Chapter: One

Introduction

1.1 Introduction:

Human infestation by *Sarcoptes scabiei var hominis*, an obligate human parasite that lives its entire life cycle in and on the skin causes scabies. Scabies affects all races and social classes worldwide, but accurate figures of its prevalence are difficult to obtain. A study by Downs *et al*. on data collected in the UK between 1967 and 1996 showed a high incidence of scabies in the late 1960s and early 1970s, a drop during the 1980s, and arise throughout the 1990s[1]. Incidence of scabies is quite high in Bangladesh-India-Pakistan subcontinent. In Bangladesh, out of total population suffering from skin diseases, 80% of them are suffering from scabies and pyogenic infection[3]. In a community based cross sectional study, scabies was found in the second position among the infectious skin diseases in a rural area of Bangladesh[4].According to Bangladesh Health Service Report 1989; scabies encountered 10.08% and 9.30% of morbidity in 1988 and 1989 respectively[5].

The scabies mite is an arthropod of the order Acarina which was 1st identified in the 1600s[2].The mite cannot fly or jump; it lives its entire 30days cycle in and on epidermis. The female mite burrows into the stratum coreum and lays eggs then passes through the stages of egg, larvae, nymph and adult mite[2]. Scabies is usually transmitted by close physical contact, such as prolonged hand-holding or the sharing of a bed[6].Itching is usually the most obvious manifestation of scabies. It is generally worst at night and when the patient is warm. The onset occurs 3–4 weeks after the infection is acquired, and coincides with a widespread eruption of inflammatory papules. Reinfection of a previously cured individual, however, provokes immediate symptoms.The pathognomonic lesions of scabies are burrows, which appear as slightly raised, brownish, tortuous lesions . Burrows occur on the wrists, the borders of the hands, the sides of the fingers and the finger web spaces, the feet, particularly the instep and, in males, on the genitalia. They are often present on the palms and soles of young children and the elderly[7].The pruritic papules that accompany the development of hypersensitivity occur predominantly around the axillae, in the areolar regions, on the abdomen, particularly the periumbilical region, and on the buttocks and thigh. Indurated, inflammatory nodules sometimes occur, particularly on the axillae, groins, scrotum and penis[8]. In addition to these primary manifestations, secondary features like excoriation or eczematous changes are common. Secondary infection, manifest as folliculitis or impetigo, may also be severe and extensive. In the

tropics and subtropics, where nephritogenic strains of β-haemolytic streptococci may be responsible for secondary sepsis, glomerulonephritis occurs as a complication of scabies[9].

There have been many suggested remedies for scabies including topical sulphar, 5% permethrin, benzyl benzoate, malathion, lindane, crotamiton , Monosulfiram and topical and systemic ivermectin. The choice of therapy is determined not only by efficacy and potential toxicity, but also by considerations such as cost, ease of application, the presence of secondary eczematization and the age of the patient[1].

Permethrin 5% cream is an effective scabicide. It should be washed off after 8–12 h, with a second application after an interval of a week. At present, it is the topical treatment of choice[1]. Permethrin is a synthetic derivative of the insecticide pyrethrum and function as a neurotoxin to mites and has low toxicity to human. But topical treatment has the disadvantage of being cumbersome, time consuming and associated with treatment failure. The failure is due to poor compliance i.e. insufficient topical application of drug, technique of application, inappropriate frequency or inadequate treatment of close contacts[10].

The only oral but highly effective scabicidal known to date is Ivermectin[2]. It was discovered in 1970s and structurally similar to macrolid antimicrobials which is isolated from the Streptomyces avermitilis. Since its discovery, it has been approved for the treatment of strongyloidiasis and onchocerciasis[2]. Ivermectin It binds to glutamate gated chloride channels (GABA mediated, present in nerve and muscle cells).This binding increase membrane permeability to chloride ions which causes hyperpolarization of nerve or muscle cell. These results in neuromuscular paralysis of the organism[11].A single dose of 200 µg/kg body weights will be effective in many cases of ordinary scabies but, presumably because of a lack of ovicidal activity, higher cure rates are obtained with two doses separated by an interval of a week[1]. Because it is effective, inexpensive, and easy to administer, ivermectin might prove particularly useful in the management of institutional outbreaks of scabies[12].

1.2 Overview of Scabies

Definition

Scabies is a well-known infection caused by a tiny burrowing mite called by *Sarcoptes scabiei var hominis* that results in a particularly relentless and devastating itch that starts out slowly and increase. Mite barely visible to the naked eye, burrows into the epidermis and lays eggs, triggering a host immune response that leads to intense itching in response to just a few mites. Scabies infestation is frequently complicated by bacterial infection, leading to the development of skin sores that, in turn, can cause more serious consequences such as septicemia, heart disease and chronic kidney diseases in severity over time[18]

