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THERAPY IN PRACTICE

Treatment of Acne Vulgaris During Pregnancy and Lactation

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Abstract Acne vulgaris is a common problem encountered by pregnant and lactating women. Unfortunately, in clinical practice, treatment is often not optimized as a result of the lack of safety data and unified recommendations on the use of the various anti-acne therapies. In this narrative review, current data on their safety is summarized. We recommend the use of topical medications as first-line treatment for acne vulgaris in pregnant and lactating women. These include antibiotics (erythromycin, clindamycin, metronidazole and dapsone), benzoyl peroxide, azelaic acid and salicylic acid. Oral agents and/or light-based therapy may be considered as second-line treatment. The former consists of oral macrolides (erythromycin and azithromycin), cephalexin or zinc compounds. Blue–violet or red light phototherapy may be used as monotherapy or in addition to topical and/or oral therapies. Hormonal therapy, antibiotics consisting of tetracyclines, co-trimoxazole and fluoroquinolones, and both oral and topical retinoids should be avoided.

1 Introduction

Acne vulgaris is a chronic dermatological disorder characterized by the presence of comedones and inflammatory papules, pustules and nodules mainly affecting sebaceous gland-rich areas of the body. It is a disease of the pilosebaceous unit and results from four major pathophysiologic factors: seborrhea, hyperkeratinization, follicular colonization with *Propionibacterium acnes* and, subsequently, the release of immune mediators that result in inflammation [1–3].

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Acne is a common condition, with a lifetime prevalence of 85 % [1]. Although it is often perceived to be a disorder afflicting only the youth, post-adolescent acne, which is defined as acne affecting people more than 25 years of age, has an incidence of up to 54 % in women and 40 % in men and is increasingly being recognized [1]. Post-adolescent acne has been consistently shown in studies to predominate in females [1], and acne is a common problem faced by pregnant women. During pregnancy, acne often worsens because of a rise in serum androgen levels [4], which results in an increase in sebum production and secretion. Acne is well known to result in significant psychosocial morbidity [5], and this is particularly significant during the perinatal period, during which time post-natal blues and depression may develop and have serious consequences.

The ubiquity and chronicity of acne vulgaris have led to a growing number of acne medications being available on the market. However, published information on the effects of these medications on the developing fetus and infant is limited. Pregnant or lactating women are often excluded from clinical trials for ethical reasons. Available information on the teratogenicity of these medications is often obtained from cases of inadvertent exposure in which a woman has used the products before she found out she was pregnant.

We reviewed the current literature to evaluate the safety of the common and newer acne medications for use in pregnancy and lactation. A PubMed search on the treatment of acne vulgaris was performed over the last 35 years, from 1 January 1977 to 7 April 2013. The evidence for the safety of these therapies in pregnancy and lactation was then evaluated with reference to PubMed articles over the same 35-year period, their manufacturers' recommendations, medicine package inserts and book chapters. As pregnant or lactating women are almost always excluded from randomized control trials, currently available evidence is limited to animal

studies, retrospective studies, case reports, anecdotal evidence and extrapolations from studies not designed to directly examine the safety of these agents in pregnancy. The results of our review are summarized and presented in a narrative manner in this article.

2 Risk Classification Systems

One of the most widely used pregnancy classifications is the US Food and Drug Administration (FDA) assessment system, which stratifies drugs into five risk categories. However, it has been heavily criticized for its focus on animal data and its readiness to label new medications as class B (safe in pregnancy). Other classification systems available include the Australian, Swedish and German systems, which rely more on human data, and recently, the more comprehensive Evidence-based Medicine system, which takes into consideration the timing of drug exposure [6]. A comparison of the US FDA and Australian pregnancy classification systems is made in Table 1.

For drug risk in lactating mothers, the more established rating systems include that from the American Academy of Pediatrics (AAP) and the Lactation Risks Categories described by Hale [7]. The former stratifies drugs into three groups: those that should be 'used with concern,' those with unknown effects but 'may be of concern' and those that are generally 'compatible with breast feeding' [8]. A newer resource is the Drug and Lactation Database (LactMed) produced by the National Library of Medicine. This peer-reviewed database provides consumers with comprehensive information about drugs that may be used in breastfeeding mothers, including serum drug levels, possible adverse effects on infants and alternative drugs to consider [9].

3 Current Practice

The lack of unified drug classification systems in pregnancy and lactation as well as the grave consequences of drug teratogenicity has led clinicians to adopt a very conservative approach when prescribing medications in these groups of women. The common perception that acne is a cosmetic problem further prompts clinicians to choose less effective treatment or even to withhold treatment completely during pregnancy and lactation.

