A Study Comparing the Use of 10% L-Ascorbic Acid and 10% Zinc Sulfate Solution in the Treatment of Melasma

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Wahyu Lestari

Abstract

Background Melasma is a hypermelanosis which is difficult to treat. There are several treatment options for melasma and one of them is topical therapy using 10% L-Ascorbic acid and 10% Zinc sulfate.

Aim To compare the efficacy and side effects of 8 weeks 10% L-Ascorbic acid solution with 10% Zinc sulfate on melasma.

Methods This is an observational study with cross sectional design and single-blind, comparing the left and right side of the faces sequentially (right-left comparison study) with each treatment 10% L-Ascorbic acid and 10% Zinc sulfate applied at night. In the morning and afternoon patients uses sunscreen SPF 30. Only new patients with melasma seen at Dermatology Polyclinic Dr M Djamil Hospital Padang from March 2012 to May 2012 were included in this study.

Results 20 melasma patients were studied. Their ages range from 25-54 years. 12 (60%) had combination triggering factors. All patients had epidermal type of melasma with 65% located over the centrofacial and 35% on the malar zones. After 2 months of treatment there was significant improvement of melasma treated with 10% Zinc sulfate and 10% L-Ascorbic acid with a P value of <0.05. Minimal side effects were found with Zinc sulfate.

Conclusion Improvement of melasma was noted with both topical 10% L-Ascorbic acid and 10% Zinc sulfate but minimal side effects were noted with the use of 10% Zinc sulfate.

Keywords: *Melasma, 10% L-Ascorbic acid, 10% Zinc sulphate*

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Introduction

Melasma, also called the 'mask of pregnancy' and cloasma, comes from the Greek 'melas" which means black, is hypermelanosis with light brown to dark brown (sometimes grayish or blue), irregular shaped on the sun-exposed areas, which develop slowly and symmetrically.[1-3] Melasma is more common in individuals from tropical countries including Indonesia. Melasma affects mainly women, and only about 10% in man. Generally, melasma is noted in adult, middle age and fertile woman.

Melasma is a cosmetic problem, especially in women, because of its location on the face.[4] Rizal Y, et al. (Indonesia, 2008) reported 405 cases of melasma in the Polyclinic of Dermato-Venereology Dr. M. Djamil Hospital Padang from 2001-2006. There were 8 male and 397 female patients.[5] Melasma can affect all races, but particularly in individuals with skin type IV-VI.[1]

The exact cause is unknown. The various precipitating factors include genetic influences, exposure to ultraviolet radiation, pregnancy, oral contraceptive, estrogen-progesterone therapy, thyroid dysfunction, cosmetics and photosensitizing and antiseizure medicine. Aetiology is unknown in a third of patients with melasma.[1-3] Diagnosis is based on symptoms and physical examination using Wood's lamp and rarely by histopathologic examination. Skin biopsy performed for histopathologic examination on the face should pay attention to the aesthetic aspect to prevent new complaint from the patients.[1-3] Current treatments include the routine use of broad-spectrum sunscreens[4] and skin lightening agents which aim to slow the proliferation of melanocytes, inhibit the formation of melanosomes and stimulate the degradation of melanosomes.[4-6]

L-Ascorbic acid 10% affects the monopherase activity of tyrosinase via its ability to reduce the enzymatically generated in the production or synthesis of melanin. This provide photo protection, preventing the absorption of UV radiation and antioxidants. Topical 10% Ascorbic acid has been shown to reduce the effect of 52% of erythema caused by UVB. Several studies have reported minimal side effects in the form of erythema which clears within 1-2 weeks, but L-Ascorbic acid is more expensive.[7]

Topical 10% Zinc sulfate has anti-inflammatory effect. Topical Zinc ions have been reported to have antioxidant effects which then provide skin photoprotection. Several studies have reported no side effects after use of 10% Zinc sulfate and the price is more economical than the other drug for depigmentation.[7,8] Sharquie KE, (Iraq, 2008) reported the use of 10% solution Zinc sulfate 2 times a day for 2 months for the treatment of melasma in 28 patients. The MASI score was reduced from 9.45 to 4.70.[9]

In this study, our aim was to compare the efficacy of 10% solution of L-Ascorbic acid and 10% solution Zinc sulfate in patients with melasma.

Patients and methods

The study was conducted at the Polyclinic of Dermato-Venereology Dr. M. Djamil Hospital Padang from March 2012 to May 2012. Diagnosis was based on anamnesis and physical examination. All patients had informed consent and explanation about the possible side effects from the medications. Inclusion criteria were adult women, aged 25-59 years with melasma. Exclusion criteria included pregnancy, lactation, hormonal contraceptive users, a malignancy of the face, history of hypersensitivity to 10% L-Ascorbic acid and 10% Zinc sulfate and had received any other form of treatment (less than 1 month ago).

