Ch 368

CHEMOPROPHYLAXIS :A SYSTEMATIC REVIEW OF THE LITERATURE AND META-ANALYSIS

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Objective : To quantify the efficacy of chemoprophylaxis against leprosy based on a systematic review of the literature and meta-analysis of trials.

Method : A literature search identified 127 published papers relating to the prevention of leprosy and the use of chemotherapy in leprosy was critically appraised. Sixteen trials were selected and grouped into three categories according to the level of randomisation of the trial groups. The Relative Risk (RR) with 95% confidence intervals was calculated from the raw data using a random effects model. To estimate the cost effectiveness of chemoprophylaxis treatment, a further analysis of the rates of disease in the trial and control groups was done. The numbers needed to be treated (NNT) to prevent one new case of leprosy was then estimated (incidence in non-exposed minus incidence in the exposed equals reduced rate, 1 divided by RR equals NNT)

Results : The overall results of the meta-analysis shows that chemoprophylaxis gives 60% protection against leprosy, and when given to close contacts of index cases, this protection increases to as much as 99% in some studies. The numbers needed to treat were found to be low in trials of household contacts and high in community based studies.

Conclusion : The evidence shows that chemoprophylaxis against leprosy is a feasible and cost-effective way to reduce the future incidence of leprosy through a targeted approach. The role of chemoprophylaxis needs to be re-examined using newer drugs.

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Ch 416

RELAPSE CASES AMONG THOSE RFT

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Objective: To find out details of relapses among those RFT

Design: Retrospective study patients returned with relapse during surveillance out of RFT.

Setting: The Leprosy Mission Hospital, a large referral centre at Naini, Allahabad, Uttar Pradesh, India.

Participants: Records of relapse cases out of surveillance

Main Outcome Measures:

Percentage of relapse out of RFT patients.

Conclusion: The trends of relapse of ratio over the past 9 years among RFT patients here were evaluated. There was a variation in the percentage of relapse among RFT patients.

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Oc 279

OCULAR COMPLICATIONS IN LEPROSY : AN EPIDEMIOLOGICAL STUDY OF 219 PATIENTS

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One hundred and thirty cases of the 219 patients surveyed were found to have ocular complications, an overall prevalence rate of 59.36%. The peak prevalence was seen in hospitalized patients (68.87%, 104/151), next in cures after discharge (55.8%, 24/43) and the lowest in newly detected cases (8%, 2/25). Visual disability rate in the study group is 21.6% including 12.33% blind sufferers. The main causes leading to visual impairments are lids involvement (lagophthalmos, ectropion) accounted for 24.66%, iris impairments 11.4%, corneal diseases 8.6%, and panophthalmitis 5.94%.. Adapting measures, such as surgical correction, self-care, functional exercise and topical medication, visual acuity of 85 cases (65%) could be improved or kept unchanged.

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Ne 99

ULTRASTRUCTURAL NEURAL-PATHOLOGY IN LEPROMATOUS LEPROSY

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Involvement of the peripheral nerves is a basic pathological phenomenon observed in leprosy whose manifestation are seen right from the early stage with hypo-anaesthetic and hypo-pigmented patches to the advanced forms of the disease with multiple deformities. In the present investigation we have studied the Schwann cell and endothelial cells of endo-neural blood vessels.

Nerve biopsies from four lepromatous leprosy patients were studied by light and electron-microscopy. The patients (BI=6+, Ridley scale) were on treatment with W.H.O. multidrug therapy for 6 month to 1 year. Ultrastructural examination showed that un-myelinated Schwann cell containing many intact bacilli with Electron Transparent Zone. Many of the blood vessels encountered on electron microscopy confirmed the light microscopic observations of intact bacilli in endothelial cells of endo-neural blood vessels . At the point of thinning the endothelial cells appeared rupturing and discharging their contents into lumen of the vessels. M.leprae were seen floating free in the plasma. The Schwann cells of myelinated aron were not affected in our series and M.leprae were not observed. Our observations suggest that the Schwann cells of non-myelinated fibres probably have a agreater affinity for M.leprae than myelinated fibres.Whether those two types of Schwann cells are metabolically different, is to be seen.

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Ne 109

PERIPHERAL NERVE SURGERY IN LEPROSY

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Leprosy is mainly disease of nerves. The skin involvement is with all probability, secondary to the neural damage at the dermal level. The involvement of peripheral nerve trunks leads to sensory-motor deficits in the limbs.

These deficits clinically manifest as (i) deformities resulting from adaptive postures consequent to muscle palsies and (ii) wounds and ulcers due to anaesthesia. Leprosy is feared for its deformities and ulcers which are also the cause of social ostracism and stigma associated with the disease.