4 Topical Therapy

As a general rule, topical agents are safer than oral medications for use in pregnancy and lactation, as systemic availability of the drug is lower.

4.1 Antibiotics

Older formulations include topical erythromycin (FDA category B), clindamycin (B) and metronidazole (B), which are generally thought to be safe for use in pregnancy and lactation [10]. When applied topically, systemic absorption of erythromycin and clindamycin has also been found to be negligible, once again implying its safety [4]. The manufacturer of topical metronidazole, however, recommends caution in its use during pregnancy as there have been reports of tumorigenicity in animal studies [11]. Newer formulations that include topical dapsone 5 % gel (C) and nadifloxacin (N) are less well studied. Embryotoxicity has been reported in animals exposed to more than 500 times the levels of topical dapsone normally prescribed in humans [12] but no adverse reproductive events have been reported in humans so far. The probable safety of topical dapsone is supported by the safe use of the oral formulation in treating conditions like dermatitis herpetiformis in pregnancy [13]. While oral dapsone has been reported to cause hemolytic anemia in breastfed infants [14], the topical formulation is likely to be safe for use in lactation because of low levels of systemic absorption, as suggested by tolerance of its use in glucose-6-dehydrogenase (G6PD) deficiency and sulfonamide allergic patients [15]. Nadifloxacin is a topical fluoroquinolone antibiotic that has been shown to be effective in treating acne vulgaris [16]. There have been no reports of reproductive adverse effects, but this is a relatively new drug and data are therefore limited.

4.2 Retinoids

There are conflicting reports on the safety of topical retinoids such as tretinoin (C), adapalene (C) and tazarotene (X) in pregnancy. Isolated cases of congenital malformations from use of these agents have been reported [17, 18], but these incidences may be coincidental. Larger scale studies have shown no increased risk of retinoid embryopathy with use of topical retinoids [19, 20]. In one of the largest prospective studies to date, Panchaud et al. demonstrated that there was no statistically significant difference in the rates of spontaneous abortions and major/minor birth defects between women exposed to topical retinoids and the control group [20].

Tretinoin and adapalene are probably compatible with lactation because of the low levels of systemic absorption [4, 21, 22]. The safety of tazarotene in breastfeeding is uncertain.

4.3 Comedolytics

These include benzoyl peroxide (C) and azelaic acid (B), which also have antimicrobial properties. Although no studies on the use of these agents in pregnant women have been done, both have minimal systemic absorption, and

Table 1 Comparison of the US and Australian drug safety in pregnancy classification systems

Category	Definition	
	US Food and Drug Administration (FDA) system	Australian system
A	Controlled studies show no risk. Adequate, well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus	Drugs taken by a large number of pregnant women and women of childbearing age with no increase in the frequency of malformations or other direct/ indirect harmful effects on the fetus
B	No evidence of risk. Animal reproduction studies have failed to demonstrate a risk to the fetus and there are no adequate and well-controlled studies in pregnant women	B1: limited experience in pregnant women and women of childbearing age, with no increase in the frequency of malformation or other direct/ indirect harmful effects on the human fetus. Animal studies reassuring
		B2: limited experience in pregnant women and women of childbearing age, with no increase in the frequency of malformation or other direct/ indirect harmful effects on the human fetus. Animal studies are inadequate/ lacking, but available data show no evidence of an increased occurrence of fetal damage
		B3: limited experience in pregnant women and women of childbearing age, with no increase in the frequency of malformation or other direct/ indirect harmful effects on the human fetus. Animal studies have shown evidence of an increased occurrence of fetal damage, the significance of which is uncertain in humans
C	Risk cannot be ruled out. Animal reproduction studies have shown an adverse effect on the fetus, but use in pregnancy may be justified if potential benefits outweigh risks	Pharmacological effects of drugs may cause harmful effects on the human fetus or neonate without causing malformations. These effects may be reversible
D	Positive evidence of human fetal risk. Investigational or marketing experience show risks to the fetus, but use in pregnancy may be justified if potential benefits outweigh risks	Suspected or proven to cause malformations or other irreversible damage on the fetus. These drugs may also have adverse pharmacological effects
X	Contraindicated in pregnancy. Studies in animals or humans and/ or investigational or marketing experience have shown positive evidence for human fetal risk, which clearly outweighs potential benefits in the patient	High risk of causing permanent damage to the fetus hence contraindicated in pregnancy or when there is a possibility of pregnancy
N	No pregnancy category has been assigned	NA

hence their use in pregnancy and lactation should not be a cause for concern [4, 10]. Salicylic acid (C) has been used as an over-the-counter dermatological agent for many years with no reports of teratogenicity. Its oral form, aspirin, is being used in low dosages to prevent pre-eclampsia [23], and this affirms its safety. There is a theoretical risk of Reye's syndrome with use of aspirin in breastfed infants [24], but this is unlikely with topical salicylic acid because of minimal skin absorption, especially if use is limited to small areas of the skin [4].