A full history was taken from each patient, including personal history (age, sex, marital state, and occupation), family history, duration of melasma, relation to pregnancy, usage of oral contraceptive pills, relation to sun exposure, and previous therapy. Clinical examination and photographs of faces (left and right) were performed before and at the end of treatment.

The melasma area and severity index (MASI) score was calculated for each patient at baseline, every 2 weeks, and at the end of the 8-week follow-up period to accurately assess the severity of melasma before, during, and after treatment. The MASI is calculated on the basis of the area of involvement, darkness of melasma, and homogeneity of hyperpigmentation.

Four areas on the face were evaluated: forehead (f), right malar (rm), left malar (lm), and chin (c), which represented 30%, 30%, 30%, and 10% of the facial skin, respectively. The area (A) of involvement in each of these four areas was given a numerical value 0 to 6 (0, no involvement; 1, 1-9%; 2, 10-29%; 3, 30-49%; 4, 50-69%; 5, 70-89%; 6, 90-100%).

The severity of melasma was based on two factors: darkness (D) and homogeneity (H). These parameters were measured on a scale of 0 to 4 (0, absent; 1, slight; 2, mild; 3, marked; 4, maximum). Melasma area severity index scores were then calculated for each half of the face by using the following equation[7]:

0.15 (HF + DF) + 0.15 AF (DMR + HMR) AMR + 0.15 (DML + HML) AML + 0.05 (HC + DC) AC.

Global evaluation of improvement in response to therapy was done by the patient at baseline, every 2 weeks and at the end of treatment (8 weeks) and was scored as marked (>75% improvement), good (50% to <75% improvement), moderate (25% to <50% improvement), or mild (<25% improvement).[7] All side effects, including erythema, burn, and itching, were registered. Reduction of ≥ 40% of the value of MASI was taken as improvement, while reduction of <40% was classified as no improvement (nominal scale).

Clinical, Wood's lamp examination and digital photographs (frontal, right, and left views) were taken before starting treatment (baseline) and for every 2 weeks of the study and 2 weeks after the end of the treatment (8 weeks).[7-9] The Wood's light examination (nominal scale) enhanced pigment differences between melasma and normal skin color.[10,11]

Each patient received 10% Zinc sulfate (Brataco® pharmaceutical, 10% Zinc sulfate solution was prepared by dissolving 10 g of Zinc sulfate crystals (ZnSO4 _7H2O) in 100mL of distilled water) drug A, on the right face and 10% L-Ascorbic acid (Skinnase® pharmaceutical) drug B, on the left face and a sunscreen. The medication was applied on the face once daily at night, while the sunscreen was applied in the morning and afternoon. Participants were asked to record the side effects that arose and given an appointment card which contained the schedule for the next visit (every 2 weeks). Informed consent was obtained before treatment. The study was conducted after obtaining approval from the Ethics Committee of Dr. M. Djamil Hospital Padang.

Statistical Analysis

Statistical analyses was used for all parameters. A Wilcoxons test was used to compare the mean of MASI change resulting from treatment. A p-value of less than 0.05 was considered significant.

Results and Discussion

A. Demographic data

Twenty women were enrolled in this study with age ranging from 25 to 54 years, with a majority (35%) of patients in the 35-39 age groups (Table 1).

Table 1 Patients' demographic data.

Age Group	Number	%
25-29 year	1	5
30-34 year	3	15
35-39 year	7	35
40-44 year	4	20
45-49 year	3	15
50-54 year	2	10
55-59 year	-	-
Occupation		
House wife	6	30
Government employee	7	35
Self employed	7	35
Others	-	-

Table 2 Characteristics of aggravating factors for melasma.

Characteristics	Number	%
History of hormonal contraception		
Yes	12	60
No	8	40
Aggravating factors		
Sun exposure	4	20
Hormonal contraception	-	-
Cosmetics	4	20
Genetics	-	-
Combined	12	60

Table 3 Pattern of melasma and Wood's lamp examination.

Patient characteristic	Number	Percentage
Pattern of melasma		
- Centrofacial	13	65
- Malar	7	35
- Mandibular	-	-
Melasma type (Wood's lamp)*		
- Epidermal	16	80
- Dermal	-	-
- Mixed	4	20
Melasma type (Wood's lamp)**		
- Epidermal	16	80%
- Dermal	1	5%
- Mixed	3	15%

