Safety of dermatologic agents in pregnancy

Compiled by: Sushil Pande, Vidya Kharkar
Department of Dermatology, KEM Hospital and Seth GS Medical College, Mumbai - 400012, India.

Address for correspondence: Dr. Sushil Pande, Department of Dermatology, KEM Hospital and Seth GS Medical College, Parel, Mumbai - 400012, India. E-mail: sushil_pande2003@yahoo.co.uk

Dermatologists need to be the familiar with the potential of medications to cause harm to the fetus or the mother. Moreover, safer alternatives are preferable in a woman of childbearing age, even if not pregnant.

The classification system indicating the level of safety of a particular drug during pregnancy was introduced by the US FDA.[1] All drugs are classified into the following categories:[1]

A) "Controlled studies show no risk. Adequate, well-controlled studies in pregnant women have failed to demonstrate risk to fetus".
B) "No evidence of risk in humans. Either animal findings show risk, but human findings do not; or, if no adequate human studies have been done, animal findings are negative".
C) "Risk cannot be ruled out. Human studies are lacking the animal studies are either positive for fetal risk or lacking as well. However, potential benefits may justify the potential risk".
D) "Positive evidence for risk. Investigational or post-marketing data show risk to fetus. Nevertheless, potential benefits may outweigh the potential risk".
X) "Contraindicated in pregnancy. Studies in animals or humans, or investigational or post-marketing reports, have shown fetal risk which clearly overweighs any possible benefit to the patient".

The following tables (Tables 1-3) enumerate the FDA category of the drugs commonly prescribed by dermatologists.

While the list of drugs appears exhaustive, it is still far

Table 1: Antihistamines[2]

Class of antihistamines	Examples	FDA class
First generation antihistamines		
Alkylamines	Chlorpheniramine	B
Ethanolaminine	Diphenylhydramine	B
Ethylenediamines	Tripelennamine	B
Phenothizines	Promethazine	C
Piperazine	Hydroxyzine	C
Piperazine	Cyproheptadine	B
Piperidines	Azatadine	B
Second generation antihistamines	Astemizole	C
	Azelastine	C
	Cetirizine	B
	Fexofenadine	C
	Loratadine	B
	Terfenadine	C

Table 2: Anti-infective agents

Anti-infectives	FDA class	Anti-infectives	FDA class
Antibacterial agents[2]			
Topical		*Systemic*	
Bacitracin	C	Penicillins	B
Mupirocin	C	Cephalosporins	B
		Erythromycin	B
		Azithromycin	B
		Clarithromycin	C
		Clindamycin	B
		Sulphonamides	B (D near term)
		Quinolones	C
		Metronidazole	B
		Vancomycin	C
Antifungals[2]			
Topical		*Systemic*	
Imidazoles	C	Griseofulvin	C
Miconazole	C	Ketoconazole	C
Ciclopirox	B	Fluconazole	C
Nystatin	B	Itraconazole	C
Naftifine	B	Terbinafine	B
Terbinafine	B		
Selenium sulphide	C		
Antiviral agents[2]			
Topical		*Systemic*	
Podophyllin	C	Acyclovir	B
Imiquimod	B	Famciclovir	B
		Valacyclovir	B
Antituberculous agents		**Antileprosy agents**	
Streptomycin	D	Dapsone	C

Isoniazid	C	Clofizamine	C
Rifampicin	C		
Pyrazinamide	C		
Ethambutol	B		
Ethionamide	C		
PAS	C		
Cycloserine	C		
Kanamycin	D[4]		
Antiretroviral agents[3]			
Nucleoside reverse transcriptase inhibitors			C
Non-nucleoside reverse transcriptase inhibitors			C
Protease inhibitors			C