4.4 Combination Therapy

Combination therapy targets different pathophysiologic events simultaneously and has been shown to have improved efficacy over monotherapy in the treatment of acne vulgaris in general [3]. The more common combinations include antibiotics with benzoyl peroxide or retinoids and retinoids with benzoyl peroxide. Theoretically, there is increased permeability of the skin with use of such combinations and thereby a risk of increased systemic exposure to the component drugs. However, studies have failed to show an increase in transdermal intake [3], and the use of combination therapy in pregnancy and lactation may therefore be assumed to be safe.

5 Systemic Therapy

Systemic therapies for acne consist of oral medications, which can broadly be divided into antibiotics, minerals, hormonal therapy and retinoids.

5.1 Antibiotics

5.1.1 Macrolides

Erythromycin (B) has traditionally been the agent of choice when a systemic antibiotic is needed during pregnancy [10]. While largely reported to be safe for use, there have

been reports of fetal cardiac malformations [25], and prolonged use of the estolate form has been associated with fetal hepatotoxicity in 10–15 % of pregnant patients [10, 26]. If there is treatment failure or intolerable side effects with erythromycin, newer macrolides such as azithromycin (B) and roxithromycin (N) may be used. These drugs are effective in the treatment of acne vulgaris, have a better side effect profile and are less frequently associated with bacterial resistance [2, 27]. However, they are much more expensive than erythromycin. Clinical experience with the newer macrolides is lacking, but they are expected to have a similar safety profile to erythromycin and have been reported to be safe for use in pregnancy [2, 28]. While macrolides as a class have been classified by AAP as safe during lactation, use of erythromycin during the 1st 2 weeks of life has been associated with subsequent development of pyloric stenosis [29].

5.1.2 Cephalosporins

Use of cephalexin (B) in lactation has been associated with infantile diarrhoea [30], but it is otherwise well established as a safe drug to use in pregnancy and lactation [10]. However, it is rarely used in the treatment acne vulgaris. While cephalosporins have been shown to have in vitro activity against *P. acne*, it is hydrophilic and therefore thought to penetrate microcomedones poorly in vivo [2]. Information regarding its efficacy in acne vulgaris is sparse, but a retrospective study of 93 patients showed that cephalexin is an effective anti-acne agent, with 78 % of patients experiencing clinical improvement after a dosing regimen of 500 mg twice daily over an average period of 8.8 months [31].

5.1.3 Tetracyclines

Tetracycline (D), while largely reported to be safe in the 1st trimester, affects calcification of the teeth if taken after the 4th month of pregnancy and causes permanent teeth discoloration. Cases of maternal liver toxicity associated with the use of tetracycline in the 3rd trimester have also been described [32, 33]. While there is a theoretical risk of bone and teeth malformation if tetracycline is used during lactation, low concentrations of fetal absorption are expected because of its strong binding with calcium ions in breast milk, and it is generally considered safe for use in breastfeeding [34]. Other anti-acne drugs from the same class include doxycycline (D), minocycline (D), lymecycline (N) and oxytetracycline (D). These drugs, while not as extensively studied, are structurally related to tetracycline and are expected to affect the fetal calcification process similarly.

5.1.4 Co-Trimoxazole

Co-trimoxazole (C) is sometimes used in the treatment of acne vulgaris recalcitrant to the macrolides and tetracyclines. Use of this drug in the 1st trimester can lead to folic acid deficiency, which may in turn result in neural tube defects, structural malformations of the cardiovascular and urinary system, and cleft lip or palate. Exposure in the 3rd trimester has been linked to small for gestational age infants, as well as hyperbilirubinemia [35]. It is considered safe for use in lactation by the AAP and LactMed except when the baby is premature, has severe jaundice or G6PD deficiency, during which there is a higher risk of kernicterus.

5.1.5 Fluoroquinolones

Levofloxacin (C), a 3rd generation fluoroquinolone, has been used successfully to treat acne vulgaris, especially in patients who have failed treatment with other agents [36]. In pregnancy, fluoroquinolones should be avoided as they may have deleterious effects on growing cartilage [37]. No adverse effects have been reported from the use of levofloxacin in nursing mothers, but pseudomembranous colitis in an infant has been reported from maternal use of ciprofloxacin [38].