Disease burden

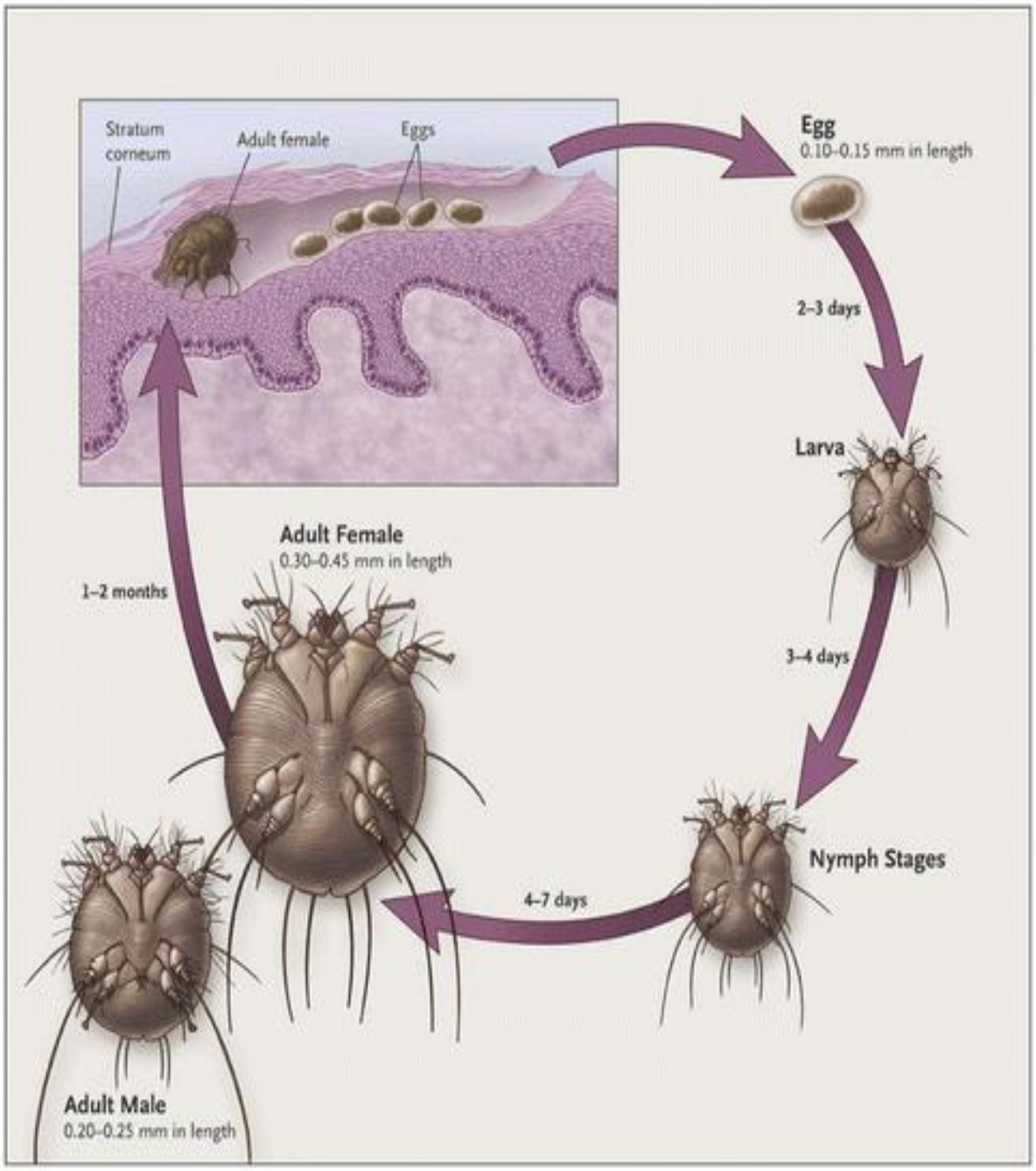
Scabies is one of the commonest dermatological conditions, accounting for a substantial proportion of skin disease in developing countries. Globally, it affects more than 130 million people at any time. Rates of scabies occurrence vary in the recent literature from 0.3% to 46%. In the developed world, outbreaks in health institutions and vulnerable communities contribute to significant economic cost in national health services. However, in resource-poor tropical settings, the sheer burden of scabies infestation, as well as their complications, imposes a major cost on health-care systems. In 2010, it was estimated that the direct effects of scabies infestation on the skin alone led to more than 1.5million YLDS (years lived with disability), and the indirect effects of complications on renal and cardiovascular function are far greater[18].

Distribution

Scabies affects people from every country. However, it is the most vulnerable, young children and the elderly in resource-poor communities who are especially susceptible to scabies as well as to the secondary complications of infestation. The highest rates occur in countries with hot, tropical climates, where infestation is endemic, especially in communities where overcrowding and poverty coexist[18].

Causes

Sarcoptes is a genus of skin parasites and part of the larger family of mites collectively known as scab mites. These organisms have eight legs as adults, and are placed in the same phylogenetic class (Arachnida) as spiders and ticks. *Sarcoptes scabiei* mites are under 0.5 mm in size but are sometimes visible as pinpoints of white. Pregnant females tunnel into the dead, outermost layer (stratum corneum) of a host's skin and deposit eggs in the shallow burrows. The eggs hatch into larvae in three to ten days. These young mites move on the skin and molt into a "nymphal" stage, before maturing as adults, which live three to four weeks in the host's skin. Males roam on top of the skin, occasionally burrowing into the skin. In general, the total number of adult mites infesting a healthy hygienic person with non-crusted scabies is small; about 11 females in burrows on average and can spread to other areas of the skin or to the skin of other people[19].They can only live off of a host body for 24-36 hours under most conditions.



Life Cycle of *Sarcoptes scabiei*

Transmission

Transmission of the mites involves close person-to-person contact of the skin-to-skin variety, so risk factors include close contact with an infected person. It is hard but not impossible, to catch scabies by shaking hands, hanging your coat next to someone who has it, or even sharing bedclothes that had mites in them the night before. Sexual physical contact, however, can transmit the disease. In fact, sexual contact is the most common form of transmission among sexually active young people, and scabies has been considered by many to be a sexually transmitted disease (STD). However, other forms of physical contact, such as mothers hugging their children, are sufficient to spread the mites. Over time, close friends and relatives can contract it this way, too. School settings typically do not provide the level of prolonged personal contact necessary for transmission of the mites [22].

Pathophysiology

The symptoms are caused by an allergic reaction of the host's body to mite proteins, though exactly which proteins remains a topic of study. The mite proteins are also present in the gut, feces of the mite, which are deposited under the skin. The allergic reaction is both of the delayed (cell-mediated) and immediate (antibody-mediated) type, and involves IgE (antibodies, it is presumed, mediate the very rapid symptoms on reinfection). The allergy-type symptoms (itching) continue for some days, and even several weeks, after all mites are killed. New lesions may appear for a few days after mites are eradicated. Nodular lesions from scabies may continue to be symptomatic for weeks after the mites have been killed[19].