The neural damage is multifactorial, inflammatory neuropathy is initiated by the bacillus to which compression neuropathy is also added when the nerve swelling reaches a threshold and can no longer be accommodated in the osseofascial tunnels through which the nerve trunks have to pass in their course. In the process, the nerve trunk is damaged.

Peripheral nerve surgery has a lot to contribute to the wellfare of a leprosy patient. First and foremost it can help relieve the compression of the nerve trunks and gives good results if steroid therapy is supplemented with. Thus, it has a role in preventing the onset of deformities. Further, if the nerve damage has become established, protective sensations can be restored in some patients by simple nerve trunk decompression because nerve fibres retain the capacity to regenerate even in badly damaged nerves.

Attempts have been made to restore nerve functions by nerve grafting procedures using both (i) autologous and homologous nerve grafts and also (ii) muscle bridge grafts of various types. Sensory nerve transfers have been attempted too in certain situations to restore protective sensations.

The above concepts will be discussed in some detail along with their merits and demerits and some likely future approaches will be outlined.

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Ne 164

INCIDENCE OF NEURITIS IN A RURAL LEPROSY PROJECT OF ORISSA WITH AN INTEGRATED POD PROGRAMME

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A leprosy project was established in a tribal area of Orissa state covering a population of 550 thousands. Routine SET activities were started to detect all the possible cases in the project area through surveys. Additionally prevention of deformity programmes (POD) were initiated as an integral part of the leprosy services. The methodology adopted in this component was, examination of patients in a systematic method of nerve function assessment.

All the patients are initially stratified into 6 risk grades depending on their possible risk of developing deformity. 36 patients were excluded as not having any risk of developing deformity among 2003 patients. Rest of the cases were followed up in the POD programme.

Among patients who had nerve function impairment and were treated with standardized steroid therapy and supportive physiotherapy, 8% had shown improvement in nerve function. The patients were further followed up to monitor the nerve function during surveillance period. 4 patients developed new nerve function impairments covering the course of MDT programme.

Nerve function assessment is done for all patients under the programme and they also are educated on self care practices. The programme also includes introducing appropriate instruction in the process of treating neuritis.

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Ne 218

ALTERED CHOLINESTERASE LEVELS IN LEPROSY NERVES

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Cholinesterases are ubiquitous enzymes which play a role in cholinergic transmission, neurogenesis and are implicated in neurodegeneration and dementia. Vertebrate cholinesterases fall into two categories, Acetylcholinesterase (AchE) and Butrylcholinesterase (BchE). These two enzymes differ in substrate specificities and inhibition by selective inhibitors. AchE preferentially hydrolyses acetylcholine or acetyl-beta-methyl choline while BchE preferentially hydrolyses butyrylcholine. Work on AchE and BchE in leprosy skin, muscle and serum have been reported. This study assessed cholinesterase levels in nerves from patients with leprosy.

These enzymes were assayed in six normal and 12 leprosy nerves in the presence of their selective inhibitors. The mean BchE level in leprosy nerves was 17.25 U/mg (SD 7.37) and

8.35U/mg (SD 6.21) in the normal nerves. The mean AchE level in leprosy nerves was

21.87 U/mg (SD 6.81) and 16.71 U/mg (SD 5.50) in the normal nerves. AchE was not significantly altered, but BchE activity was significantly elevated in leprosy nerves when compared to normal nerves ($P>0.05$).

The results show that in leprosy patient nerves there is a significant increase in BchE activity and not in AchE as compared to normal nerves. The possible role of these enzymes in leprosy neurodegeneration will be discussed.

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Ne 290

TRIPOD TRIAL PREPARATION FOR A CLINICAL TRIAL IN A FIELD SETTING *Alison M.Anderson*

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The TRIPOD trial is a double blind, placebo controlled, multi-centre trial of the use of Predinisolone in three aspects of leprosy treatment - prophylactic use for the prevention of nerve function impairment, treatment of early sensory nerve function impairment and treatment of longstanding nerve function impairment. The trials are run in field clinics of six centres spanning two countries, with local paramedical staff taking the primary responsibility for trial patients. In designing a trial to run under these conditions, without compromising safety and scientific standards, several key issues were addressed in the design phase, in the preparation phase and during the trial.

DESIGN - The design conforms to acceptable standards in terms of trial size and randomisation. Randomisation and balance of patients between countries and individual centres needed to accommodate the possibility of between country/centre differences and early curtailment.

MANUFACTURE & DRUG DELIVERY - Drugs were locally made for the trial, minimising cost of manufacture and cost of importation. Spot checks of the manufacturer were made during the process. QC samples were independently assessed. Drugs were packed in unique numbered packs under strict supervision.

STANDARDISATION & TRAINING - Between centre differences were minimised by the use of agreed, simplified, standardised entry, exit and outcome criteria, and measurement techniques. Centres took part in training and reliability testing before the trial started.