5.2 Minerals

5.2.1 Zinc

Zinc sulfate (N) and zinc gluconate (N) have been shown to be effective in the treatment of acne vulgaris at elemental doses of 30–150 mg daily [36]. Zinc is an essential trace

Table 2 Teratogenicity of isotretinoin[a]

Features
External abnormalities
Ears—anotia, micropinna, small/absent external auditory canal
Eyes—microphthalmia
Facial dysmorphism
Cleft palate
Internal abnormalities
Central nervous system—cerebral abnormalities, cerebellar malformation, hydrocephalus, microcephaly, cranial nerve deficit
Cardiovascular system
Thymus gland abnormality
Parathyroid hormone deficiency
Suboptimal IQ
Spontaneous abortion
Premature births

[a] Accutane [Package Insert], Welwyn Garden City, UK; Roche Lab. Inc; 2012

Table 3 Summary of the use of acne drugs in pregnancy and lactation

Medication	Pregnancy rating		Lactation rating		Recommendations	
	FDA[a]	Aus[b]	AAP[c]	LactMed	Pregnancy	Lactation
Topical						
Erythromycin	B	A	Compatible	Acceptable	Safe for use	Safe for use
Clindamycin	B	A	Compatible	Acceptable	Safe for use	Safe for use
Metronidazole	B	B2	Of concern	Unlikely to be of concern with topical application	Likely safe for use Reports of tumorigenicity in animal studies [10] No adverse reproductive events in humans	Likely safe for use
Dapsone	C	B2	Compatible	Avoid in G6PD deficiency, newborn/ premature infants	Likely safe, but studies lacking Embryocidal effects in animal studies when administered >500× the levels in humans [11] Oral dapsone used to treat dermatitis herpetiformis in pregnancy [12]	Likely safe, but studies lacking Oral dapsone may cause hemolytic anemia in breastfed infants [13], but unlikely with topical dapsone due to low systemic absorption
Nadifloxacin	N	Not rated	Not rated	Not rated	Likely safe, but studies lacking	Likely safe, but studies lacking
Tretinoin	C	D	Not rated	Low risk	Avoid if possible Reported case of otocerebral abnormalities [17]	Likely safe, due to low systemic absorption [19]
Adapalene	C	D	Not rated	Low risk	Avoid if possible Reported case of oculocerebral malformations [18]	Likely safe, due to low systemic absorption [20]
Tarazotene	X	Not rated	Not rated	Low risk	Contraindicated in pregnancy	Avoid in lactation. Safety in breastfeeding poorly defined, excretion levels into breast milk not determined
Benzoyl peroxide	C	Not rated	Not rated	Low risk	Safe for use	Safe for use, systemic absorption minimal
Azelaic acid	B	B1	Not rated	Low risk	Safe for use	Safe for use, systemic absorption minimal
Salicylic acid	C	Not rated	Not rated	Not rated	Likely safe Low dose aspirin used for treatment of pre-eclampsia [21]	Likely safe, systemic absorption minimal if used on small areas of skin Possible risk of Reye's syndrome with use of aspirin [22]
Systemic						
Erythromycin	B	A	Compatible	Acceptable	Likely safe for use in pregnancy Reported cases of cardiovascular anomalies [23] and hepatotoxicity [24] in humans	Safe for use after first few weeks of birth Reported case of pyloric stenosis when exposed during early neonatal days [27]
Azithromycin	B	B1	Not rated	Acceptable	Likely safe for use, but studies lacking	Likely safe, but studies lacking.
Roxithromycin	N	B1	Not rated	Not rated	Likely safe for use, but studies lacking	Likely safe, but studies lacking.
Cephalexin	B	A	Not rated	Acceptable	Safe for use	Likely safe, but reported cases of diarrhea in the breast-fed infant [28]