Signs and symptoms

The characteristic symptoms of a scabies infection include intense itching and superficial burrows[20]. The burrow tracks are often linear, to the point that a neat "line" of four or more closely placed and equally developed mosquito-like "bites" is almost diagnostic of the disease. Because the host develops the symptoms as a reaction to the mites' presence over time, there is typically a delay of three to four weeks between the onset of infestation and the onset of itching. Similarly, symptoms often

persist for one to several weeks after successful eradication of the mites. As noted, those re-exposed to scabies after successful treatment may exhibit symptoms of the new infestation in a much shorter period—as little as one to four days[21].

Itching

In the classic scenario, the itch is made worse by warmth, and is usually experienced as being worse at night, possibly because there are fewer distractions. As a symptom, it is less common in the elderly[20].

Rash:

Commonly involved sites of rashes of scabies

The superficial burrows of scabies usually occur in the area of the finger webs, feet, ventral wrists, elbows, back, buttocks, and external genitals. Except in infants and the

immunosuppressed, infection generally does not occur in the skin of the face or scalp. The burrows are created by excavation of the adult mite in the epidermis[20].
In most people, the trails of the burrowing mites are linear or *s*-shaped tracks in the skin often accompanied by rows of small, pimple-like mosquito or insect bites. These signs are often found in crevices of the body, such as on the webs of fingers and toes, around the genital area, in stomach folds of the skin, and under the breasts of women[23].

Symptoms typically appear two to six weeks after infestation for individuals never before exposed to scabies. For those having been previously exposed, the symptoms can appear within several days after infestation. However, it is not unknown for symptoms to appear after several months or years.[16]Acropustulosis, or blisters and pustules on the palms and soles of the feet, are characteristic symptoms of scabies in infants[23].

Crusted scabies

Also called Norwegian scabies, crusted scabies is a severe form of scabies. People who have crusted scabies have 100s or even 1,000s of mites in their skin. By comparison, most people who get scabies have 15 to 20 mites on their skin. Crusted scabies develops in people who have a weak immune system due to a medical condition, the elderly, and people who are living in institutions. Crusted scabies develops when the person's body cannot develop any resistance to the mites. Without resistance, the mites quickly multiply. A common sign of crusted scabies is widespread crusts on the skin. These crusts tend to be thick, crumble easily when touched, and look grayish in color. Sometimes the crusts appear on 1 or a few areas of the body such as the scalp, back, or feet[24].

Sequelae

Scratching can lead to inoculation of the skin with bacteria (particularly *Staphylococcus aureus* and *Streptococcus pyogenes*), leading to the development of impetigo (skin sores), especially in the tropics. Impetigo can, in turn, be complicated by deeper skin infection such as abscesses, as well as serious invasive disease and sepsis in infants. In tropical settings, scabies-associated skin infection is a common risk factor for immune-mediated complications such as acute post-

streptococcal glomerulonephritis and possibly rheumatic heart disease. Evidence of renal damage can be found in up to 10% of children with infected scabies in resource-poor settings and, in many, this persists for years following infection contributing to permanent kidney damage. Recurrent infestations are common[18].

Diagnosis

Diagnosis of scabies is based on clinical recognition of the typical features. These comprise an itchy patient with linear burrows and vesicles around the wrists and especially finger webs, on the soles of the feet and ankles, and sometimes on the head in infants. Prolonged itching leads to the development of scabies nodules, which in adults are often found on the genital area, especially the penis and scrotum as well in areas around the breast. Additionally, asymptomatic family members may also have burrows in the finger webs. Itching occurs only if the individual reacts to the presence of the mite.

An uncommon but important clinical variant is “crusted scabies”. This condition occurs particularly in some immuno-suppressed patients, including those with HIV/AIDS, and is characterized by hyper-infestation with millions of mites, producing widespread scale and crust, often without significant itching. Patients with crusted scabies are important to identify as they are a significant source of reinfection to the rest of the surrounding community[18].

Ink test

The burrows of scabies mites can be identified by using an ink test. Ink is rubbed around an area of itchy skin before being wiped off with an alcohol pad. If scabies burrows are present, some of the ink will remain and will have tracked into the burrows, showing up as a dark line.

To confirm the diagnosis, a skin sample may be gently scraped from the affected area so it can be examined under a microscope for evidence of scabies mites, their eggs and faces.

Management

There are a number of treatments for scabies which have various level of effectiveness.[2] Most treatment modalities available are topical e.g. Sulphur, Benzyl benzoate, Malathion, Crotamiton, Monosulfiram, Permethrin, Lindane.[7] 5 to 10% sulfur in paraffin, an agent used widely in Africa and South America; 1% lindane, which is no longer used in many Western countries because of concerns regarding neurotoxicity; 10 to 25% benzyl benzoate, which is often used in Europe and Australia; malathion; 10% crotamiton and 5% tea-tree oil is used in combination with benzyl benzoate.[12]

Permethrin 5% cream is the most widely used and most effective & safe medication for scabies. The only oral but highly effective scabicidal known to date is Ivermectin.[2] A recent Cochrane review of randomized controlled trials of drug treatments for scabies concluded that topical permethrin appears to be the most effective treatment for scabies, whereas ivermectin appears to be an effective oral agent.[29] Best results are obtained by treating the whole household at the same time. Secondary management involves prompt treatment of the complications of scabies, such as impetigo using appropriate antibiotics or antiseptics[18].

Brief information about Permethrin & Ivermctin are given below;

Permethrin

Permethrin is a synthetic pyrethroid used as an approximate 2 :3 mixture of the 3-phenoxybenzyl (6) *cis*- and *trans*- 3-(2,2-dichlorovinyl)-2,2 dimethylcyclopropanecarboxylate.[27]

Dosages formulation

Permethrin is available as a 5% cream (Elimite) for the topical treatment of scabies and as a 1% cream rinse (Nix) for treatment of head lice.[27]

Pharmacokinetics

After application of the permethrin 5% cream, mean systemic absorption is less than 1–2% owing to its minimal percutaneous absorption.