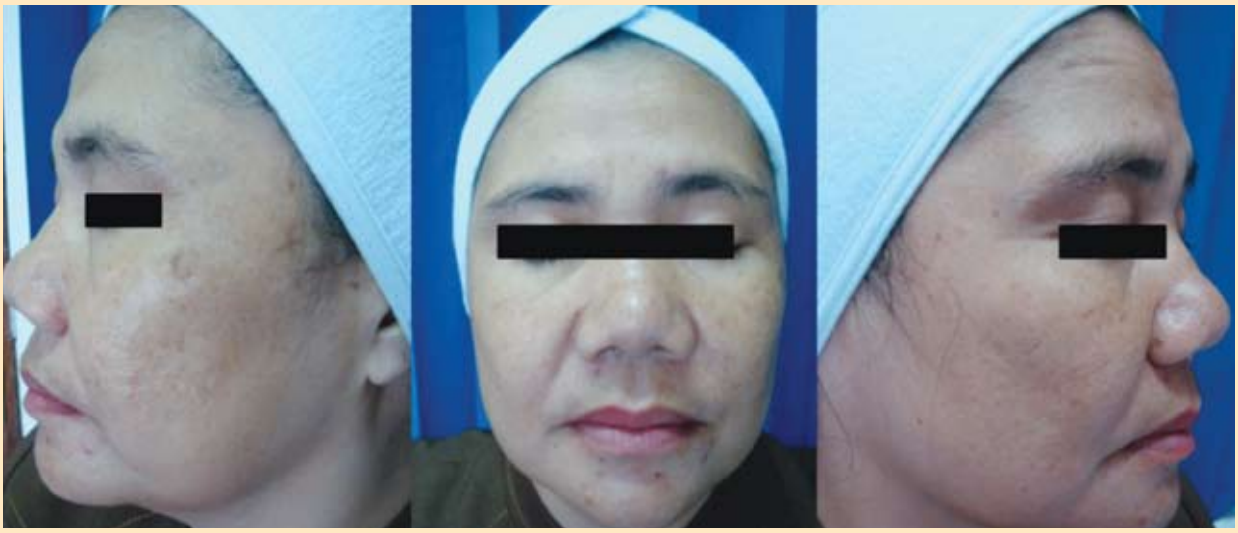
Table 4 Evaluation of response to treatment of melasma with 10% L-Ascorbic acid and 10% Zinc sulfate.

Characteristics	Clinical response				
Before therapy	**Excellent**	**Good**	**Moderate**	**Mild**	**Worst**
Ascorbic acid 10%	-	-	-	-	20
Zinc sulfate 10%	-	-	-	-	20
After therapy (2 weeks)					
Ascorbic acid 10%	-	-	-	-	20
Zinc sulfate 10%	-	-	-	-	20
(4 weeks)					
Ascorbic acid 10%	-	-	9	11	-
Zinc sulfate 10%	-	-	9	11	-
(6 weeks)					
Ascorbic acid 10%	-	-	15	5	-
Zinc sulfate 10%	-	-	16	4	-
(8 weeks)					
Ascorbic acid 10%	-	-	16	4	-
Zinc sulfate 10%	-	-	17	3	-

Table 5 MASI score and treatment with 10% *Ascorbic acid* (drug 1, *left face*) and 10% Zinc sulfate (drug 2, *right face*).

Day	Group	Average Score	SD	P
Day 0	Drug 1 Drug 2	11.23 10.35	3.42 3.65	0.1
Day 14	Drug 1 Drug 2	10.67 9.14	2.98 2.86	0.1
Day 28	Drug 1 Drug 2	7.49 6.57	2.42 2.02	0.08
Day 42	Drug 1 Drug 2	5.12 5.02	2.54 1.98	0.06
Day 56	Drug 1 Drug 2	4.34 4.06	1.23 1.04	0.05

