YEAR BOOK OF DERMATOLOGY - 2019

FUNGAL INFECTIONS

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Foreword
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Section 1: Epidemiological Studies

ARTICLE 1

Antifungal Activity of Silver Nanoparticles on Fluconazole Resistant Dermatophytes Identified by (GACA)4 and Isolated from Primary School Children Suffering from Tinea Capitis in Ismailia – Egypt

Amin ME, Azab MM, Hanora AM, et al. Antifungal activity of silver nanoparticles on fluconazole resistant dermatophytes identified by (GACA)4 and isolated from primary school children suffering from Tinea capitis in Ismailia – Egypt. ***Cell Mol Biol. 2017;63(11):63-7.***

Abstract

The treatment of fungal infections in the recent times have become challenging due to the problems like relapses and drug resistance. The available antifungal drugs have seen the emergence of resistant strains due to improper usage. This study was conducted to determine the antimycotic activity of silver nanoparticles in cases of tinea capitis who are resistant to fluconazole. The results showed that the silver particles can be used for the treatment of tinea capitis caused by *Trichophyton violaceum* but not for *Microsporum canis* or *Microsporum gypseum*.

COMMENT

The treatment of dermatophytosis ranges from topical and systemic therapy depending upon the site and the extent of involvement. Tinea capitis usually affects children and systemic agents are the mainstay of treatment. The gold standard agent for the treatment of tinea capitis in children is griseofulvin. The other agents which can be used are terbinafine, itraconazole and fluconazole.

This study was performed to determine the antimycotic effect of silver nanoparticles against fluconazole resistant species of dermatophytes. This study was conducted in cases of tinea capitis who did not respond to fluconazole. The study included 112 cases of which 70 samples showed culture positivity. The organisms isolated were *Trichophyton violaceum, Microsporum gypseum* and *Microsporum canis*. The susceptibility of silver nanoparticles was tested with disk diffusion technique and other methods. The results showed that only *Trichophyton violaceum* was susceptible to silver nanoparticles whereas the other two species did not respond to it. The drawback of this study is that fluconazole is not usually preferred in the treatment of tinea capitis in the presence of other agents. The result showed that only one organism is

susceptible to this drug and the others do not and hence this drug can be given only to those cases which are caused by *T.violaceum* which can be determined only by culture.

Key Message

- ***Silver nanoparticles effective in fluconazole resistant cases caused by Trichophyton violaceum.***

ARTICLE 2

Interdigital Tinea Pedis Resulting from *Fusarium* Species in Dakar, Senegal

Diongue K, Diallo MA, Ndiaye M, et al. Interdigital tinea pedis resulting from *Fusarium* species in Dakar, Senegal. ***J Mycol Med. 2018;28(1):227-31.***

Abstract

Tinea pedis is a dermatophyte infection involving the soles of the foot. Interdigital type of tinea pedis is also encountered. This study was conducted to highlight the incidence of *Fusarium* as a cause of interdigital type of tinea pedis. *Fusarium* as the causative agent of tinea pedis is not common. This article shows that fusarium can be a causative agent and should be treated early before hematogenous dissemination occurs.

COMMENT

Fungal infection of the interdigital web spaces are caused by dermatophytes and *Candida* yeasts. Rarely it can be caused by *Fusarium* species. In this study which was conducted in Dakar, it was observed that *Candida* was most common cause of interdigital fungal infection followed by *Fusarium* and trailed by dermatophytes. This was a retrospective study conducted to highlight the fact that *Fusarium* species should be considered while treating cases of interdigital tinea pedis. The study was performed with KOH examination and fungal culture. It was found that *Fusarium* was the causative agent in 45% of cases and was common in the age group belonging to fourth decade. Also, it was seen commonly in immunocompetent individuals. The early recognition of this entity is important because if untreated or improperly treated it may lead to the hematogenous dissemination of the fungus.

Key Messages

- ***Fusarium species can be considered as the differential in the interdigital fungal infections***
- ***Early recognition is required to prevent hematogenous dissemination.***

ARTICLE 3

Emergence of African Species of Dermatophytes in Tinea Capitis: A 17-Year Experience in a Montreal Pediatric Hospital

Marcoux D, Dang J, Auguste H, et al. Emergence of African species of dermatophytes in tinea capitis: A 17-year experience in a Montreal pediatric hospital.
Pediatr Dermatol. 2018;35:323-8.

