Guidelines for the management leishmaniasis; Sri Lanka College of Dermatologists

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List of Abbreviations

CL	Cutaneous leishmaniasis
MCL	Muco-cutaneous leishmaniasis
VL	Visceral leishmaniasis
SSG	Sodium stibogluconate
LN	Liquid nitrogen cryotherapy
HS	Hypertonic sodium chloride solution
MOH	Medical officers of health
PHM	Public health midwives
PHI	Public health inspectors
PCR	Polymerase chain reaction
EDTA	Ethylene diamine tetra acetic acid
ECG	Electrocardiogram
TB	Tuberculosis
IV	Intravenous
IM	Intramuscular
FBC	Full blood count
NSAID	Non steroidal anti-inflammatory drug

Introduction

Leishmaniasis is a disease caused by the protozoa - *Leishmania*. Several species of the genus *Leishmania* can cause leishmaniasis, and in Sri Lanka the disease is caused by *Leishmania donovani*. It is transmitted by a bite of an infected female sandfly. Sandflies acquire the parasites by feeding on infected humans or animals such as dogs, foxes and rodents.

Leishmaniasis can be classified according to the clinical presentation as cutaneous, muco-cutaneous, diffuse cutaneous and visceral leishmaniasis. Clinical picture varies according to the causative species and host factors. The most common clinical type identified in Sri Lanka is cutaneous leishmaniasis.

Cutaneous leishmaniasis commonly presents as papules, nodules or ulcerated lesions over exposed areas mainly involving face and limbs. Lesions are mostly single. However multiple skin lesions can occur. Mucosal lesions are rare. It will take few weeks to several months for the skin lesions to appear following a bite of an infected sandfly. A single bite of an infected sandfly is sufficient to cause the disease, since a sandfly can inject more than 1000 parasites per bite. Living in endemic areas, travelling to endemic areas and outdoor occupations are the main risk factors in developing the disease.

An increasing incidence of leishmaniasis is noted worldwide. During the period of last twelve years an outbreak of cutaneous leishmaniasis has been reported in Sri Lanka especially in North Central, North Western and Southern provinces. The main aim of preparing these guidelines is to provide guidance to the medical professionals in diagnosis, management and control of leishmaniasis in Sri Lanka.

Diagnostic methods

The diagnosis is mainly based on the clinical history and examination findings.

Clinical criteria suggesting the diagnosis of cutaneous leishmaniasis

Typical clinical cases are those having discrete papules, nodules or non-healing noduloulcerative

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skin lesions on exposed sites if they met at least four of the following five clinical criteria:

1) Living in an endemic area, or having visited an endemic area during the period of onset of the lesion
2) Mostly asymptomatic: painless and non itchy lesions
3) Presence of lesions for several weeks to months
4) Poor response to conventional antibiotics
5) History of similar lesions in the household or locality

The clinical diagnosis can be aided by the following confirmatory tests.

Confirmatory tests

1) Smear (tissue impression / slit skin smear / needle aspirate)
2) Histopathology (biopsy)
3) PCR (biopsy / needle aspirate)
4) Culture (needle aspirate / biopsy)
5) Serology - Rapid detection test of rK 39 Ag (1.5 ml blood in two plain bottles for suspected mucocutaneous and visceral leishmaniasis)

Culture specimens should be transported in culture medium; PCR specimen in 1cc sterile normal saline. PCR specimens can be transported at room tem-perature. Specimens for serology should be sent at 4°C, and specimens for culture should be sent at room temperature (24° - 26°C) within 24 hours. (It is advisable to contact the relevant parasitology department before sending the specimen for specifications)

Slit skin smears

1. A convenient location for obtaining specimens from ulcerative lesions is the area immediately adjacent to or beneath the active border
2. Pinch the skin to exclude blood and use a scalpel blade to incise several millimeters long and deep slit into the upper dermis
3. Consider starting the incision in the active border and proceeding radially out from the ulcer across several millimeters of intact skin
4. Obtain tissue juice and flakes of tissue by scarping the upper dermis with a scalpel blade
5. Make a thin smear
6. Air dry the slide and fix in 90% methanol
7. Stain with Giemsa stain