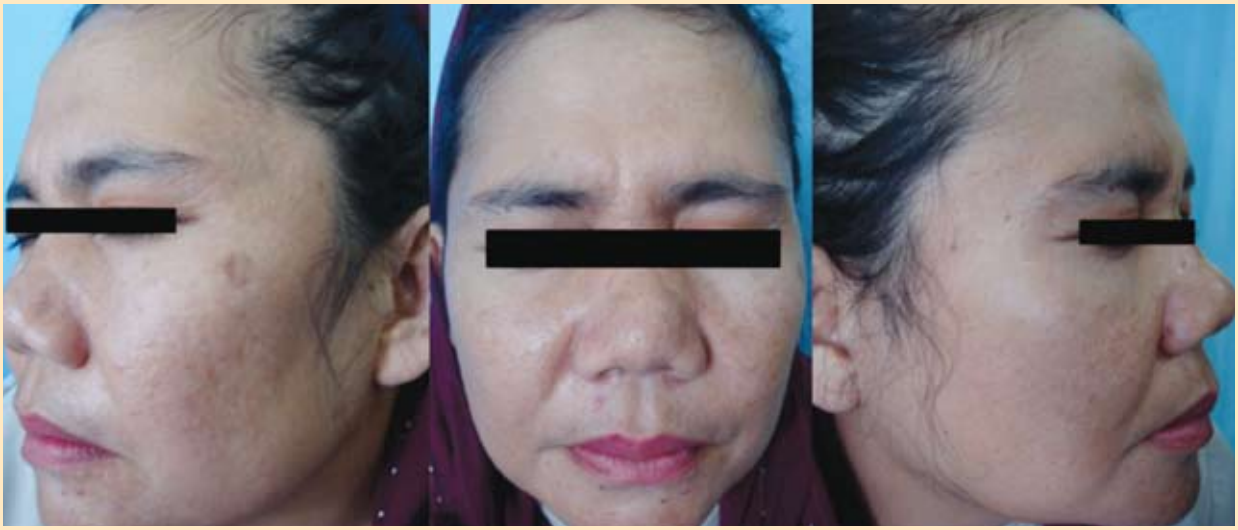
1. Before Treatment



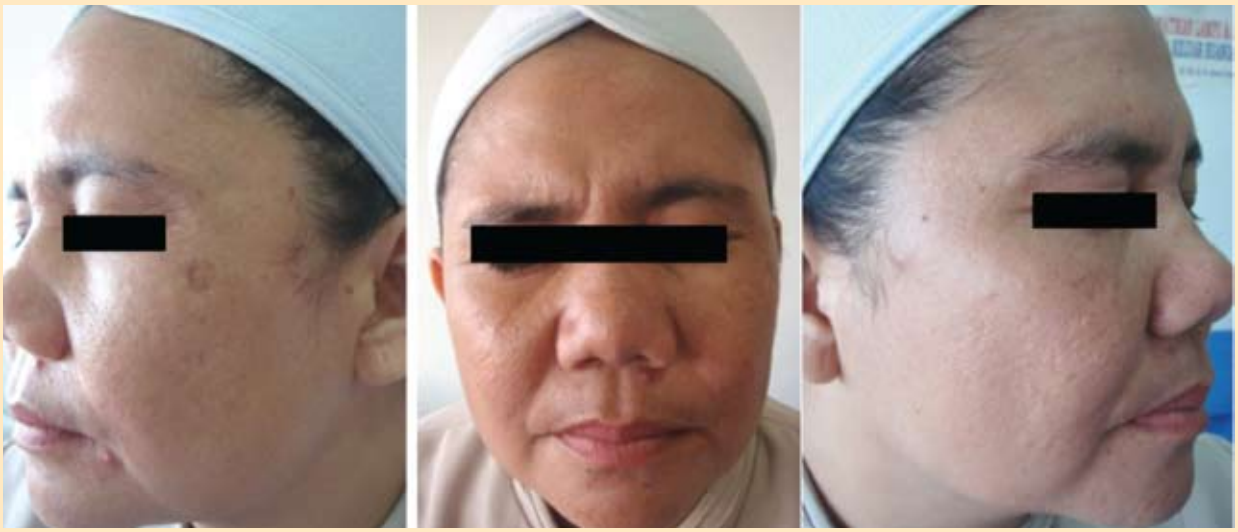
10% Ascorbic acid : left face

10% Zinc sulfate : right face

2. After Day 28



3. After Day 56



60% (n=12) had a combination of aggravating factors. Guinot C, et al. (Tunisia, 2010) reported that 60% of melasma appeared at the age of 30 years and the most common precipitating factors were sun exposure, pregnancy and oral hormonal contraception.[13]

Majority (65%) of the patients in this study have centrofacial patterns of melasma which is similar with other reports and the mandibular type is noted to be rare.[13,14] Our study did not have any patients with mandibular type.

The results of Wood's lamp examination showed that at the beginning of the study there were 16 patients (60%) with epidermal melasma and mixed type[4]. This is similar with previous studies with epidermal melasma being more common, approximately 72%.[14] After 8 weeks of treatment, 1 patient (5%) had dermal and 3 patients (15%) had mixed type. In this study, 1 patient with mixed type resulted into a dermal type probably indicating treatment success in removing epidermal melasma. This suggests that there is a reduction and or disappearance of the epidermal component, although this difference was not significant in both groups.

Several studies have reported topical treatment of melasma using these medications removing only the epidermal component.[14] No improvement of melasma with 10% L-Ascorbic acid and 10% Zinc sulfate were noted at 2 weeks therapy. After 4 weeks there was mild to moderate improvement. However, after 6 weeks treatment, there was moderate improvement in both treatment sites. After 2 months of treatment there was significantly more improvement with 10% L- Ascorbic acid as compared to Zinc sulfate 10%($p < 0.05$).

Up to day 28 of therapy, there was no significant difference between 10% L-Ascorbic acid and 10% Zinc sulfate (mean of 10% L-Ascorbic acid was 7.49±2.42 and the mean 10% Zinc sulfate was 6.57±2.02 (Table 5)).