SUPERVISION, SAFETY & CONTROL - The trial is integrated into the routine clinic programme and run by staff in the clinics. Safety is assured through an hierarchy of clinic and centre managers, backed up by a local trial co-ordinator and in-country directors. A supervision programme ensures that clinics maintain the standards set. A co-ordinating committee remote from the field provides technical backup, reviews outcome data and makes safety checks.

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Ne 346

LEPROUS NEUROPATHY : MORPHOLOGICAL STUDY OF BIOPSIED PERIPHERAL NERVES

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Hansen's disease is an infectious disease presenting itself as neuropathy and skin lesion. Mycobacterium leprae is the pathogen of leprous neuropathy but the mechanism of nerve damage is uncertain. Perineurial thickening and infilteration of M.leprae and/or cell are the main pathological characteristics of Hansen's disease on nerve biopsy. Here, we report the morphological study of perineurium in biopsied nerves.

Biopsied peripheral nerves from ten leprosy patients (6 tuberculoid patients and 4 lepromatous patients) were examined from morphological aspect.

Light microscopial examination showed that the perineurium was markedly thickened by infiltrated cells in tuberculoid type and mycobacterium leprae in lepromatous type. Schwann cells markedly decreased in number and nerve fibre disappeared without regeneration in severe cases. In mild cases, subperineurial edema was present. The nerve fibre density was normal or mildly decreased. Ultrastructural examination showed the abnormalities of basal lamina on perineurial cells. The basal lamina of the perineurium completely disappeared in several cases. In mild cases, subperineurial edema was present. The nerve fibre density was normal or mild decreased. Ultrastructural examination showed the abnormalities of basal lamina on perineurial cells. The basal lamina of the perineurial disappeared in several cases and showed splitting even if the perineurial looked like the normal complete structure in light microscopy. Both types of leprous neuropathy had same changes with regard to abnormality of the basal lamina. There are many

M.leprae Schwann cells in fibroblasts and perineurial cells on the nerve of lepromatous patients, although few M.leprae in the nerve of tuberculoid patients. Previous studies indicated that the pathogeneris of leprous neuropathy was due to destruction of axon. This study provides that these abnormalities of perineurium are characteristic in both types of leprous neuropathy. The perineurium acts as a barrier between the interior of the nerve and extraneural fluid environment. The damaged perineurium light lose the normal function and allow tissue-damaging factors to enter the nerve resulting in degenerating nerve fibres.

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Im 133

A STUDY ON THE REPRODUCTIBILITY OF TWO SPECIFIC SEROLOGICAL ASSAYS FOR DIAGNOSIS OF LEPROSY

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Diagnosis is the first step in the treatment and control of any disease, both in the individual as well as in the community. Over the years a variety of serological assays have been described for diagnosis of leprosy. Serum antibody competition test based enzyme linked immunosorbent assay (SACT-ELISA) and phenolic glycolipid based enzyme linked immunosorbent assay (PGLELISA) have been reported to be useful and have been studied widely. One of the important characteristics needed for an immunodiagnostic test, is reproducibility of the results. Regarding these two assays there is no such information available in the literature. Therefore, an attempt was made to find out variations (with-in and between the assays) in the results of these two tests. In the present report, the findings, in brief, for same have been described.

The reproducibilities of these two assays were estimated using sera with different levels of anti-Mycobacterium leprae antibodies. From the findings it appears that with-in assay reproducibility of SACT-ELISA is better for sera having low and middle levels of antibodies whereas with PGLELISA it was better with sera having high and low levels of antibodies. Between assay variations were not promising for both the assays. Regarding the percent positivities of both the assays, the PGL ELISA showed better reproducibility than SACT-ELISA. The results would be presented and discussed in details.

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Im 316

SCREENING NEW LEPROSY ANTIGENS FOR POTENTIAL AS LEPROSY SKIN TESTS

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Elimination of leprosy will require new tools to identify trends in leprosy infection in the community. A leprosy-specific skin test could answer the critical question of how MDT programmes impact the transmission of leprosy. Present leprosy skin tests composed of fractions of the leprosy bacillus do not have the requisite specificity to detect leprosy exposure in communities with high levels of tuberculosis. We have demonstrated that levels of the cytokine interferon-gamma (IFN-) produced in a simple overnight whole blood culture with leprosy antigens are increased in healthy contacts of leprosy patients. The 35kD antigen (Triccas, 1996), the 45kD antigen (Vega-Lopez, 1998) and a newly expressed M. leprae homologue of the early secreted antigen of TB of 6kD (ESAT-6 ML) were employed in overnight whole blood assays and interferon-gamma was measured in supernatants. Short-term cultures were compared with longer (5-day) culture and with T-cell proliferation in Nepali leprosy patients, leprosy contacts and unexposed subjects. These data indicate the potential of these three relatively leprosy-specific antigens for leprosy skin tests.