Abstract

Tinea capitis is the dermatophyte infection of the scalp commonly seen in children. The etiological agents of tinea capitis differs in different parts of the world depending on the geographical conditions. This study was conducted in Canada in patients of tinea capitis. The infection was common in African migrants and infection in family members was also seen. *Microsporum audouinii* was the commonest isolate and it was resistant to terbinafine.

COMMENT

Tinea capitis is common in children before puberty due to the absence of sebum secretion which acts as a natural fungistatic action. The causative agent of tinea capitis differs in parts of the world due to change in the geographical factors required by the fungus. This retrospective study was performed because it was found that the rise in dermatophytosis caused by African species was noted in countries receiving African migrants. This study was conducted in Canada and the retrospective data suggests that there was six times the increase in dermatophytosis caused by African species.

The incidence of tinea capitis was high among children of African immigrants. Boys were commonly affected and preschool children were more affected. *Microsporum audouinii* was the common organism isolated

and this agent is known to cause epidemics of tinea capitis. The isolate in this study was resistant to terbinafine. This study shows the importance of the geographical factors and immigration in isolation of new species in a new territory.

Key Messages

- ***Microsporum audouinii was the common organism isolated and this agent is known to cause epidemics of tinea capitis. The isolate in this study was resistant to terbinafine***
- ***This study shows the importance of the geographical factors and immigration in isolation of new species in a new territory.***

ARTICLE 4

Topical Tavaborole in the Treatment of Onychomycosis Complicated by Dermatophytoma: A Post-hoc Assessment of Phase II Subjects

Aly R, Winter T, Hall S, et al. Topical tavaborole in the treatment of onychomycosis complicated by dermatophytoma: A Post-hoc assessment of phase II subjects.
J Drugs Dermatol. 2018;17(3):347-54.

Abstract

Tavaborole is an antifungal medication approved by FDA in the treatment of onychomycosis in the year 2014. This study was conducted to determine the efficacy of topical tavaborole in the treatment of onychomycosis which is complicated by the formation of dermatophytoma. This randomized controlled trial is in the phase II and the results are from this phase. The results show that topical tavaborole is effective in the treatment of onychomycosis as well in cases of onychomycosis complicated by dermatophytoma formation.

COMMENT

Onychomycosis is the fungal infection of the nail caused by dermatophytes as well as non-dermatophytes. The diagnosis of onychomycosis is made clinically though various conditions like nail psoriasis and other conditions may mimic the presentation. Adding to this difficulty is the formation of dermatophytoma, an entity which is not known to many. A dermatophytoma presents as linear white/yellowish discoloration of

the nail plate due to the formation of biofilm by the dermatophytes which is composed of fungal filaments and spores attached together by an extracellular polysaccharide material leading to poor treatment response even after oral antifungal therapy.

The ideal treatment for the treatment of onychomycosis with dermatophytoma is by surgical/chemical treatment. This study was conducted to determine the efficacy of topical tavaborole in the treatment of onychomycosis complicated by dermatophytoma formation.

This study is a randomized controlled trial, still in the phase II has published its results. The results show that 24% of the patients of onychomycosis treated by this drug had complete resolution of the condition by 6 months and follow-up for 1 year showed that 26% of the patients had complete resolution. The findings show that topical tavaborole is quite effective in the treatment of onychomycosis complicated by dermatophytoma, the treatment of which was considered to be surgical/chemical in the past.

Key Message

- ***Topical tavaborole is effective in cases of onychomycosis complicated by dermatophytoma formation.***

ARTICLE 5

In vitro Antifungal Susceptibility Profiles of 12 Antifungal Drugs against 55 *Trichophyton schoenleinii* Isolates from Tinea Capitis Favosa Patients in Iran, Turkey and China

Deng S, Ansari S, Ilkit M, et al. In vitro antifungal susceptibility profiles of 12 antifungal drugs against 55 *Trichophyton schoenleinii* isolates from Tinea capitis Favosa patients in Iran, Turkey, and China.
Antimicrob Agents Chemother. 2017;61(2):e01753-16.

Abstract

Trichophyton schoenleinii, a dermatophyte causes superficial fungal infections of which it is the causative agent of inflammatory type of tinea capitis, favus. This study was conducted to evaluate the most susceptible antifungal agent against *Trichophtyton schoenleinii*. In this in vitro study, the samples of the fungus was obtained from the last 30 years from Iran to China. The results showed that ketoconazole and terbinafine were the most potent antifungal agents against *T. schoenleinii*.