Needle aspirates

1. Draw up 0.1-0.2 ml of sterile 0.9% saline into a 1-3 ml syringe
2. Insert the needle (23-27 gauge) through intact skin into the dermis of the active border
3. Repeatedly move the needle back and forth under the skin tangentianally to the ulcer simultaneously rotating the syringe and applying gentle suction
4. If no aspirate or smear is obtained inject 0.05-0.1 ml saline under the skin and resume suction
5. After the aspirate is obtained withdraw the needle from the skin and discharge the aspirate in to the bottles with culture medium and with sterile normal saline

Biopsy specimens

1. Clean skin with 70% alcohol
2. Inject anaesthetic (1% lignocaine with epinephrine 1: 100000) through intact skin into the dermis underlying the area (avoid high concentrations of anaesthetic which would inhibit parasitic growth)
3. Clean with 70% alcohol, it is preferable not to use iodine because it could inhibit parasitic growth in culture
4. Use a scalpel blade to debride scabs and devitalized tissue from the relevant areas
5. Then apply pressure with a sterile gauze to achieve haemostasis
6. Obtain sterile full thickness punch biopsy specimens from the active border of the lesion. Divide the specimen into three (or obtain multiple biopsy specimens)
   I. One sterile portion for leishmanial and other cultures in culture medium / normal saline
   II. One portion for impression smears
   III. One for histologic examination in 10% formaline
7. In an ideal set up a separate biopsy of 2 mm should be taken for culture

Tissue impression smears

1. Grasp the biopsy specimen with the forceps
2. Gently press the tissue with rolling or circular motion to a glass slide. Repeat on a parallel row down the slide
3. Air dry the slide. Fix in absolute methanol and stain with Giemsa

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Indications for treatment

Cutaneous leishmaniasis may heal spontaneously with an atrophic scar. However, all lesions with evidence of disease activity should be offered treatment. This may reduce the size of the resultant scar and also prevent the spread of the disease.

Decisions regarding treatment should be taken by a Consultant Dermatologist following complete evaluation of the clinical picture.

Treatment options available are;

1) Standard therapy

   This includes;

   a) Sodium stibogluconate
      Intralesional
      Intramuscular
      Intravenous

   b) Cryotherapy

2) Alternative therapies

Treatment of leishmaniasis with sodium stibogluconate (SSG)

SSG is a pentavalent antimony compound. Mode of action of SSG is not clearly understood. This is probably by direct inhibition of DNA topoisomerase I leading to inhibition of both DNA replication and transcription.

SSG is used as a standard therapy for leishmaniasis. It is being used extensively worldwide. However SSG resistance is reported[1,2].

A vial contains 100 ml of 100 mg/ml pentavalent antimony. This can be used for intralesional, intramuscular and intravenous injections depending on type of disease, site involved, number of lesions, clinical setting and type of species involved. SSG vial should be stored in a dark place below 25°C. Once opened, the vial should be used only for one month.

Intralesional SSG (I/L SSG)

Most established treatment for cutaneous leishmaniasis.

Indications

1. Where the lesions are small (<3-4 cm in diameter)
2. Where the number of lesions are less than 5
3. Lesions where the surrounding tissue is not hard
4. Where the lesion is accessible and the patient is co-operative
5. In patients who have not responded to standard cryotherapy this has to be judged by the clinical improvement

Avoid in (see Figure 1)

1. Lesions on cartilaginous part of the ear
2. Eye lid
3. Periorbital skin
4. Nose

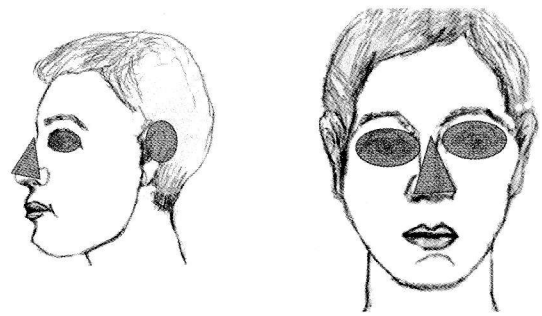

Figure 1.

Technique

Aim of the treatment is to infiltrate the part of infected dermis with SSG. This includes the area immediately surrounding the lesion and base of the lesion.