Permethrin is metabolized through ester cleavages and virtually all of the absorbed permethrin is excreted in the urine within 1 week.[27]

Mechanism of action

It acts on the nerve cell membrane to disrupt the sodium channel current by which the polarization of the membrane is regulated. Delayed repolarization and paralysis of the mite are the consequences of this disturbance.[28]

Indications

1. Scabies

Multiple compiled trials comparing permethrin 5% cream, crotamiton, topical lindane, and oral ivermectin suggest that permethrin 5% cream is the treatment of choice for scabies, as noted by the 2007 Cochrane Review.[27]

2. Pediculosis

Pyrethrins with piperonyl butoxide and permethrin 1% cream rinse (Nix) are approved by the FDA for the treatment of head lice and are available over the counter[27]

How to use Permethrin Cream

Apply the medicine from your head to the soles of your feet, including under your nails and in skin folds such as between the toes, as directed. Massage the cream into the skin. Wash off the cream after 8-14 hours by showering or taking a bath.
They should be reapplied in 7–10 days because neither is reliably ovicidal.[28]

Adverse effect

There have been no reported adverse reactions other than local irritation[27]

Contraindications

Permethrin Cream, 5% is contraindicated in patients with known hypersensitivity to any of its components, to any synthetic pyrethroid or pyrethrin[28]

Ivermectin

Ivermectin is a semisynthetic antihelminthic derived from the fermentation products of *Streptomyces avermitilis.* It is the 22,23-dihydro derivative of avermectin B1.[29]

Dosages formulation

Ivermectin is available as topical as well as oral formulation. In oral form 3mg & 6mg tablet is available.

Pharmacology

Peak serum levels is about 4 hours

Plasma half-life is about 18 hours

Metabolism is primarily hepatic, with excretion in feces

Bioavailability is increased when the drug is administered with a high-fat meal.[29]

Mechanism of action[29]

I. Ivermectin binds selectively to glutamate-gated chloride ion channels found in invertebrate nerve and muscle cells.
II. Binding results in increased permeability of cell membranes to chloride ions
III. Hyperpolarization of the nerve or muscle cells resulting in death of the parasite.

Indication

1. FDA – approved indication

- Onchocerciasis
- Strongyloidiasis

. 2. Off-label indication

- Scabies
- Pediculosis
- Filariasis
- Cutaneous larva migrans

- Infestations caused by *Ascaris lumbricoides*, *Enterobius vermicularis* (pinworm), *Mansonella ozzardi*, *Gnathostomia spingerum*, *Mansonella streptocera*, and *Trichuris trichiura* (whipworm)[29]

Therapeutic guidelines

Dose range from 150 to 400 µg/kg.
In the treatment of scabies, 200 µg/kg (which is roughly 1 mg/10 pound body weight) is commonly given as a single dose, and repeated in a week to 10 days.
For lice, a single 400 µg/kg dose has been given on day 1 and day 8.[29]

Adverse effect

There are few significant adverse reactions. The following reactions to ivermectin have been reported in >10% of patients in the setting of helminthic infestations. They are less common in the setting of scabies infestation.[29]

1. Mazzotti-type reaction: The overall incidence of rashes, including edema and urticaria, is 23% in the setting of helminthic infestation.
2. Pruritus (28% in the setting of helminthic infestation)
3. Fever (23% in the setting of helminthic infestation)
4. Lymphadenopathy or lymph node tenderness

Less frequent reactions include tachycardia, facial edema, orthostatic hypotension, diarrhea, and nausea. CNS symptoms like ataxia, headache are rarely occur.

Contraindication[29]

1. Ivermectin should not be used during pregnancy, as safety in pregnancy has not been established.
2. Use of ivermectin is not recommended during lactation.
3. It is not recommended for children under 15 kg or age <5years as well as for geriatric patients.

Control and elimination

Population control of scabies and its complications has been identified by some countries as a public health priority and an International Alliance for the Control of

Scabies (IACS) is now working as a global network committed to this goal. Treatment of individuals with scabies and their contacts is unlikely to achieve this goal, and so there is increasing interest in implementing a mass drug administration (MDA) strategy. Large studies of MDA using oral ivermectin versus topical treatment are under way. An important aspect of control and elimination programmes is their integration into existing clinical and public health programmes and systems[18].

1.3 Rationale of the research:

Scabies is an ectoparasitic disease which is a common diseases in OPD of dermatology dept. of most of the hospitals. It is highly contagious and prevalence of scabies is more common in congested or densely populated area like slum area. Individual with close contact with the infected person should be treated with scabicidal. Oral treatment is more convenient and cost effective than topical treatment. In this study, we will evaluate efficacy of oral ivermectin and topical permethrin in the treatment of scabies. It would be helpful to select more effective and easily administrable drug in the treatment of scabies in the endemic area like Bangladesh and at the same time it will help us to reduce the use of excess amount of scabicide that will be cost effective.

1.4 Hypothesis:

Topical Permethrin is more efficacious than oral Ivermectin in the treatment of scabies.

1.5 Objectives:

a. General objective

- To evaluate the efficacy of oral Ivermectin and topical Permethrin in the treatment of scabies.

b. Specific objective

- To see the effectiveness of oral Ivermectin in the treatment of scabies.
- To see the effectiveness of topical Permethrin in the treatment of scabies.
- To identify side effects of oral Ivermectin and topical Permethrin

1.6 Literature Review:

Relevant previous works:

Incidence of scabies is quite high in Bangladesh-India-Pakistan subcontinent. In Bangladesh, out of total population suffering from skin diseases, 80% of them are suffering from scabies and pyogenic infection[3].
There are numerous publications regarding effectiveness of various scabicide in all around the world.