Table 3 continued

Medication	Pregnancy rating		Lactation rating		Recommendations	
	FDA[a]	Aus[b]	AAP[c]	LactMed	Pregnancy	Lactation
Tetracyclines (and its derivatives)	D	D	Compatible	Short-term use acceptable	Avoid in pregnancy Fetal teeth discoloration reported [30] and maternal hepatotoxicity [31] reported	Likely safe Theoretical risk of affecting bone growth, but low levels of fetal absorption as the drug binds to calcium in the maternal milk
Co-trimoxazole	C	C	Compatible	Avoid in jaundiced, ill, premature infants; or in G6PD deficiency	Avoid in pregnancy Reports of neural tube defects, structural malformations of the cardiovascular and urinary system, cleft lip or palate with use in 1st trimester. Small for gestational age infants and hyperbilirubinemia reported with 3rd trimester use [33]	Avoid in neonates that are premature, has severe jaundice or has G6PD deficiency, due to a higher risk of kernicterus [5].
Levofloxacin	C	Not rated	Not rated	Short term use acceptable	Avoid in pregnancy Possible deleterious effects on growing cartilage [35]	Avoid in lactation Perforated pseudomembranous colitis reported in a breast fed infant whose mother consumed ciprofloxacin [36]
Zinc salts	N	Not rated	Not rated	Not rated	Likely safe, but studies lacking.	Likely safe, but studies lacking.
Oral contraceptive pills	X	B3	Compatible	Avoid <4 weeks postpartum	Avoid in pregnancy Higher incidence of Down's syndrome reported [38] Risk of feminization of the male fetus, hypospadias [1]	Avoid in lactation Reported to decrease milk production [39] Risk of feminization of the male fetus [1]
Cyproterone acetate	X	B3/D[d]	Not rated	Not rated	Avoid in pregnancy Risk of feminization of the male fetus, hypospadias [1]	Avoid in lactation Risk of feminization of the male fetus [1]
Spironolactone	C	B3	Compatible	Appears acceptable		
Isotretinoin	X	X	Not rated	No recommendation made	Contraindicated in pregnancy Teratogenic agent (see Table 2)	Avoid in lactation. Safety in breastfeeding poorly defined, excretion levels into breast milk not determined
Light-based treatment						
Blue/red light phototherapy	NA	NA	NA	NA	Safe for use	Safe for use Blue light used to treat neonatal hyperbilirubinemia [42]
ALA-PDT	C[e]	Not rated[e]	Not rated[e]	Not rated[e]	Likely safe Used in treatment of condyloma acuminata with no reports of adverse pregnancy events [43]	Likely safe, but studies lacking

G6PD glucose-6-phosphate dehydrogenase

[a] US Food and Drug Administration Classification System

[b] Australian Classification System

[c] American Academy of Pediatrics (AAP) Classification System

[d] Dose dependent

[e] Ratings for aminolevulinic acid

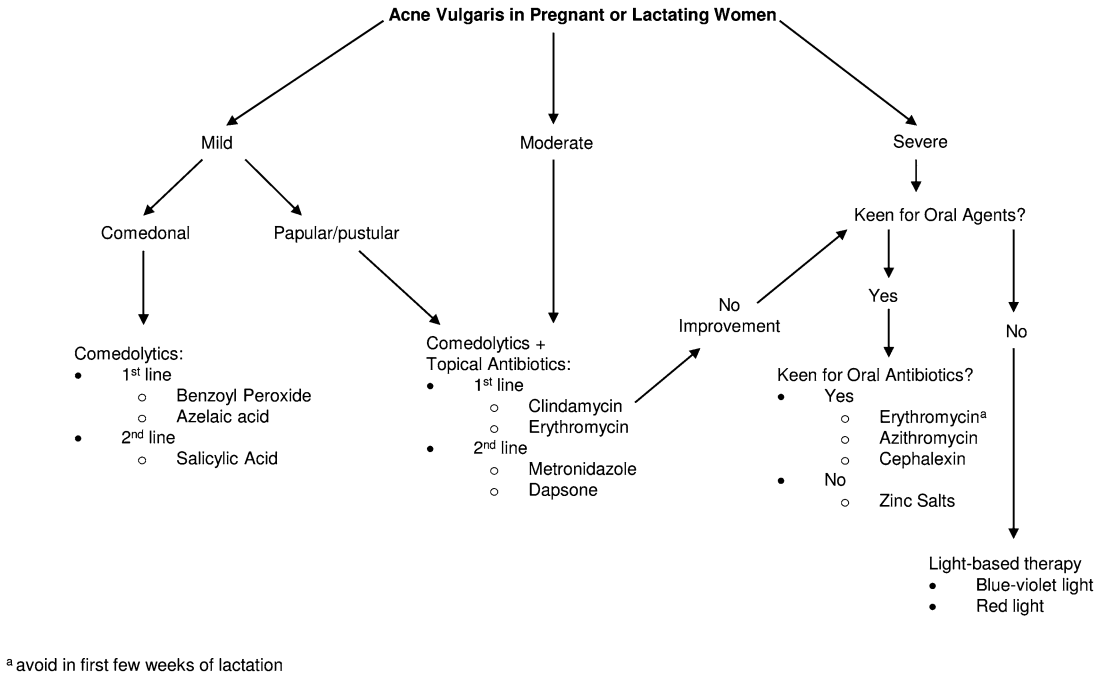

Fig. 1 Suggested treatment algorithm for acne vulgaris in pregnant and lactating women

element that is needed for proper functioning of several enzymes in our body. Studies have consistently proven that at doses below 75 mg/day of elemental zinc, no harm is posed to the growing fetus [39]. Literature on the use of zinc salts in lactation is sparse, but no adverse effects have been reported thus far.