First clean the skin carefully and then mark out the area to be treated.

Then inject at right angles to the lesion to infiltrate in a "V" shaped pattern, ending with advancing the needle into the base of the lesion. It is important to inject into dermis. It is certain that you are in the dermis if there is resistance to injection. Usually you need to inject until the skin surface has blanched (see Figure 2[3]).

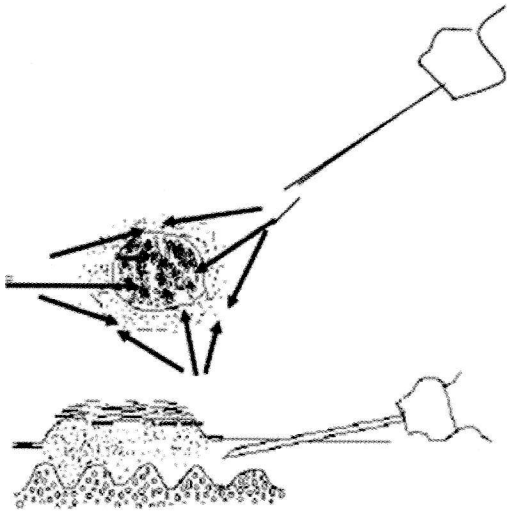

Figure 2.

Dosage and duration of treatment

1 to 3 ml is given in every 5-7 days for a total of 2-5 times. If does not respond, can go up to 10 weeks. One study shown successful results with I/L SSG given on day 1,3,7,10 and day 30[6].

I/L SSG therapy do not require hospital admissions, monitoring investigations or restriction of exercise.

Intramuscular SSG

Positive smear, demonstration of parasite on histology, overwhelming evidence of leishmaniasis on histology or positive PCR is a pre-requisite for intramuscular SSG. Pre treatment evaluation should be done before commencing on the treatment. This includes ECG (to look for arrhythmias), full blood count (to look for cytopenia) and serum creatinine (to access renal function).

Indications

1. Large diameter (>5cm lesions) lesions
2. Large number of lesions (more than five lesions)
3. Lesions at the sites those are difficult to inject (lesions affecting cartilaginous part of the ear, periorbital skin, eye lid and nose)
4. Where there is lymphatic spread (with nodular lymphatic spread)
5. Children who need treatment but cannot be restrained for intralesional treatment
6. In whom 10 weeks intralesional SSG has failed

Technique

Calculated volume to be given intramuscularly in two divided doses to upper outer quadrant of each buttock. Injections have to be given daily for 14 days. If the response is poor by 14th day, the treatment can be continued for further 7 days. In the event of severe myalgia every other day dose can be given.

Dose

10 - 20mg / kg / day

Cautions and monitoring

Relatively safe drug, few side effects experienced.

1. Anaphylactic response

   Need resuscitation kit ready before injections. In whom anaphylactic reactions developed no more injections to be given.

2. Cardiac arrhythmias

   Dose dependent cardiac arrhythmias can occur. But they are usually mild and no treatment is required. Patients with irregular cardiac rhythm or a history of cardiac disease should not be given the treatment.

3. Renal and hepatic side effects

   Reversible elevation of liver enzymes and abnormal renal function tests may occur. Occasionally these can cause problem. If there is evidence of these either before or during treatment the treatment needs to be stopped. No special monitoring is required except stopping treatment. Treatment can be restarted once the baseline investigations returned to normal.

4. Immunosuppression

   The drug is mildly immune suppressive. Patients should not be treated with the drug if they have fever or pulmonary TB.

   Other known adverse effects include metallic taste, nausea, vomiting, diarrhoea, abdominal pain, pancreatitis, skin eruptions, hypotension, occasional anemia and thrombo-cytopenia which are often dose dependant. Myalgia is a common adverse effect.

Cautions

Patients should avoid heavy physical exercise and alcohol during treatment and one week after.

Review the patients after one month and after three months to see the response. Further follow up may be necessary in some patients.

Intravenous SSG

Indications

1. Visceral leishmaniasis
2. Diffuse cutaneous leishmaniasis
3. South American cutaneous leishmaniasis

Method of administration

As thrombophlebitis is common IV cannula site need to be changed frequently. This can be given via a series of butterfly needles or IV cannulae or peripherally inserted central catheter. IV SSG should be diluted in 5% dextrose to be given over 30 minutes.