According to Reena Sharma, Archana Singal; Both permethrin and ivermectin in both single and two dose regimen are equally efficacious and well tolerated in scabies[6]

Munazza Saqib, Lamees Mehmood Malik, Muhammad Jahangir conducted an experimental study among 120patient in the Department of Dermatology Unit I, AllamaIqbal Medical College/Jinnah Hospital, Lahore. To compare the efficacy of single topical permethrin and single oral ivermectin in treatment of scabies and found no significant difference regarding efficacy of topical permethrin and oral ivermectin when used in treatment of scabies[7].

Aisha Mushtaq, Khawar Khurshid, Sabrina Suhail Pal conducted an interventional (quasi experimental) study, To compare the efficacy and safety of oral ivermectin with topical permethrin in treating scabies in outpatient clinic of Dermatology Department, Unit II, Mayo Hospital, Lahore. Hundred patients belonging to either sex and from 12 to 60 years of age were divided into two groups. Oral ivermectin was given to group A in a single dose of 200µg/kg body weight. Group B was given single application of topical permethrin 5% cream at night on whole body for 12 hours. Investigations were carried out at presentation and at 2ndweek while patients were followed up at 2nd and 4th weeks. Permethrin showed marginal better efficacy (88.1%) in completely clearing scabietic lesions at fourth week of therapy as compared to ivermectin(79.5%). Seven patients in ivermectin group had side effects as headache, increase in itching and secondary bacterial infections as compared to permethrin group in which one patient had erythema ($p<0.05$)[9].

Glaziou et al. conducted an investigator blinded trial in French Polynesia, comparing a single oral dose of ivermectin with topical therapy with a 10% benzyl benzoate for the treatment of scabies. One month later,70% patient with ivermectin had been cured as compared with only 48% of the patient treated with benzyl benzoate[13].

In Nigeria, Halima M. Sule and Tom D. Thacher conducted a trial comparing oral ivermectin with topical 25% benzyl benzoate lotion in 210 patients of scabies. After 4 weeks, 95% patient of ivermectin group and 86% patient of topical treatment group were completely cured. The improvement in severity score was greater in the ivermectin group than in topical treatment group (P<.001)[14].

In India Usha V et al had compared the efficacy of oral ivermectin with topical permethrin among 85 patients and observed a cure rate of 95% and 100% respectively at the end of 4 weeks and p value was 0.22[15].

In Bangladesh, Tahmida Hasan et al had observed the efficacy of single dose of ivermectin in 60 scabies patients. There was significant reduction of the lesions at the end of 4 weeks. Complete clearance within 2 weeks was observed in 70% and within 4 weeks in 95% patients[16].

M Zakir Hossain et al had conducted a clinical trial comparing the efficacy of ivermectin and topical permethrin among 40 patients. 55% patient of ivermectin group and 75% patient of permethrin group were cured. Here ivermectin was found less effective than permethrin[17].

Sullivan JR et al stated that ivermectin was successfully used as a sole agent to combat endemic scabies in a ward of a rural nursing home where previous topical therapies including permethrin, benzyl benzoate and precipitated sulfur had failed.[25]

Meinking TL et al conducted an open label study in which they administered ivermectin in a single oral dose of 200µgm/kg body weight to 22 patients of scabies..After 4 weeks 21 patients were completely cured.[26]

Chapter: Two

Materials and Methods

2. Materials and Methods

2.1 Type of study

This will be a Quasi – experimental study.

2.2 Place of study:

Department of Dermatology and Venereology at Shaheed Suhrawardy Medical College Hospital, Dhaka.

2.2 Period of the study:

August 2016 to January 2017

2.3 Study population:

Patients suffering from scabies attending in the outpatient department of Dermatology & Venereology at Shaheed Suhrawardy Medical College & Hospital, Dhaka will be undertaken as study population.

2.4 Sample size and the statistical basis:

100 patients will be taken, out of which 50 patients will be treated with oral Ivermectin and 50 patients will be treated with topical Permethrin. Following formula & purposive sampling will be carried out;

Sample size:

Sample size is selected using the following statistical formula:

$$n = \frac{z^2 pq}{d^2}$$

Z= Standard normal deviation = 1.96

P= Unknown Prevalence is .5= 50%

q = (1-p) = 0.50

d= Degree of allowable error

These assuming a 50% prevalence of Scabies and degree of allowable error 5%, we get the required sample size:

$n= (1.96)^2 \times .5 \times .5 /(0.05)^2= 384$

Due to lack of time, resources, accessibility and availability a total of 100 patients will be taken for the study.

2.5 Screening method:

Patients will be selected by taking complete history and diagnosed clinically by the presence of erythematous papuleS, excoriation and burrows in the typical distributions (finger webs, wrists; axillae, areola, umbilicus, genitalias) and also by microscopy of mite.

2.6 Sampling method:

Purposive sampling

2.7 Inclusion and exclusion criteria:

2.7.1Inclusion criteria

Newly diagnosed patients of scabies, of either gender, above 12 years of age, willing to participate, and give written informed consent.

For inclusion, the patients had to satisfy the presence of at least three of the following clinical criteria;

(a) Demonstration of burrow

(b) Presence of pruritic lesions at the classical sites

(c) Nocturnal pruritus

(d) Family history of similar illness

(e) Microscopic examination of mite

2.7.2 Exclusion criteria:

(a) Pregnant and lactating women

(b) Patients with immunodeficiency or severe systemic disease

(c) With heavily crusted or nodular lesions

(e) Secondary infection or eczematization and coexisting dermatological disease

(d) Patients with a history of treatment with anti-scabetic or topical steroid in the previous 4 weeks

(d) With known hypersensitivity to the trial drugs were also excluded

2.8 Operational definitions:

Scabies

Scabies is epidermal infestation by the mite *Sarcoptes scabiei var hominis,* transmitted by skin-to-skin contact and fomites. Lesions appear as red, scaly, excoriated papules and nodules that favor webs, flexor wrist, elbows, axillae, areolae, genitalias. Scratching may cause skin break down and an additional bacterial infection of the skin. Cutaneous lesions will be graded as mild (lesion count<10), moderate (lesions 11-50) and severe (lesions >50).