5.3 Hormonal Therapy

Hormonal therapy includes oral contraceptive pills (OCP) (X) and androgen receptor blockers such as cyproterone acetate (X) and spironolactone (C), which are especially useful in controlling acne vulgaris linked to hyperandrogenism. These anti-androgenic agents should be avoided during pregnancy and lactation, as they have been associated with hypospadias and feminization of the male fetus [1]. A higher incidence of Down syndrome has also been noted with use of OCPs in early pregnancy [40]. Hormonal therapy should be avoided in lactation for two reasons: the estrogen content in OCPs has been reported to decrease milk production [41], and there is a theoretical risk of fetal feminization, especially in neonates who might be less capable of metabolizing the additional hormones.

Table 4 Combined acne severity classification

Severity	Definition		
	Comedones	Inflammatory lesions	Total lesion count
Mild	Fewer than 20	Fewer than 15	Fewer than 30
Moderate	20–100	15–50	30–125
Severe	More than 100	More than 50 or more than 5 cysts	More than 125

5.4 Retinoids

5.4.1 Isotretinoin

The teratogenic effects of isotretinoin (X) are well established (Table 2). It should be avoided throughout pregnancy. The gravity of isotretinoin use in pregnancy is highlighted by the establishment of iPLEDGE by the US FDA in 2006, a risk management program aimed at eliminating fetal exposure to isotretinoin [42]. The manufacturer of isotretinoin has advised against its used in lactation, though no adverse effect on the nursing baby has been described. Acitretin, a similar drug from the same class, has been studied extensively and is rated by the AAP as being usually compatible with feeding.

6 Light-Based Therapy

6.1 Blue–Violet and Red Light Phototherapy

This is thought to work via the absorption of light by endogenous porphyrins produced by *P. acnes*, which leads

to porphyrin activation, singlet oxygen production and subsequently bacterial death. Red light activates porphyrins to a lesser extent than blue light, but penetrates deeper into the skin [43]. Because it uses a specific, safe wavelength of light, blue light and red light are generally considered safe for use in pregnant and lactating women. Its safety is further affirmed by the use of blue light phototherapy to treat neonatal hyperbilirubinemia [44].

6.2 Photodynamic Therapy (PDT)

This is a two-step process that involves the application of a photosensitizing agent such as aminolevulinic acid (ALA) (C) prior to exposure to visible light. The preferential accumulation of photosensitizers in sebaceous glands helps augment the response to light therapy [43]. The safety of photosensitizers such as ALA in pregnancy and lactation is not well established, with both animal and human studies lacking. However, ALA-PDT has been used successfully to treat condyloma acuminata in pregnant women with no report of adverse pregnancy events [45]. Also, systemic absorption of the topically applied photosensitizer is expected to be insignificant, assuming the area of application is small.

7 Recommendations

In deciding whether to treat acne in pregnancy and lactation, as well as in choosing a specific therapy, the physician should consider the severity of acne, the potential risk of the drug in question and the patient's tolerance for risk taking. A summary of the risk categories of the drugs used for acne is presented in Table 3 and a suggested treatment algorithm is shown in Fig. 1. The clinical classification of the severity of acne in the algorithm is in accordance with the Combined Acne Classification System [46], and this is detailed in Table 4.

As with established guidelines [47, 48], we recommend the use of topical anti-acne medications as first-line treatment because of their low systemic exposure compared to drugs taken orally. However, women should be advised against applying copious amounts of topical drugs on inflamed skin over prolonged periods of time and over a large body surface area, as this may increase systemic absorption. Topical antibiotics are all likely to be safe, although information on newer agents such as nadifloxacin and dapsone is lacking. Comedolytics, consisting of topical benzoyl peroxide, salicylic acid and azelaic acid, are also safe in pregnancy and lactation. Benzoyl peroxide and azelaic acid have comparable efficacy [49] and contain antibacterial properties in addition to being a comedolytic [47]. Hence, their use is recommended over salicylic acid, which has only moderate comedolytic effects [48]. There are conflicting reports on the safety of topical retinoids in pregnancy; hence we advise against their use, especially since there are alternative comedolytic agents available.

If treatments with topical agents fail, systemic agents or phototherapy may be considered. Macrolides and cephalosporins are generally safe for use in pregnancy and lactation. We recommend erythromycin and azithromycin in view of their established effectiveness and their safety profile. Cephalexin has a good safety profile in pregnancy and lactation, but its efficacy is less well established compared to the macrolides. We do not recommend the use of co-trimoxazole and fluoroquinolones because of their associated risks. Zinc salts are an alternative for those who prefer not to consume antibiotics, but patients should be aware that results may be poorer than with the use of oral antimicrobial agents [50]. Light-based treatment consisting of blue–violet and red light phototherapy can be used safely, and they can be used as either as monotherapy or in addition to topical and oral therapies.