Filtration, cardiac monitoring and keeping the infusion in dark place are not necessary as given in earlier guidelines. Patients need to be advised to avoid exercise and alcohol during treatment and one week thereafter.

Dose and duration of treatment

20 mg / kg / day for 20 days for cutaneous leishmaniasis, 30 days for mucosal involvement and for visceral leishmaniasis.

Monitoring

Twice weekly monitoring of FBC, blood urea and electrolytes, liver function tests, serum amylase and ECG.

Treatment be interrupted if

- FBC changes become significantly abnormal (when pancytopenia occurs)
- Blood urea and electrolytes become significantly abnormal
- Liver transaminases exceed 15 times the upper limit of normal
- Serum amylase exceeds 4 times the upper limit normal or if other features of pancreatitis develop
- ECG changes become significantly abnormal (QTc prolongation >500 milliseconds)

Commonest reason for interruption of treatment is musculoskeletal symptoms. This may settle with NSAIDs. Treatment can usually be recommenced once the abnormality returns to normal.

Military personnel treated with IV SSG for 20 days should be given 20 days sick leave and advised to avoid exercise and alcohol for one week after treatment. They may also need few weeks of gradually increasing exercise to regain full fitness[4].

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Treatment of leishmaniaisis with liquid nitrogen cryotherapy

Liquid nitrogen is nitrogen in a liquid state at an extremely low temperature. It is produced industrially by fractional distillation of liquid air. At atmospheric pressure, liquid nitrogen boils at - 195°C (77 K; - 321°F) and is a cryogenic fluid which can cause rapid freezing on contact with living tissue, which may lead to frostbite. It will destroy parasites in cutaneous leishmaniasis.

Indications

1. Cutaneous leishmaniasis
   a. Papules, nodules, plaques, nodular ulcerative lesions
   b. Small lesions; size ≤ 3cm diameter
   c. Total number of lesions 1 to 5
2. Mucocutaneous leishmaniasis with cutaneous extension

Avoid in

1. Patients with keloid tendency
2. Facial lesions > 2 cm diameter - due to the risk of ulceration and permanent scarring it is better to use intralesional therapy (sodium stibogluconate or hypertonic saline) on these lesions
3. Thin superficial ulcerative lesions without indurations (cryotherapy may worsen ulcers)

Procedure

Use either cotton swabs attached to ekels or cryoguns. Perform two freeze-thaw cycles per site. Freezing is performed until it makes a 1-2 mm white margin around the site. Freezing times vary from 15 to 20 seconds.

Applications as described above should be repeated until the entire lesion is included. The numbers of applications vary from one to six or more depending on the lesion size.

Patients with secondary infections can be treated with oral and/ or topical antibiotics before any cryotherapy. After each cryosession, topical and/or oral antibiotics can be prescribed accordingly if indicated.

Frequency

- Weekly for one month (1st to 4th cryosessions)
- Fortnightly (every other week) for one month (5th and 6th cryosessions)
- Monthly for one month (7th cryosessions)
- If no response after 7th cryosession change to intralesional sodium stibogluconate

Cure - complete flattening of the lesion is considered as total clearance.

Side effects

1. Painful procedure.
2. Ulceration - marked on lesions where there are secondary bacterial infections prior to cryotherapy, therefore can minimize ulceration by treatment with oral and/ or topical antibiotics before any cryotherapy.
3. Scarring - marked on badly ulcerated lesions.
4. Post inflammatory depigmentation - returns to normal skin colour within 6-8 months. Re-assure the patients.

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Alternative therapies

A = Double blind study
B = Clinical trial more than or equal 20 subjects
C = Clinical trial less than 20 subjects
D = Series more than or equal 5 subjects
E = Anecdotal case reports

Pentamidine isothionate - B

20 patients with recurrent CL were included. Treated with 3 IV or 2 IM pentamidine isothionate.

4 mg / kg on alternate days. All were cured within 1-3 months[1].