Table 3: Miscellaneous agents

Agent	FDA class	Agent	FDA class
Anti-acne agents[2]			
Systemic		*Topical*	
Isotretinoin	X	Erythromycin	B
Tetracycline	D	Clindamycin	B
Erythromycin	B	Benzoyl peroxide	C
		Metronidazole	B
		Tretinoin	C
		Adapalene	C
		Azelaic acid	B
		Tazarotene	X
Agents to treat psoriasis[2]			
Systemic		*Topical*	
Acitretin	X	Tazarotene	X
Methotrexate	X	Calcipotriene	C
Cyclosporine	C	Glucocorticoids	C
Psoralens	C		
Analgesic agents			
Aspirin (full strength)	D	Rofecoxib	C[4]
Aspirin (low dose		Ketorolac	C
< 150 mg/day)	C[3]	Other NSAIDs	C
Ibuprofen	B (I trimester) D (II & III trimester)		
Hormonal agents[3]			
Androgens	D	Old contraceptive pills	X
Danazol	X	Non-steroidal estrogen	X
Estrogens (synthetic)	X		
Glucocorticoids[3]			
Systemic		*Topical*	
Cortisone	C	Fluticasone	C[4]
Hydrocortisone	C	Mometasone	C[5]
Prednisolone	C	Clobetasol	No data
Dexamethasone	C		
Beclomethasone	C[4]		
Betamethasone	C[4]		
Cytotoxic/Immunosuppressives/Immunomodulators			
Methotrexate	D[3]	5-Fluorouracil	D
Cyclophosphamide	D[4]	Azathioprine	D[4]
Hydroxychloroquine	C[4]	Gold salts	C
Mesalamine (5-ASA)	C		
Agents for gastroenterological diseases[3]			
H2 receptor antagonists			
Cimetidine	B	Famotidine	B
Ranitidine	B	Nizatidine	C
Promotility drugs			
Metaclopramide	C	Cisapride	C
Proton pump inhibitors			
Omeprazole	C	Lansoprazole	B
Prostaglandins			
Misoprostol	X		
Agents for neurological diseases			
Antidepressants			
Amitryptyline	D	Imipramine	D
Clomipramine	C	Doxepin	C
Sertraline	C	Amphetamine	C
Fluoxetine	C	Venlafaxine	C
Antianxiety agents[3]			
Alprazolam	D	Midazolam	C
Buspirone	D	Diazepam	D
Lorazepam	C		
Sedative/hypnotics			
Cyproheptadine	B	Promethazine	C
Phenobarbital	D		
Vitamins[3,4]			
Vitamin B1	C	Vitamin B2	C
Vitamin B6	A	Vitamin B12	C
Folic acid	A	Vitamin C	C
Vitamin E	C	Vitamin D	A, D
Vitamin A	A (X in high doses)		
Miscellaneous agents[3,4]			
Insulin	B	Potassium iodide	D
Heparin	C	Ketanserine	D
Nifedipine	C	Diltiazem	C
Spironolactone	X		
Iron	C		
Ethanol	X (if used in large doses)		
Permethrin (topical)	B[4]		

from complete. Moreover, adequate data is not available about the safety of many drugs.

Drugs which are absolutely contraindicated, including those agents in risk category X, should be strictly avoided. Occasionally, it may be necessary to treat a woman during pregnancy or lactation with a category C drug after weighing the pros and cons of both options and discussing them with the patient. Rarely, limited use for drugs even in category D under close supervision may be necessary.[5] Non-prescription drugs should also be avoided as far as possible.

REFERENCES

1. Sannerstedt R, Lundborg P, Danielsson BR, et al. Drugs during pregnancy: an issue of classification and information to prescribers. Drug Saf 1996;14:69-77.
2. Hale EK, Pomeranz MK. Dermatologic agents during pregnancy and lactation: an update and clinical review. Int J Dermatol 2002;41:197-203.
3. Mutalik N, Salvi V. Drugs in pregnancy. In: Salvi V, editor. Medical and surgical disorders in pregnancy, Mumbai: Jaypee Brothers Medical Publishers; 2003. p. 337-413.
4. Drugs in pregnancy and breastfeeding, Created:11/17/2000 Last update: 11/30/2002 http://www.perinatology.com/exposures/druglist.htm Last accessed: 20/12/2003.
5. Physician Desk References. 57th ed. Montwale NJ: Thomson PDR; 2003. p. 3054.
6. Kacew S. Fetal consequences and risks attributed to the use of prescribed and over-the-counter (OTC) preparations during pregnancy. Int J Clin Pharmacol Ther 1994;32:335-43.

Castellani's paint

Manish K. Shah
Hon Dermatologist, Bhatia General Hospital, Tardeo, Mumbai - 400007, India.