On day 56 of therapy, there were significant differences: 10% L-Ascorbic acid was 4.34±1.23 and the 10% Zinc sulfate 4.06±1.04. It appears that 10% Zinc sulfate gave better results than 10% Ascorbic acid.

Sharquie KE, et al. (Iraq, 2008) reported the treatment of melasma with 10% solution Zinc sulfate twice daily for 2 months for treatment of melasma. The MASI scores decreased from 9.45 to 4.70 after treatment. Side-effects appeared in 3 patients with a mild stinging sensation.[12] Another study reported the use of Ascorbic acid with iontophoresis in 29 patients for 12 weeks. The MASI score decreased from 4.8 to 2.78 after treatment. Side-effects such as itching, erythema and burning occured in some patients.[6] Ochiai Y, et al. (Japan, 2006) reported the use of Ascorbic acid for treatment of hyperpigmentation. After 3 weeks there was suppression of the elevated intracellular peroxide after UVB irradiation, and enhanced cellular tolerance against UVB and reactive oxygen species such as hydrogen peroxide and tert-butyl hydroperoxide. Ascorbic acid reduced the production of interleukin-1a and prostaglandin E2 in UVB-irradiated keratinocytes and suppressed melanocyte proliferation in conditioned culture medium prepared from UVB-irradiated keratinocytes.[13]

Conclusions

Both 10% L-Ascorbic acid and 10% Zinc sulfate reduced the MASI score in melasma patients although 10% Zinc sulfate gave better results with minimal side effects. Clinical improvement was noticed after 1 month of treatment based on reduction in the MASI score. Side effects in patients treated with 10% L-Ascorbic acid included redness and pain, whereas 10% Zinc sulfate only caused a mild itch which resolved within a week. However, further research is needed using a larger number of patients and a longer observation period.

Acknowledgement

We would like to thank Skinnase® pharmacy for their support.

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Acne Management Clinical Practice Guideline (CPG)

Asmah J.

The Acne Management Clinical Practice Guideline (CPG) was launched on 5th June 2012 in Institut Perubatan Respiratori (IPR), Kuala Lumpur by Dato' Dr Zaininah Mohd. Zain, the Director of Kuala Lumpur Hospital on behalf of the Director General of Health, Dato' Dr Hasan Abdul Rahman.

This is the first evidence based CPG launched for dermatology under the guidance of Health Technology Assessment Section, Ministry of Health. The CPG was developed for almost 3 years as all evidence had to be reviewed thoroughly. The development committee also had to assess its relevance in Malaysian Health Care system. It serves as a guide for local doctors especially in primary care to optimize treatment before referral is made to a dermatologist or plastic surgeon for other specific treatment or management.

This topic was initially chosen as acne is a common problem among adolescents and young adults. It has a wide spectrum of clinical severity with different types of treatment modalities. There is also a wide variation in the prescribing patterns; hence the treatment may not be standardized to our expectation. It also provides a very good reference for medical students to improve their knowledge.

The development committee consists of a group of dermatologists, Datin Dr Asmah Johar (Chairperson), Dr. Noor Zalmy Azizan, Dr. Chang Choong Chor, Dr. Ng Ting Guan, Dr. Lee Yin Yin and other relevant personnel involved were Ass. Prof. Dr. Leelavathi Muthupalaniappen (Family Medicine Specialist), Dr. Norraliza Md. Zain (Family Medicine Specialist), Dr. Siti Irma Fadhilah Ismail (Clinical Psychologists), Dr. Zahara Abdul Manaf (Dietitian), Ms Lui Wei Qi (Pharmacist), Dr. Mohd. Aminuddin Mohd. Yusof (Public Health Physician) and Mariammah Krishnasamy (Scientific Officer).

The review committee consists of senior dermatologist, Datuk Dr. Roshidah Baba, Head of Dermatology Services (Chairperson), Puan Sri Datuk Dr. Suraiya H. Hussein, Dr. Choon Siew Eng, Dr. Pubalan Muniandy, Dr. Rohna Ridzwan, Dr. Ting Hoon Chin, Dr. Mohd. Noh Idris, Dr. Mardziah Alias and other members include Dr. Suraya Yusoff (Psychiatrist) and Datin Dr. Rugayah Bakri (from Health Technology Assessment).

The CPG addresses on various sections including recently updated and more established acne pathophysiology, risk and aggravating factors including the role of diet and supplements and quality of life assessment. For dermatologists, it offers a good review on pharmacology and non-pharmacology treatment response up to 31st July 2011.