Rifampicin - A

46 patients with CL included. 32 received rifampicin 600 mg twice daily for 4 weeks and others received placebo for 4 weeks. Rifampicin group 73.9% had complete healing compared to 4.3% in placebo group. Statistically significant difference observed. Oral

rifampicin was well tolerated and suitable for if injections cannot be given[2].

Allopurinol + low dose meglumine antimonate - B

A treatment of either daily allopurinol (20 mg / kg) + meglumine antimoniate (30 mg / kg) or meglumine antimoniate (60 mg / kg / day) was given for 20 days to 72 patients with CL. Complete healing in 80.6% of those on Allopurinol (20 mg/kg) + meglumine antimoniate compared to 74.2% of those on high dose meglumine antimoniate alone. No significant difference[3].

Azoles - B

106 patients received fluconazole 200 mg daily and 103 received placebo for 6 weeks. Complete healing in 79% in fluconazole group and 34% in placebo group[4].

200 patients were studied. Itraconazole (100 mg) twice daily for 6-8 weeks was superior to meglumine antimoniate in achieving complete clinical and parasitological cure with fewer side effects (75% compared to 65%)[5].

Hypertonic sodium chloride solution - B (Annexure 1)

Hypertonic sodium chloride solution injections were given at 7-10 day intervals with a 96% cure rates within 2-7 weeks (compared to sodium stibogluconate). This was cheap, safe and effective[6].

Gamma interferon - E

Systemic monotherapy with Gamma interferon (100 mg/m 2 of body surface daily) given subcutaneously for 28 days can be effective for complicated cases of human CL[7].

Miltefosine - B

28 patients were given miltefosine 2.5 mg/kg/day orally for 28 days. A cure rate of 92.9% was achieved at 3 months of treatment[8]. Drug comes in tablet form. It is a relatively safe drug and has an advantage in using in resource poor setting. Drug resistance has been reported.

Imiquimod 5% - D

Combination treatment with imiquimod 5% and meglumine antimoniate gave superior results with rapid healing and better cosmetic outcome[9].

Paromomycin ointment - A

A randomized controlled study involving 120 patients with ulcerated lesions compared the therapeutic efficacy and safety of two paromomycin containing topical preparations with meglumine antimoniate. Paromomycin applied twice daily for 30 days. By 12 weeks 70% and 79.3% achieved cure[10].

Photodynamic therapy (PDT) - B

60 patients were included. Topical PDT was given weekly for 4 weeks. Complete cure was seen in 93.5% patients treated with topical PDT versus 41.2% in the topical paromomycin group making PDT a safe and effective treatment[11].

Direct current electrotherapy - B

146 lesions from 54 patients were treated with weekly sessions of Direct Current Stimulation (5-15 Ma for 10 minutes). This produced total clearance in 95.5% of treated lesions for 4-6 weeks[12].

CO_2 laser - B

183 lesions from 123 patients were treated with CO_2 laser with maximum power of 100W and a pulse width of 0.5 - 5 seconds, and 250 lesions from 110 patients were treated with meglumine antimoniate 50 mg / kg daily for 15 days. The CO_2 laser was 1.12 times more effective than meglumine antimoniate with shorter healing time (1 month vs 3 months) and fewer side effects[13].

Oral zinc sulphate - B

104 patients with CL randomly assigned to 2.5, 5, or 10 mg / kg zinc sulphate orally. A controlled group received no treatment. At the end of 45 day follow up an 83.9% cure rate was achieved for the 2.5 mg / kg group, 93.1% for the 5 mg / kg group, and 96.9% cure rate was seen in the 10 mg / kg group. No healing signs were observed in the control group[14].

Pentoxyphilline - A

64 patients studied systemic meglumine antimoniate 20 mg / kg / day combined with pentoxyphilline 400 mg three times daily for 20 days is more effective than meglumine antimoniate alone[15].

AmBisome (Liposomal amphotericin B for the treatment of Visceral Leishmaniasis) - Annexure 2.

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Health education on leishmaniasis

What is leishmaniasis?

Leishmaniasis is a parasitic disease spread by the bite of an infected sandfly.

How long will it take for the skin lesion to appear following the bite of an infected sandfly?

A few weeks to several months.

Why do we treat?