8 Conclusion

The level of evidence on the safety of acne therapies in pregnancy and lactation is low. Based on available data, we recommend the use of the following topical medications as first-line treatment: antibiotics (erythromycin, clindamycin, metronidazole and dapsone), benzoyl peroxide, azelaic acid and salicylic acid. Oral agents and/or light-based therapy may be considered as second-line treatment. The former consists of oral macrolides (erythromycin and azithromycin), cephalexin or zinc compounds. Blue–violet or red light phototherapy may be used as monotherapy or in addition to topical and/or oral therapies.

Conflict of interest The authors declare that they have no conflicts of interest.

References

1. Kamangar F, Shinkai K. Acne in the adult female patient: a practical approach. Int J Dermatol. 2012;51(10):1162–74.
2. Mays RM, Gordon RA, Wilson JM, et al. New antibiotic therapies for acne and rosacea. Dermatol Ther. 2012;25(1):23–37.
3. Feneran AN, Kaufman WS, Dabade TS, et al. Retinoid plus antimicrobial combination treatments for acne. Clin Cosmet Investig Dermatol. 2011;4:79–92.
4. Bozzo P, Chua-Gocheco A, Einarson A. Safety of skin care products during pregnancy. Can Fam Phys. 2011;57(6):665–7.
5. Fried RG, Wechsler A. Psychological problems in the acne patient. Dermatol Ther. 2006;19(4):237–40.
6. Wong JW, Heller MM, Murase JE. Caution advised in interpretation of US FDA risk classification for dermatological medications during pregnancy. Dermatol Online J. 2012;18(10):15.