COMMENT

The epidemiological and mycological study of dermatophytosis has to be performed because of its importance in the changing pattern of causative agents of dermatophytosis and the susceptibility to antifungal agents. Favus is the inflammatory type of tinea capitis which is rare and seen commonly in the Kashmir valley. This type of tinea capitis is caused by *Trichophyton schoenleinii* although other dermatophytes belonging to the zoophilic and geophilic types can cause the condition.

Griseofulvin is considered to be the gold standard drug for the treatment of tinea capitis in children, but the susceptibility of agents to the drug has decreased and this may lead to the administration of larger doses and longer duration of treatment. Other drugs like terbinafine and itraconazole have shorter duration of treatment and have fungicidal effect even after stoppage of the drug. So this study was conducted to determine the most potent antifungal agent for favus. Isolates from 55 tinea capitis patients belonging to Iran, China and Turkey were chosen and cultured and later tested for drug susceptibility. Various antifungal agents that were tested are griseofulvin, fluconazole, itraconazole, terbinafine, ketoconazole, miconazole and amphotericin B.

The results showed that except for fluconazole and flucytosine all the other drugs had inhibitory effect on *T. schoenleinii*. The most potent drugs to act against this organism were terbinafine and ketoconazole. This study gives us knowledge regarding the choice of antifungal agents in favus (tinea capitis) which is the least researched entity. The study results show that this can be applied to all geographical regions. More studies are required to support this.

Key Messages

- ***All drugs except fluconazole and flucytosine had inhibitory effect on T. schoenleinii***
- ***The most potent agents were terbinafine and ketoconazole.***

ARTICLE 6

Characterizing the Clinical Isolates of Dermatophytes in Hamadan City, Central West of Iran, Using PCR-RLFP Method

Farokhipor S, Ghiasian SA, Nazeri H, et al. Characterizing the clinical isolates of dermatophytes in Hamadan city, Central west of Iran, using PCR-RLFP method.
J Mycol Med. 2018;28(1):101-5.

Abstract

Dermatophyte infections are encountered all over the world most commonly in the tropical regions. The diagnosis is mainly clinical but in order to know the epidemiological features, one should perform cultures and subcultures to identify the species causing the infection. This study was performed to analyse the use of molecular techniques like polymerase chain reaction and restricted fragment length polymorphism for the epidemiology of dermatophytic infections.

COMMENT

Fungal culture and subculture techniques are performed for the identification of the species in clinical or research purposes. But the disadvantage of the above techniques is that they are time consuming and the results are not accurate all the time. This study was performed to determine the epidemiology of the dermatophytes using molecular techniques like PCR and RFLP.

The samples collected were examined by direct microscope and cultures and later the isolates were identified using PCR technique using the Mval enzyme. The results showed that most common type of infection noted was tinea pedis followed by others. *Trichophyton interdigitale* was the common isolate followed by *Trichophyton rubrum*.

The study showed that molecular techniques can be used in epidemiological studies for faster and accurate identification of the causative species of dermatophytes.

The last decade has seen lot of new developments in the field of biotechnology and molecular sciences which has led to easier and faster diagnosis of many diseases. The disadvantage of the above techniques is that the facility is not available in all centres in developing nations and also the cost of the techniques is quite high which is not affordable for everyone in the developing nations.

Key Message

- ***The study showed that molecular techniques can be used in epidemiological studies for faster and accurate identification of the causative species of dermatophytes.***

ARTICLE 7

A Comparative Study of the Various Patterns of Oro-cutaneous Fungi and their Sensitivity to Anti-fungals between HIV Patients and Normal Healthy Individuals

Vijendran P, Verma R, Hazra N, et al. A comparative study of the various patterns of oro-cutaneous fungi and their sensitivity to anti-fungals between HIV patients and normal healthy individuals.
Medical Journal Armed Forces India. 2018.

Abstract

Human immunodeficiency virus infection can have cutaneous manifestations in the form of cutaneous infections like bacterial, fungal and viral as well as other malignancies like Kaposi sarcoma. This study was performed to determine the etiological agents, clinical spectrum and drug sensitivity among HIV population and comparing it with normal healthy individuals.