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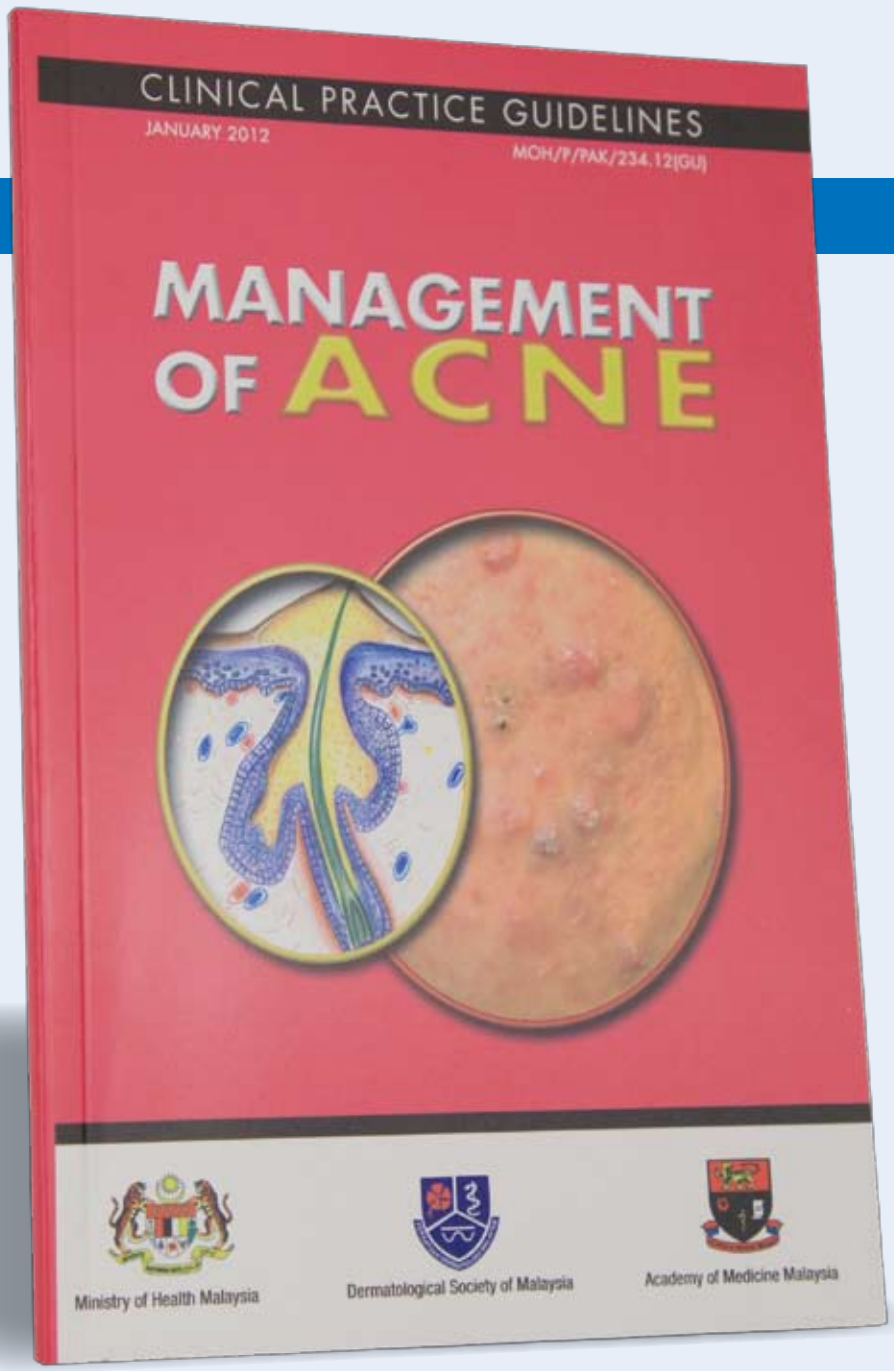
This CPG has an important guide on appropriate treatment algorithm, recommendations and a quick reference. Provision of well designed training module for implementation and patient information leaflet will encourage utilization of CPG. Download is available from the Ministry of Health website.



2013 American Academy of Dermatology Annual Meeting

Organizers American Academy of Dermatology

Venue Miami, Florida

Date March 1-5, 2013

Program website www.aad.org

The International Affairs Committee of the American Academy of Dermatology (AAD) offers attendance scholarships to two (2) young dermatologists per country to attend the AAD's 2013 Annual Meeting, March 1-5, 2013 in Miami, Florida.

Publication in Dermatology from Malaysia

Title

Jernel Dermatologi Malaysia, Volume 1

Now also known as Malaysian Journal of Dematology

Chief Editor

Founding editor Chow Kim Weng followed by Rosidah Baba, Mardziah Omar, Najeeb Safdar, Henry Foong and currently Rohna Ridzwan

Publisher

Published for Persatuan Dermatologi Malaysia (Dermatological Society of Malaysia), 1987

KDN 1505(6813)/10

ISSN 1511-5356 (YEAR 1999)

Synopsis

Jernel Dermatologi Malaysia is currently known as Jurnal Dermatologi Malaysia according to the updated Malay thesaurus. The journal is written in English, published annually but as off 2009, there are 2 issues published yearly. Initial paper written focus on review article by invitation only, case reports and case series. With the inception of post-graduate training for Masters in Advance Dermatology in Malaysia, original papers and clinical trials were written to be shared not only among Malaysian community but also to those in Western Pacific Region after it was accepted by Western Pacific Research Index Medicus in November 2010.