Address for correspondence: Manish K. Shah, Hon Dermatologist, Bhatia General Hospital, Tardeo, Mumbai - 400007, India.
E-mail: appletrue@hotmail.com

Castellani's paint was perfected in 1905 by Aldo Castellani (1878-1971), an Italian physician and a specialist in tropical diseases. Castellani's paint is an excellent preparation for tinea cruris and moniliasis of intertriginous areas.[1] It is effective in pustular dermatoses of the hands and feet,[2] and has also been recommended for pruritus ani and pruritus vulvae.[3] Colorless Castellani's paint may be used to reduce secondary bacterial contamination in onycholysis and in chronic paronychia.[4]

CASTELLANI'S PAINT[5]

Basic fuchsin	0.3
Ethyl alcohol 95%	10.0
Boric acid	1.0
Phenol liquef.	4.0
Acetone	5.0
Resorcinol	10.0
Water to	100.0

Sig: Apply to affected areas at night with a cotton-tipped applicator daily at night. Then dry and dust with talc.

A colorless variety exists that is cosmetically more acceptable and less irritating, but purportedly less effective:

Alcohol 90%	8.5%
Boric acid	0.8%
Phenol	4.0%
Acetone	4.0%
Resorcinol	8.0%
Water to	100.0%

ROLE OF THE INGREDIENTS

Magenta or basic fuchsin:[6] Basic fuchsin is a dark purple liquid that appears red on the skin and can stain. It has local anesthetic, bactericidal (Gram positive) and fungicidal properties. It has also been reported to stimulate granulation tissue and epithelialization.

Ethyl alcohol: This has been used in Castellani's paint for its cooling properties.

Boric acid: Boric acid presumably has been included for antiseptic properties. It is rarely used topically nowadays because it is toxic when absorbed.

Phenol: Phenol is basically a caustic agent, which at lower concentrations inhibits nerve endings, acting as an anti-pruritic. However, high concentrations over large areas on the body can be toxic, particularly for the kidneys.

Acetone: Acetone is a solvent with cooling and cleansing properties.

Resorcinol: Resorcinol is an important constituent of Castellani's paint. It has anti-pruritic, keratolytic, anti-mycotic and anti-eczematous properties.

PRECAUTIONS

Initial irritation or stinging may occur, and can be circumvented by using half-strength Castellani's paint for the first few times. Castellani's paint is preferably

avoided in infants and children because of the potential for percutaneous absorption of phenol.[7] Rarely, allergic eczematous contact dermatitis to resorcinol in Castellani's paint used to mark radiotherapy ports has been reported.[8] Patients need to be warned regarding the staining of the clothes with Castellani's paint.

CASTELLANI'S PAINT IN CONTEMPORARY PRACTICE

Castellani's paint dramatically improves inflamed tinea cruris and intertrigo of the groins, particularly in patients with a history of long-term topical steroid application. Applying Castellani's paint is an effective way to dry oozing lesions, particularly in the groins and the toe webs.[9]

REFERENCES

1. Litt JZ. Alternative topical therapy. Dermatol Clin 1989;7:43-52.
2. Rees RB. A compilation of alternative therapies. Dermatol Clin 1989;7:53-62.
3. Griffiths WAD, Wilkinson JD. Topical therapy. In: Champion RH, Burton JL, Burns DA, Breathnach SM, editors. Rook/Wilkinson/Ebling Textbook of Dermatology. Oxford: Blackwell Science; 1998.
4. Domonkos AN, Arnold HL Jr, Odom RB. Andrews' Diseases of the skin. Philadelphia: WB Saunders Company; 1982.
5. Arndt KA, Bowers KE. Manual of dermatologic therapeutics. Philadelphia: Lippincott, Williams & Wilkins; 2002.
6. Rogers SC, Burrows D, Neill D. Percutaneous absorption of phenol and methyl alcohol in Magenta paint BPC. Br J Dermatol 1978;98:559-60.
7. Marks JG Jr, West GW. Allergic eczematous contact dermatitis to radiotherapy dye. Contact Dermatitis 1978;4:1-2.
8. Bielan B. 'If it's wet, dry it; if it's dry, wet it.' Occup Health Saf 1978;47:23-4.