Burrow

Burrow is the pathognomic lesion of scabies, which is a thin, thread like, linear lesion, that is 1 to10mm in length and is a tunnel caused by the movement of the mite in the st.corneum, usually in areas with few or no hair follicles, usually where stratum corneum is thin and soft, i.e. interdigital webs of hands, wrists, shaft of penis, elbows, feet, buttocks, and axillae.

Itch

Itch (Latin: pruritus) is a sensation that causes the desire or reflex to scratch. Itch has resisted many attempts to classify it as any one type of sensory experience.

Pruritus will be graded as mild, moderate and severe on the basis of sleep disturbance.

Ivermectin:

Ivermectin is a medication that is effective against many types of parasites. It is used to treat head lice, scabies, strongyloidiasis and lymphatic filariasis among others. It can be either applied to the skin or taken by mouth. Adverse effect of ivermectin in a single oral dose is very infrequent. Most reported adverse effects occur in the treatment onchocerciasis and strongyloidiasis from veterinary formulation included headache, dizziness nausea, vomiting, ataxia and seizures.

Permethrin:

Permethrin is a medication and chemical widely used as an insecticide and insect repellent. Permethrin is a first-line treatment for scabies. It is used as 5% cream. There have no serious reported adverse reaction other than local irritation like pruritus, burning, erythema etc.

2.9 Outcome variables

a. Main outcome variables

- Cutaneous lesions
- Burrows
- Nocturnal pruritus
- Microscopy
- Any adverse effect of Ivermectin &Permethrin

b. Confounding variable :NA

2.10 Procedures of preparing and organizing material:

Patients of clinically diagnosed case of scabies attending in OPD of Dermatology & Venereology in Shaheed Suhrawardy Medical College Hospital, Dhaka fulfilling inclusion criteria will be included in the study after taking informed written consent.

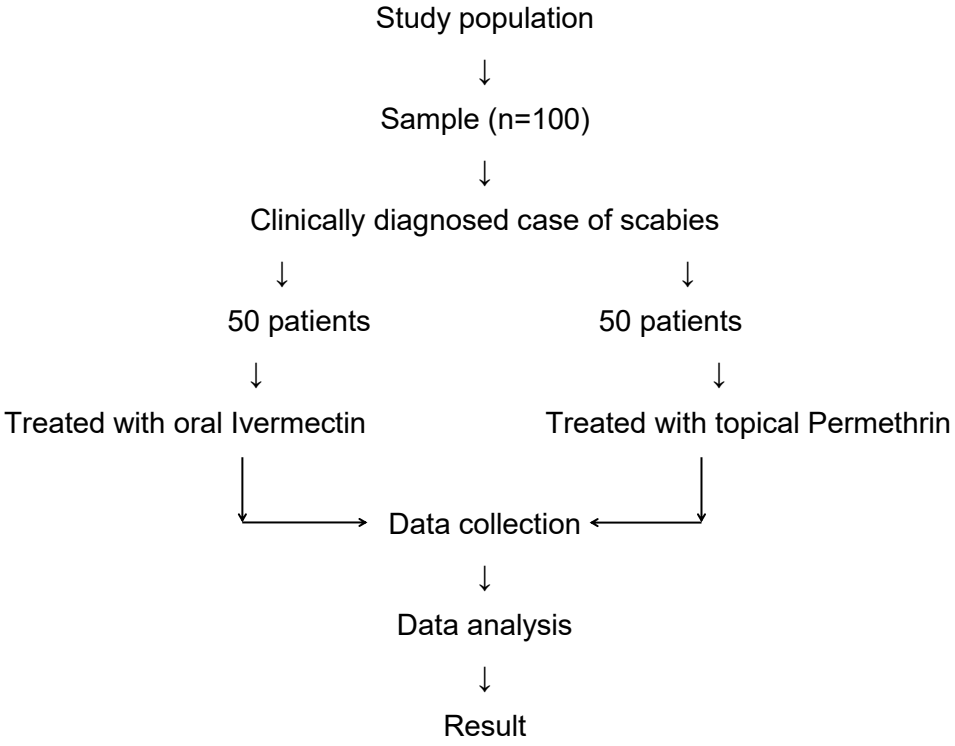
2.11Equipment to be used:

- Predesigned case record from
- Informed written consent form

2.12 Procedures of collecting data:

All patients diagnosed of scabies on history and examination will be recruited as per inclusion criteria. They will be divided by using random number table into group A and group B. Oral Ivermectin will be given to group A in a single dose of 200µg/kg body weight. Group B will be given single application of topical Permethrin 5% cream at night on whole body for 12 hours. Those patients will not respond to first treatment will be given second dose at 2nd week in their respective group. Patient will be followed up on day 7, 14 and assessed for the efficacy and safety. The medicine will be purchase by the patients himself or herself

2.13Flow chart showing the sequence of tasks



2.14 Time table

Activity	August'16	September to December 2016				January'17
Problem definition						
Approach to patients						
Research Design						
Dta collection						
Data analysis						
Report writing						
Submission						

2.15 Professional assistance from experts:

Analysis was done with the help of professional statistician.

2.16 Procedure of data analysis:

Data will be processed and analyzed using computer software with Statistical Packages for Social Science SPSS – 22.0 version (SPSS Inc. Chicago, IL,USA).Data were analyzed using Chi-Square test and paired "t" test. Level of significance was set at .05 and $P<0.05$ was considered significant.

2.17 Quality assurance strategy:

It is extremely important that data collection will be of good quality. Regular instruction from supervisor will be taken. Patients will be examined carefully; regular follow up will be strictly maintained.