7. Hale T. Medications and mothers' milk. 14th ed. Amarillo: Hale Publishing; 2010.
8. American Academy of Pediatrics Committee on Drugs. Transfer of drugs and other chemicals into human milk. Pediatrics. 2001;108:776.
9. LactMed: A New NLM Database on Drugs and Lactation. http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?LACT.
10. Hale EK, Pomeranz MK. Dermatologic agents during pregnancy and lactation: an update and clinical review. Int J Dermatol. 2002;41(4):197–203.
11. Rozex [package insert]. Watford: Galderma; 2012.
12. ACZONE (dapsone) gel [package insert]. Irvine: Allergan, Inc.; 2013.
13. Tuffanelli DL. Successful pregnancy in a patient with dermatitis herpetiformis treated with low dose dapsone. Arch Dermatol. 1982;118(11):876.
14. Sanders SW, Zone JJ, Foltz RL, et al. Hemolytic anemia induced by dapsone transmitted through breast milk. Ann Intern Med. 1982;96(4):465–6.
15. Webster GF. Is topical dapsone safe in glucose-6-phosphate dehydrogenase-deficient and sulfonamide-allergic patients? J Drugs Dermatol. 2010;9(5):532–6.
16. Jung JY, Kwon HH, Yeom KB, et al. Clinical and histological evaluation of 1% nadifloxacin cream in the treatment of acne vulgaris in Korean patients. Int J Dermatol. 2011;50(3):350–7.
17. Selcen D, Seidman S, Nigro MA. Otocerebral anomalies associated with topical tretinoin use. Brain Dev. 2000;22(4):218–20.
18. Autret E, Berjot M, Jonville-Béra AP, et al. Anophthalmia and agenesis of optic chiasma associated with adapalene gel in early pregnancy. Lancet. 1997;350(9074):339.
19. Loureiro KD, Kao KK, Jones KL, et al. Minor malformations characteristic of the retinoic acid embryopathy and other birth outcomes in children of women exposed to topical tretinoin during early pregnancy. Am J Med Genet A. 2005;136(2):117–21.
20. Panchaud A, Csajka C, Merlob P, et al. Pregnancy outcome following exposure to topical retinoids: a multicentre prospective study. J Clin Pharmacol. 2012;52(12):1844–51.
21. Leachman SA, Reed BR. The use of dermatologic drugs in pregnancy and lactation. Dermatol Clin. 2006;24:167–97.
22. Akhavan A, Bershad S. Topical acne drugs: review of clinical properties, systemic exposure, and safety. Am J Clin Dermatol. 2003;4:473–92.
23. Trivedi NA. A meta-analysis of low-dose aspirin for prevention of preeclampsia. J Postgrad Med. 2011;57(2):91–5.
24. The WHO Working Group, Bennet PN (ed). Drugs and human lactation. Oxford: Elsevier; 1988. p. 325–6.
25. Källén BA, Otterblad Olausson P, Danielsson BR. Is erythromycin therapy teratogenic in humans? Reprod Toxicol. 2005;20(2):209–14.
26. McCormack WM, George H, Donner A, et al. Hepatotoxicity of erythromycin estolate during pregnancy. Antimicrob Agents Chemother. 1977;12(5):630–5.
27. Hayashi N, Kawashima M. Efficacy of oral antibiotics on acne vulgaris and their effects on quality of life: a multicenter randomized controlled trial using minocycline, roxithromycin and faropenem. J Dermatol. 2011;38(2):111–9.
28. Czeizel AE, Rockenbauer M, Olsen J, et al. A case–control teratological study of spiramycin, roxithromycin, oleandomycin and josamycin. Acta Obstet Gynecol Scand. 2000;79(3):234–7.
29. Sorensen HT, Skriver MV, Pedersen L, et al. Risk of infantile hypertrophic pyloric stenosis after maternal postnatal use of macrolides. Scand J Infect Dis. 2003;35:104–6.
30. Harmon T, Burkhart G, Applebaum H. Transfer of probenecid and cephalexin into breast milk. Ann Pharmacother. 2006;40(5):986–9.
31. Fenner JA, Wiss K, Levin NA. Oral cephalexin for acne vulgaris: clinical experience with 93 patients. Pediatr Dermatol. 2008;25(2):179–83.
32. Rothman KF, Pochi PE. Use of oral and topical agents for acne in pregnancy. J Am Acad Dermatol. 1988;19(3):431–42.
33. Wenk RE, Gebhardt FC, Bhagavan BS, et al. Tetracycline-associated fatty liver of pregnancy, including possible pregnancy risk after chronic dermatologic use of tetracycline. J Reprod Med. 1981;26(3):135–41.
34. Spencer JP, Gonzalez LS 3rd, Barnhart DJ. Medications in the breast-feeding mother. Am Fam Phys. 2001;64(1):119–26.
35. Ho JM, Juurlink DN. Considerations when prescribing trimethoprim-sulfamethoxazole. CMAJ. 2011;183(16):1851–8.
36. Katsambas A, Dessinioti C. New and emerging treatments in dermatology: acne. Dermatol Ther. 2008;21(2):86–95 (Review).
37. Briggs GG, Freeman RK, Yaffe SJ, eds. Drugs in pregnancy and lactation. 5th ed. Baltimore: Williams & Wilkins; 1998.
38. Harmon T, Burkhart G, Applebaum H. Perforated pseudomembranous colitis in the breast-fed infant. Pediatr Surg. 1992;27(6):744–6.
39. Dréno B, Blouin E. Acne, pregnant women and zinc salts: a literature review. Ann Dermatol Venereol. 2008;135(1):27–33.
40. Martínez-Frías ML, Bermejo E, Rodríguez-Pinilla E, et al. Periconceptional exposure to contraceptive pills and risk for Down syndrome. J Perinatol. 2001;21(5):288–92.
41. Tankeyoon M, Dusitain N, Chalapati S, et al. Effects of hormonal contraceptives on milk volume and infant growth. WHO Special Programme of Research, Development and Research Training in Human Reproduction. Task force on oral contraceptives. Contraception. 1984;30:505–22.
42. Maloney ME, Stone SP. Isotretinoin and iPledge: a view of results. J Am Acad Dermatol. 2011;65(2):418–9.
43. Ross EV. Optical treatments for acne. Dermatol Ther. 2005;18(3):253–66.
44. McDonagh AF, Lightner DA. 'Like a shrivelled blood orange'—bilirubin, jaundice, and phototherapy. Pediatrics. 1985;75(3):443–55.
45. Yang YG, Zou XB, Zhao H, et al. Photodynamic therapy of condyloma acuminata in pregnant women. Chin Med J (Engl). 2012;125(16):2925–8.
46. Lehmann HP, Robinson KA, Andrews JS, et al. Acne therapy: a methodological review. J Am Acad Dermatol. 2002;47:231–40.
47. Archer CB, Cohen SN, Baron SE. Guidance on the diagnosis and clinical management of acne. Clin Exp Dermatol. 2012;37(Suppl 1):1–6.
48. Strauss JS, Krowchuk DP, Leyden JJ, et al. Guidelines of care for acne vulgaris management. J Am Acad Dermatol. 2007;56(4):651–63.
49. Graupe K, Cunliffe WJ, Gollnick HP, et al. Efficacy and safety of topical azelaic acid (20 percent cream): an overview of results from European clinical trials and experimental reports. Cutis. 1996;57(1 Suppl):20–35.
50. Dreno B, Moyse D, Alirezai M, et al. Multicenter randomized comparative double-blind controlled clinical trial of the safety and efficacy of zinc gluconate versus minocycline hydrochloride in the treatment of inflammatory acne vulgaris. Dermatology. 2001;203(2):135–40.