- To prevent and to minimize the disfiguring scars (especially facial lesions)
- To avoid secondary infections
- To control the spread of the disease in the population

Importance of health education

- Health education is a core element in implementation of any disease prevention and control program.
- Multidisciplinary working groups need to be established.

The target groups for health education

- Medical officers of health (MOH)
- Public health midwives (PHM)
- Public health inspectors (PHI)
- All the hospital staff including doctors, nurses, paramedical and minor staff
- Community leaders
- School children and school teachers
- Patients with leishmaniasis and families
- People living in endemic areas
- Defense personnel in endemic areas

Objectives of health education in leishmaniasis control

- To assist in forming a state health policy to control the spread of leishmaniasis
- To enable the community to obtain clear and accurate information (preferably in their own language) about the disease, treatment measures, access to treatment, mode of transmission and control measures
- To establish links and collaboration with experts involved with health promotion and disease control
- To obtain the community participation in the control of the disease
- To conduct training courses for health authorities and health personnel in endemic areas and to organize and conduct primary health education programs for community health workers and leaders, school teachers and communities in endemic and non endemic areas

Prevention of cutaneous leishmaniasis

- Sandflies are generally more sensitive than mosquitoes to insecticides

- Therefore the indoor spread of the disease can be minimized by residual spraying of indoor rooms, use of repellants and the use of impregnated bed nets
- Early detection and treatment would reduce the spread of the disease
- Identification of animals acting as reservoirs needs to be done
- Improve the disease awareness among the general public and health care personnel

Protective measures against sandfly bites

- Apply repellants on uncovered skin and under the ends of sleeves and pant legs
- As repellants are effective for 4-6 hours, re-application is necessary
- Long sleeved shirts and ankle long pants are recommended for outdoor wear
- Keep the indoors and outdoors clean
- Use insecticide treated bed nets
- Indoor residual spraying in areas with high case load

Surveillance

- If a suspected case of leishmaniasis is found it should be notified to the MOH of the residing area of the patient by using the health notification form (H544)
- Once the MOH receives the notification PHI will visit the patient's residence and carry out the investigation within 7 days
- For each and every clinically confirmed case of leishmaniasis MOH team is supposed to fill the special investigation form and send it to the epidemiology unit

How patients can seek treatment?

Treatment and investigations are available at skin clinics in government hospitals.

How to obtain more details about the disease?

- Skin clinics in government hospitals
- MOH office
- Regional epidemiology unit
- Sri Lanka College of Dermatologists, No. 6, Wijerama Mawatha, Colombo 07

Annexure 1

Hypertonic sodium chloride solution (7% to 10%)

Intralesional hypertonic sodium chloride solution (HS) can act by its osmotic effect to destroy the parasite as well as the surrounding tissue of the granuloma (Sharquie 1995; Sharquie 1997). It seems a cheap, safe, and effective local method for treating cutaneous leishmaniasis.

Indications (Same as with sodium stibogluconate)

1. Cutaneous leishmaniasis (CL) only
2. Where the lesions are small (< about 3-4cm in diameter) even if they are multiple
3. Where the lesion is accessible and the patient is co-operative

Disadvantages and side effects

1. Hypertonic saline need prolong therapy in *L. donovani* CL
2. Painful procedure (same as with sodium stibogluconate)
3. Post inflammatory hyperpigmentation - fades over 6-8 months, reassure the patient (same as with sodium stibogluconate)

Avoid

Should not use in intramuscular or intravenous administration, as sodium chloride above 3% can cause phlebitis and tissue necrosis

Efficacy of hypertonic saline

Sharquie KE et al (1995 and 1997) reported that intralesionally administered 7% hypertonic sodium chloride (96.05% cure rate) is as effective as sodium stibogluconate (96.42% cure rate) against CL caused by *L. major* and *L. tropica* in Iraq.

Ranawaka RR *et al* (2010 and 2013) reported that intralesional sodium stibogluconate (98-100% cure rate within 1-6 injections, average being 3.24) is more effective than 7% and 10% hypertonic saline (92.2% cure rate within 1-10 injections; average being 5.27) against CL caused by *L. donovani* in Sri Lanka.