2.18Ethical implication

The researcher will be duly careful about ethical issues related to this study. In this study the following criteria will be set to ensure maintaining the ethical values.

1. All patients were given an explanation of the study including the risks and benefits.
2. All patients were included in the trial after taking their informed consent.
3. The researcher was also explain them that they have the right to refuse or accepts to participate in the study.
4. The patient was not gained financially from the study.
5. All data obtained during the study period from the patient remain confidential.
6. Permission was granted by the ethical committee and informed consent was taken from all patients.

Chapter: Three

Results and Observation

Results and Observation:

This clinical trial was conducted in the Department of Dermatology and Venereology, Shaheed Suhrawardy Medical College and Hospital, Dhaka between the periods of August 2016 to January 2017 for duration of 6 months. The study was conducted to find out the effectiveness and safety of oral Ivermectin and topical Permethrin in the treatment of scabies. Patients presented with scabies willing to give the consent and comply with the study procedure was included in the study. Pregnant and lactating women, patients with immunodeficiency or severe systemic disease or with heavily crusted or nodular lesions or secondary infection or eczematization and coexisting dermatological disease and with known hypersensitivity to the trial drugs were also excluded from the study.

A total of 100 patients with scabies were enrolled in the study. They were randomized into two groups. Group A Ivermectin (n=50) and Group B Permethrin (n=50). All patients completed 2 weeks study period were reviewed after 7^{th} day and 14^{th} day.

Table-1: Distribution of patients according to sex:

Sex	Group-A Ivermectin (n=50) No. (%)	Group-B Permethrin (n=50) No. (%)	p value
Male	27 (54.0)	26 (52.0)	0.841^{ns}
Female	23 (46.0)	24 (48.0)	
Total	**50 (100.0)**	**50 (100.0)**	

Chi-square test was done to measure the level of significance, ns= not significant
Figure within parentheses indicated in percentage

Table 1 shows the distribution of patients according to sex. In group A male was predominant than female which was 27 (56.7%) cases and 23 (43.3%) cases respectively. In group B male was predominant than female which was 26 (53.3%) cases and 24 (46.7%) cases respectively. The difference between these two group was not statistically significant (p=0.795).

Table-2: Distribution of patients according to age group

Age (in years)	Group-A Ivermectin (n=50) No. (%)	Group-B Permethrin (n=50) No. (%)	p value
13 – 22	06 (12.0)	12 (24.0)	
23 – 32	13 (26.0)	14 (28.0)	
33 – 42	15 (30.0)	11 (22.0)	
43 – 52	10 (20.0)	08 (16.0)	
>52	06 (12.0)	05 (10.0)	
Total	**50 (100.0)**	**50 (100.0)**	
Mean ± SD	37.86±12.81	34.28±12.74	0.156^{ns}

T test was done to measure the level of significance
Figure within parentheses indicates in percentage
ns = not significant

Table 2 shows the distribution of patients according to age group A majority of the patients were in the age group of 33-42 years which as 15 (30.0%) cases followed by 23-32 years were 13 (26.0%) cases, 43-52 years were 10 (20.0%) cases, >52 years and 13-22 years were6 (12.0%) cases respectively. In group B majority of the patients are in the age group 23-32 years 14 (28.0%) followed by 13-22 years 12 (24.0%), 33-42 years 11 (22.0%),43-52years 8 (16.0%) and >52 years5 (10.0%) cases respectively.

The difference between the ages of the two groups was not significant (p=0.156)

Table-3: Distribution of patients according to site of involvement.

Site of involvement	Group-A Ivermectin (n=50) No. (%)	Group-B Permethrin (n=50) No. (%)	p value
Finger webs	45 (90.0)	47 (94.0)	0.714 ns
Wrist	48 (96.0)	46 (92.0)	0.677 ns
Periumbilical region	47 (94.0)	45 (90.0)	0.714 ns
Genitalias	48(96.0)	49 (98.0)	1.000 ns
Areola	23 (46.0)	24 (48.0)	
Axillae	35 (70.0)	33 (66.0)	

*Chi-square test was done to measure the level of significance

Figure within parentheses indicates in percentage

ns = not significant

Table 3 shows the distribution of patients according to site of involvement. In group A shows that the most common site was the wrist and genitalias 48 (96.0%) followed by periumbilical region 47 (94.0%), finger web 45 (90.0%) lower on axillae35 (70.0%) and areola 23 (46.0%). In group B shows that the most common site was genitalias 49 (98.0%) followed by finger web 47 (94.0%), wrist 46 (92.0%), periumbilical region 45 (90.0%), axillae33 (66.0%) and areola 24 (48.0%).The differences among the site of involvement of two groups were not significant.

Table-4: Distribution of patients according to clinical findings of integumentary system.

Clinical findings of integumentary system	Group-A Ivermectin (n=50) No. (%)	Group-B Permethrin (n=50) No. (%)	p value
Erythematus papules	47 (94.0)	49 (98.0)	0.617^{ns}
Excoriation	44 (88.0)	42 (84.0)	0.564 ^{ns}
Burrow	12 (24.0)	15 (30.0)	0.499 ^{ns}
Nocturnal pruritus	50 (100.0)	50 (100.0)	1.000 ^{ns}

*Chi-square test was done to measure the level of significance
Figure within parentheses indicates in percentage
ns = not significant

Table 4 shows the distribution of patients according to clinical finding of integumentary system. In group A, Erythematous papules were present in 47 cases, Excoriation was present in 44 cases, Burrow was present in 12,and Nocturnal pruritus was present in 50 cases. In group B Erythematous papules were present in 49 cases, Excoriation was present in 42 cases, Burrow was present in 15 cases, and Nocturnal pruritis was present in 50 cases.

Table-5: Efficacy of Ivermectin & Permethrin at 1st & 2ndweek (n= 100) after treatment according to scoring.