Title
Dermatologi Asas

Author
BA Adam

Publisher
Universiti Malaya
1991

Synopsis
Malay textbook in Dermatology for medical students and medical officers.

Title
Current treatment in Dermatology

Author
Adam, Basheer A

Publisher
Universiti Malaya
1994

Synopsis
Dermatology Textbook in English for medical students and medical officers.

Title
Consensus statement - The Management of Psoriasis

Author
Chow Kim Weng &nd the team from Malaysian Dermatological Society

Editor
Academy Medicine of Malaysia
1996

Synopsis
Guideline of psoriasis care for Malaysian dermatologists.

Title
A Guidebook on Histological Diagnosis of Inflammatory Skin Diseases

Editor
P]ayalakshmi, H H Suraiya, A Kreetharan

Published
2001

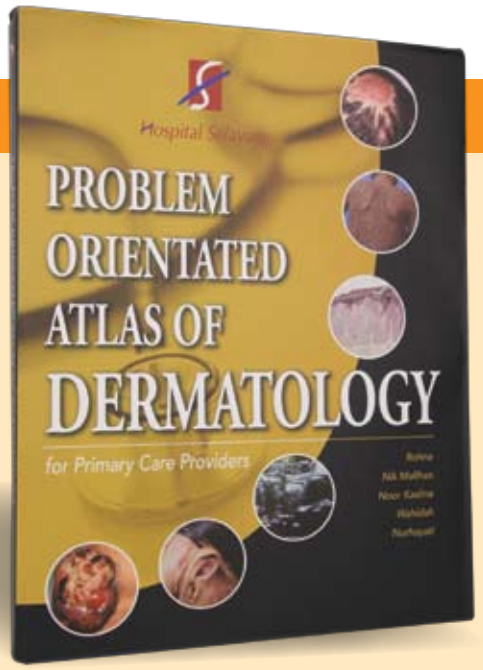
Synopsis
This book is to be commended for the Medical Officer or GP confronted with a patient with a skin disease and could also be useful for the 1st year trainee specialist in dermatology.

Title
Contact & Occupational Dermatitis - Lecture Notes for Beginners

Author
Rohna Ridzwan

Publisher
Self
2012
ISBN 978-967-10420-1-4

Synopsis
Quick hand book for primary, secondary and tertiary dermatology care providers to recognising and managing contact and occupational dermatitis.



Title

Problem Orientated Atlas of Dermatology for Primary Care Providers

Author

Rohna Ridzwan, Nik Malihan, Noor Kaslina, Wahidah, Nurhayati Mokhty

Publisher

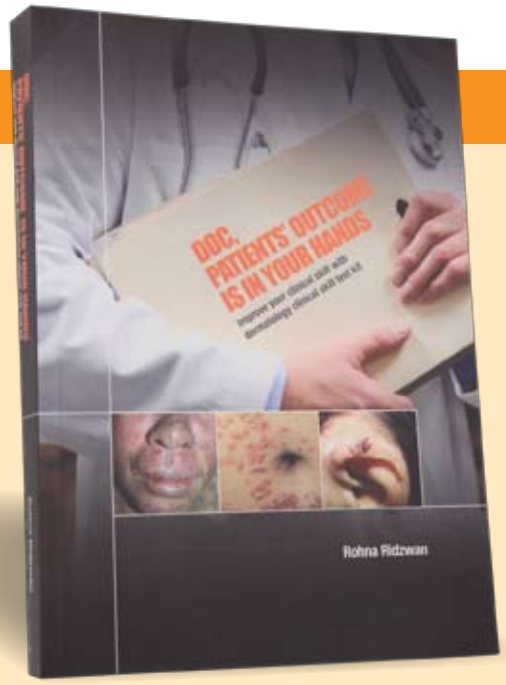
Selayang Hospital

2004

ISBN 983-420140-0-6

Synopsis

Problem orientated approach to diagnosing skin lesions according to sites and characteristic of skin lesion.