COMMENT

The HIV virus causes depletion of the helper T cells thereby leading to decrease in host immunity and leads to development of opportunistic infection. Among these, cutaneous infections are the most common manifestation. Atypical presentations are commonly encountered in HIV individuals and resistance to therapy is commonly encountered. This study was conducted to find out the clinical spectrum, etiological agents of fungal infections caused in HIV patients and comparing them with normal healthy population.

Skin samples in the form of swabs and scales were collected from the inguinal, dorsum of tongue and toe web spaces and direct microscopy and culture was performed.

The results showed that HIV patients are more commonly affected from fungal infections compared to normal population. It was also observed that HIV patients harbor fungi even without clinical manifestation. This should be kept in mind while treating patients with HIV.

Key Messages

- ***HIV patients are more commonly affected from fungal infections compared to normal population***
- ***HIV patients harbor fungi even without clinical manifestation.***

ARTICLE 8

Frequency of Fungal Species of Onychomycosis between Diabetic and Non-diabetic Patients

Sultana S, Jaigirdar QH, Islam MA, et al. Frequency of fungal species of onychomycosis between diabetic and non-diabetic patients.
Mymensingh Med J. 2018;27(4):752-6.

Abstract

Onychomycosis is the fungal infection of the nails caused by either dermatophytes or yeasts or non dermatophytic organisms. Onychomycosis can be frequently in diabetic patients or sometimes in cases of immunosuppressed patients. The present study was performed to find out the differences in causative agents of onychomycosis between diabetics and nondiabetics. The result showed that dermatophytes was commonly isolated in diabetic patients whereas *Candida* species and other non-*Candida albican* species.

COMMENT

This study was performed to isolate the common organisms causing onychomycosis in diabetic and nondiabetic population. The causative agents in normal individuals and diabetic individuals vary and the importance in treatment duration depending upon the organisms grown.

This was a cross-sectional study conducted in Bangladesh and clinically diagnosed patients of onychomycosis were divided into diabetic and non-diabetic groups. Routine investigations like direct microscopy and culture was performed in all the samples. The results were later then compared between the two groups.

The results showed that *T. rubrum* and *T. mentagrophytes* were commonly seen in diabetic patients whereas in non-diabetic patients *Candida albicans* and other species of *Candida* was seen. This information is important because the management between the two categories differs. Terbinafine is usually not effective against yeasts but effective against dermatophytes. Also the duration of treatment can vary between the two groups. The drawback of this study is the small sample size and more studies with larger sample size is required to determine the accurate pattern of onychomycosis among diabetics.

Key Message

- ***Onychomycosis caused by dermatophytes was commonly seen in diabetic patients whereas Candida species and other non-Candida albican species were isolated in non-diabetic patients.***

ARTICLE 9

Examining the Accuracy of Visual Diagnosis of Tinea Pedis and Tinea Unguium in Aged Care Facilities

Goto T, Nakagami G, Takehara K, et al. Examining the accuracy of visual diagnosis of tinea pedis and tinea unguium in aged care facilities.
J Wound Care. 2017;26(4):179-83.

Abstract

This study was conducted to determine the accuracy of the visual diagnosis to aid in detecting skin problems like onychomycosis and tinea pedis in elderly population which are residing in the nursing homes and long-term health care facilities. This is a cross-sectional study in which a dermatologist performs a clinical examination in the intertriginous area of the finger and foot, later based on suspicion direct microscopy with KOH and culture was performed. It was found that scaling was more commonly observed in cases of tinea infection and not in others. The study showed that tinea infections are seen in elderly individuals but correlation was not found between the results.

COMMENT

Skin disorders are commonly found in elderly population and is frequently found in elderly people residing in old age homes and orphanages. This cross-sectional study was performed to determine the accuracy of visual diagnosis by a dermatologist to aid in detecting skin problems like onychomycosis and tinea pedis.

The study was conducted by macroscopic examination of the skin lesions in the two intertriginous area and foot and nails for detecting tinea pedis and onychomycosis. After examination, cases who are clinically suspicious of tinea infection were subjected to direct microscopic examination and culture for confirmation of the clinical diagnosis.

The results showed that scaling was commonly observed in elderly patients having tinea pedis and onychomycosis. The accuracy of diagnosis with clinical examination alone is low and hence other investigations are required to improve the diagnosis rate. Also, the correlation between the two methods were not satisfactory.