Efficacy	Group-A Ivermectin (n=50) No. (%)	Group-B Permethrin (n=50) No. (%)	p value
Base line	8.26 ± 2.22	7.59 ± 2.01	0.117ns
7th Days	4.54±2.05	1.64±1.84	<0.001s
14th Days	2.68±2.35	0.36±1.10	<0.001s

* t-test was done to measure the level of significance.

Table 5 shows the distribution of patients according to scoring. The mean scoring with SD in group A and group B were 8.26 ± 2.22 and 7.59 ± 2.01minutes respectively at the time of observation. The difference between the mean score of the two group is not significant (p=0.117) The mean scoring with SD in group A and group B were 4.54 ± 2.05 and 1.64 ± 1.84 minutes respectively at 7th days. The difference between the mean score of the two group is significant (p<0.001). The mean scoring with SD in group A and group B were 2.68± 2.35 and .36± 1.10 minutes respectively at 14th day difference between the mean score of the group is significant (p<0.001).

Table 6: Adverse Effects of Ivermectin & Permethrin

Adverse effect	Group-A Ivermectin (n=50) No. (%)	Group-B Permethrin (n=50) No. (%)	p value
Nausea	2 (4.0)	0	
Vomiting	1 (2.0)	0	
Headache	1 (2.0)	0	
Pruritis	0	1 (2.0)	
Burning	0	2 (4.0)	
Total			

*Chi-square test cannot be done to measure the level of significance

Figure within parentheses indicates in percentage.

Chapter: Four

Discussion

Discussion:

Scabies is one of the most common infectious diseases in our country. In this study, we evaluated the efficacy & safety of oral Ivermectin and topical Permethrin in the treatment of scabies.

Hundred patients diagnosed of scabies on history and examination was recruited as per inclusion criteria. They were divided by using random number table into group A and group B. Oral Ivermectin were given to group A in a single dose of 200µg/kg body weight. Group B were given single application of topical Permethrin 5% cream at night on whole body for 12 hours. Patients were followed up on day 7, 14 and assessed for the efficacy and safety.

In the present study male patients were predominant than female in group A and B. In group A male was 27 (56.7%) and female was 23 (43.3%) cases respectively. In group B male was 26 (53.3%) and female was 24 (46.7%) cases respectively. The difference between these two group was not statistically significant (p=0.795). Similar results were found in a study that overall males are more affected by scabies than females[16].

According to age majority of the patients were in both groups were from 13-22 to 33-42 years in this study. The difference between the age group was not statistically significant (P = 0.156). In general, prevalence of scabies is more in children & young adult but it can affect all ages[3,16] .

In the study shows that the most common site was the wrist and genitalias48 (96.0%) followed by periumbilical region 47 (94.0%), finger web 45 (90.0%) lower on axillae35 (70.0%) and areola 23 (46.0%). In group B shows that the most common site wasgenitalias49 (98.0%) followed by finger web 47 (94.0%), wrist 46 (92.0%), periumbilical region 45 (90.0%), axillae33 (66.0%) and areola 24 (48.0%). The differences among the site of involvement of two groups were not significant. Almost similar results were found in a study that the most common site was the genitalia (98%) followed by wrist(96%) then periumbilical region(94%), and web space(94%) lower on axilla (70%) and areola (48%)[17].

Nocturnal pruritus was the most common clinical findings of integumentary system followed by erythematous papules, excoriations and burrows. There is no significant difference between the two groups in clinical features.

The cure rate was more in case of single application of topical Permethrin than single oral Ivermectin at 1st week, which was significant (p=<0.001). At 2nd week topical Permethrin has more cure rate than oral Ivermectin & it was also significant (p=<0.001). According to Aisha Mushtaq et al. topical Permethrin is used nowadays for being safer and more effective than the previously used other drugs[9].

The scoring of follow up and observation shows that the outcome of patients with topical Permethrin was better than the oral Ivermectin. Some previous study documented that single oral Ivermectin provide a cure rate of 70% whereas topical Permethrin was associated with 98.0% cure rate at 2nd week of treatment. Significantly According to Reena Sharma, Archana Singal; Both Permethrin and Ivermectin in both single and two dose regimen are equally efficacious and well tolerated in scabies[6].Usha and Nair have shown efficacy of Ivermectin 200µg/kg to be equivalent to topical 5% Permethrin[15].According to Munazza S, Lamees MM, M Jahangir there is no significant difference regarding efficacy of topical Permethrin and oral Ivermectin when used in treatment of scabies[7]. Ivermectin is known to have limited ovicidal activity. So that single oral dose is not appropriate for the treatment. On the other hand, Permethrin have ovicidal property,s o single application may be appropriate[15].

In the present study there was no clinically significant difference in nature, frequency, of severity of adverse events between the two treatment groups, as reported in earlier studies[15].

Chapter: Five

Conclusion and Recommendations

Conclusion

In conclusion, our study demonstrated that administration of single application of topical Permethrin was an effective and safe treatment for the treatment of scabies. Treatment with Permethrin has the benefits of rapid resolution of skin lesions and itching compared to oral Ivermectin.

Recommendations:

A Quasi – experimental study was conducted in Department of Dermatology at Shaheed Suhrawardy Medical College Hospital, Dhaka for 6 months duration. The objective of the study was to evaluate the efficacy of oral Ivermectin and topical Permethrin in the treatment of scabies.

Following recommendations are made based on the study findings:

- This study consists of small number of patients & shorter durations; it emphasizes the fact that further evaluation of the role of oral Ivermectin and topical Permethrin in the treatment of scabies in larger number of patients with longer duration will provide better clarification.
- More follow up should be done to evaluate the better outcome of the patients.
- Longitudinal studies (Cohort study) with larger samples can evaluate the effective and long term outcome for the patients.

Limitation of the study:

In our country, OTC drugs are available. Many patients had to be withdrawn from the study because they use OTC drugs in case of Ivermectin group for immediate relief.

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