Title

Doc, patients' outcome is in your hands. Improve your clinical skill with dermatology clinical skill test kit

Author

Rohna Ridzwan

Publisher

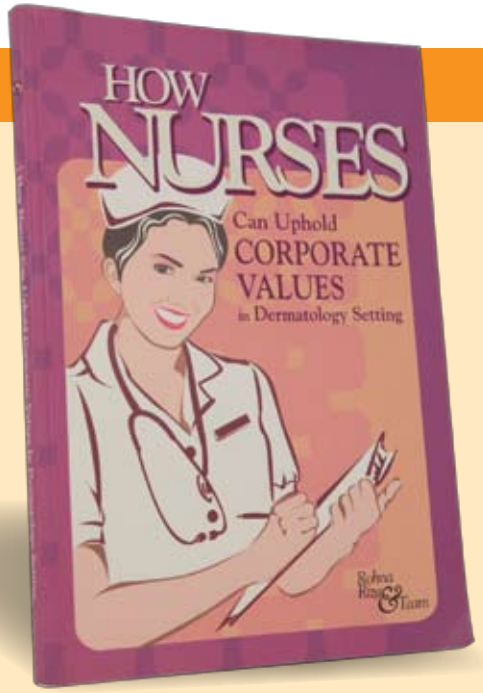
Self

2011

ISBN 978-967-10420-0-7

Synopsis

Skin slides with multiple choice questions. Patients' outcome can be predicted by the diagnosis chosen by the doctor.



Title

How nurses can uphold corporate values - In dermatology setting

Author

Rohna Ridzwan, Riza & Team

Publisher

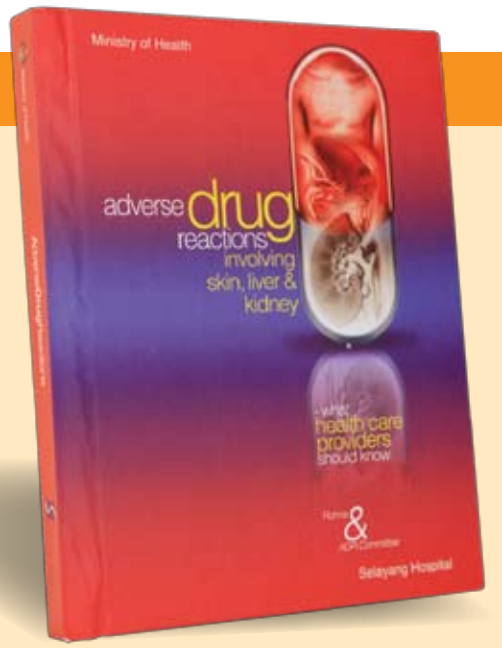
Selayang Hospital

2004

ISBN 983-42140-1-4

Synopsis

This book aid nurses to prioritize scheduling of patients with skin diseases, being professional, courteous and caring to patients in the clinic, ward and in day care centre.



Title

Adverse drug reactions involving skin, liver & kidney - what health care providers should know

Editor

Rohna Ridzwan, Tan Soek Siam, Ghazali TV Ahmad Kutty

Publisher

Ministry of Health, Malaysia

2006

ISBN 983-42140-2-2

Synopsis

This book alert first line health providers on the early signs of adverse drug reactions and reduce delay in therapy.

Title

Rahsia Jerawat Terbongkar - Bagaimana Mengawal Jerawat Dalam Masa 60 Hari

Author

Hasseenah Hassan

Publisher

Self

2012

Ebook available through http://www.drhasseenah.com/jerawa

Synopsis

Controlling acne written in Malay by a private clinician practising aesthetic medicine.

Title

Penyakit Kulit Kanak-Kanak

Author

Wan Ghazali Wan Mohamed

Publisher

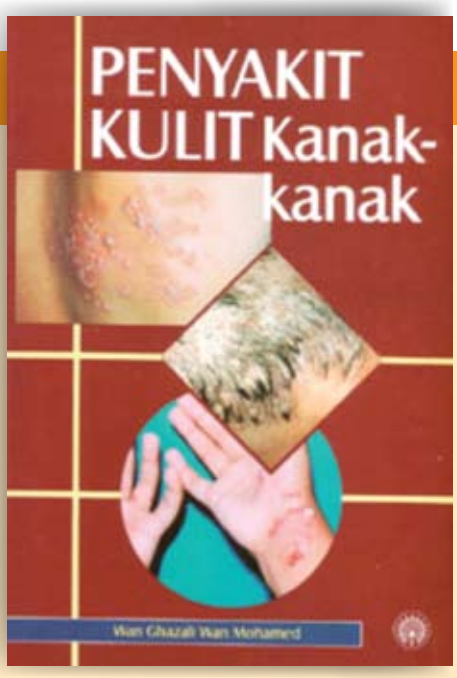
Kuala Lumpur; Dewan Bahasa Pustaka

2002, 2006

ISBN 9836271961

Synopsis

Malay textbook on skin diseases in children for the general public especially parents and kindergarten supervisor.



contents

GENERAL DERMATOLOGY

PAEDIATRIC DERMATOLOGY

DERMATOLOGY THERAPEUTICS

ANOUNCEMENT