Key Message

- ***The accuracy of diagnosis of tinea pedis and onychomycosis with clinical examination alone is low and hence other investigations are required to improve the diagnosis rate.***

ARTICLE 10

Incidence and Biodiversity of Yeasts, Dermatophytes and Non-dermatophytes in Superficial Skin Infections in Assiut, Egypt

Moubasher AH, Abdel-Sater MA, Soliman Z. Incidence and biodiversity of yeasts, dermatophytes and non-dermatophytes in superficial skin infections in Assiut, Egypt.
J Mycol Med. 2016;27:166-79.

Abstract

This study was conducted to determine the incidence of yeasts, dermatophytes and non-dermatophyte infections and to isolate the causative organism causing each. The results showed that yeasts were the common agents isolated and onychomycosis cases were commonly found followed by tinea capitis.

COMMENT

This study is a prospective study in which patients presenting with dermatophytosis, onychomycosis were clinically examined and subjected to direct microscopic examination, fungal culture and identification. The samples were collected form hair, nail clippings and skin scrapings.

The results showed that onychomycosis was the commonly seen followed by tinea capitis in this study culture was positive in 96 cases and KOH positivity was seen in 45 cases. Yeasts were grown majority in culture followed by non-dermatophyte organisms. Dermatophytes were grown in approximately 16% of the cases and this was leaded by *Aspergillus* species.

It can be concluded that yeasts were commonly isolated followed by non-dermatophyte organisms. The study recommends direct microscopy and culture for mycological evaluation of the fungal specimens.

This study shows that etiological agents of fungal infections vary across the globe and treating physicians must be aware of the same to aid in proper drug selection and treatment.

Key Messages

- ***Yeasts were the common agents isolated and onychomycosis cases were commonly found followed by tinea capitis in this study***
- ***Dermatophytes were not commonly isolated in this study.***

ARTICLE 11

A Phase 2, Controlled, Dose-Ranging Study of SB208, an Investigational Topical Nitric Oxide-releasing Drug, for the Treatment of Tinea Pedis

Elewski BE, Kircik LH, Stasko N, et al. A Phase 2, Controlled, Dose-Ranging Study of SB208, an Investigational Topical Nitric Oxide-releasing Drug, for the Treatment of Tinea Pedis.
J Drugs Dermatol. 2018;17(8):888-93.

Abstract

Tinea pedis is the dermatophytic infection of the feet, the treatment of which depends on the type and extent of involvement. This randomized controlled trial was conducted to evaluate the effectiveness of the new drug SB208, a topical nitric oxide-releasing drug for the treatment of tinea pedis. The results showed that the drug provided good mycological cure and can be considered as an alternative agent for the treatment of dermatophytosis, in particular tinea pedis.

COMMENT

This randomized controlled trial was conducted to evaluate the safety and efficacy of the new drug SB208, a topical nitric oxide releasing drug for the treatment of tinea pedis. This drug is a new drug of berdazimer sodium and hydrogel which releases nitric oxide at the lesional area.

The study was performed by comparing the effect of the active drug and vehicle alone in patients at day 14 and 42. The drug was administered once daily. The patients were selected after clinical examination and followed by fungal culture and cases positive by fungal culture alone were included in this study. After 14 days culture was performed to assess the mycological cure.

At day 14 more patients in group treated with SB208 had mycological cure than the vehicle group. At day 42, greater number of patients in SB208 group showed mycological cure compared to vehicle group. The drug was considered to be relatively safe and had no major side effects. This shows that the drug is effective and well tolerated in the treatment of tinea pedis.

Key Messages

- ***SB208 is a novel topical nitric oxide-releasing agent for the treatment of tinea pedis***
- ***The drug was considered to be relatively safe and had no major side effects.***

YEAR BOOK OF DERMATOLOGY - 2019
FUNGAL INFECTIONS

Key Features

- The Year Book of Dermatology – 2019 *Fungal Infections* brings to you a collection of meticulously chosen articles focusing on the recent advances in the management of fungal infections
- Articles selected from various peer reviewed journals that were published in the last 12-month period
- The book is divided into sections covering articles on epidemiology, diagnosis and management of fungal infections
- Each article has been reviewed by subject reviewers who have written comments on value of the article, previous knowledge on the subject, what the article adds to the prevailing knowledge and practices, strong points and weaknesses of the article and other similar observations
- Each article is accompanied by key messages, summarizing the article as well as highlighting the clinical experience of the reviewers
- A must read book for dermatologists, physicians, and postgraduate students.

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