There was no significant difference in treatment response in sodium stibogluconate and HS with regard to the size, the type (nodulo-ulcerative or papular) or the location (head, neck, upper and lower extremities) of the lesions.

Safety of hypertonic saline

Between 7% and 10% hypertonic saline was as equally effective and safe on CL caused by *L. donovani* in Sri Lanka. Except for post-inflammatory hyper-pigmentation which faded-out over 6-8 months there were no systemic or significant local side effects with either sodium stibogluconate or 7 to 10% HS.

15% or above hypertonic saline is not safe due to cutaneous necrosis (30%) caused by intralesional injections. Between 11% and 14% safety of hypertonic saline is not studied and should avoid until proven otherwise.

Preparation of hypertonic sodium chloride

7% HS and 10% HS are prepared by dissolving 12.2 g and 18.2 g of medical sodium chloride in 200 ml of 0.9% sodium chloride (normal saline) solutions respectively. The solutions are sterilized in an autoclave at 121°C for 20 minutes in a screw-capped bottle. Fresh solutions are prepared monthly.

(Technique and dosage of therapy are as same as with sodium stibogluconate)

Technique for infiltration

A disposable 2 cc syringe with a fine-gauge needle is used. The lesion is infiltrated with the drug solution thoroughly until complete blanching of the base of the lesion is achieved. The amount of solution required is 0.2-4 ml per lesion, depending on the size of the lesion. No local anesthesia is added. The solutions are injected intralesionally and not subcutaneously.

Dosage of therapy

Same as with sodium stibogluconate; 1 to 3 ml given in every 5-7 days for a total of 2-5 times. If not responding can go up to 10 weeks.

Cure - Cure is defined as total clearance of the lesion without any palpable lesions.

Advantages

1. very cheap < 1 US$ per 100ml
2. could easily be prepared at all centers
3. minimal local side effects (3% cutaneous necrosis with 10% HS, necrosis not reported with 7% HS)
4. No systemic side effects
5. Resistance not reported (resistance to sodium stibogluconate had reported from many parts of the world (6, 7)

Therefore we can introduce hypertonic saline to endemic areas and train medical officers at peripheral hospitals to treat CL patients. That would be beneficial to the government and convenient to the local farmers who have to travel 90-120 km from highly endemic areas (Padaviya and Padavi Sripura respectively) to the treatment centers (Teaching Hospital Anuradhapura).

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Annexure 2

AmBisome (Liposomal amphotericin B for the treatment of visceral leishmaniasis)

Introduction

Liposomal amphotericin B is a lipid formulation of amphotericin B, in which the drug is packaged along with cholesterol and other phospholipids within a small unilamellar Liposome[1]. The mechanism of action is thought to be drug binding to parasite ergosterol precursors such as lanosterol causing disruption of parasite membrane. The highly specialized liposomal formulation has several characteristics that increases its' efficacy against visceral leishmaniasis while minimizing toxicity. This is used with or after an antimony compound for visceral leishmaniasis unresponsive to antimonials alone.

Although transient rise in creatinine can occur, acute and chronic renal toxicity from liposomal ampho-tericin B is low even with doses of up to 15 mg /kg[2]. Liposomal amphotericin B requires a fairly reliable cold chain, as exposures to temperature above 25°C or below 0°C will alter characteristics of liposome. Such changes may increase toxicity or decrease efficacy[3].

It is administered by IV infusion.

WHO consensus on treatment of visceral leishmaniasis[3]

Zoonotic visceral leishmaniasis

A total liposomal amphotericin B dose of 20 mg/kg is adequate to treat immunocompetent children and adults in these regions. The exact dosing schedule can be flexible (divided into doses of 10 mg/kg on 2 consecutive days or in smaller divided doses), but liposomal amphotericin B pharmacokinetics suggest that the initial dose will provide better tissue levels if at least 5 mg/kg is given.

Anthroponotic visceral leishmaniasis

As monotherapy, liposomal amphotericin B can be given at a total dose of 20 mg/kg in one or two injections in all endemic foci; meanwhile, 10-15 mg/kg for South Asia may be adequate to achieve high cure rates, as is suggested in some limited trials.

Use of combination antileishmanial drug regimens should be promoted to prevent the development of resistance to existing drugs.

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