a special interest in acne use treatment algorithms similar to that recommended by the Global Alliance to Improve Outcomes in Acne, emphasizing combination therapy with topical retinoids and topical antimicrobials for mild-to-moderate acne and adding BPO and oral agents for severe acne. This group’s recommendations for the treatment of acne in Asian patients are generally in agreement with the Global Alliance guideline. Physicians and other care providers should also be educated on the current guidelines for effective acne therapy and need to incorporate them into practice.

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