G-N-3

THINK ABOUT CRYPTOCOCCAL MENINGITIS

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Cryptococcus neoformans is regarded as an opportunistic infectious agent for human beings and untreated cryptococcal meningitis has a very high mortality rate. However, occasional cases of cryptococcal meningitis occur in apparently normal individuals. This study aims to identify cellular and humoral immunity defects in cryptococcal meningitis. From May 1996 to June 1999, all patients with CSF culture confirmed cryptococcal meningitis are studied. Peripheral lymphocyte count, HIV antibody titre, serum immunoglobulin levels are measured; lymphocyte subset profile by flow cytometry and lymphocyte function test are performed for those with no obvious causes of immunocompromise found. A total of 6 patients are identified and two had lymphopenia with positive HIV antibody tests; one patient had dermatomyositis and lymphopenia while taking oral prednisolone and cyclophosphamide. For the three patients with no obvious cause found, one had reduced CD4+ T helper cells on lymphocyte subset profile and diagnosed as idiopathic CD4 lymphopenia; the other two had normal lymphocyte subset profiles but impaired lymphocyte function tests in terms of proliferative response to phytohaemagglutinin and pokeweed mitogen. All six patients have normal serum immunoglobulin levels. In conclusion, it seems that all patients with cryptococcal meningitis are immunocompromised in some ways though the exact underlying causes need further investigations, this is important as immunocompromised patients with cryptococcal meningitis require long term prophylactic antifungal agents until immunocompetence is restored

G-N-4

IN VIVO NEUROPROTECTION OF MELATONIN AGAINST FOCAL CEREBRAL ISCHAEMIA IN THE RAT

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Background and Purpose: Melatonin, the neurohormone secreted predominantly by the pineal gland, plays a key role in the synchronisation of diurnal rhythms in mammals. Melatonin protects against experimental brain injury and global cerebral ischaemia. Deficiency of Melatonin after pinealectomy was found to increase the infarction volume of middle cerebral artery occlusion (MCAO) in rats. In this study, the neuroprotective effects of exogenous Melatonin were tested in a MCAO stroke model.

Methods: Adult male Sprague-Dawley rats were anaesthetised with sodium pentobarbital to undergo 3-hour or permanent endovascular right-sided MCAO. Melatonin (1.5, 5, 15, or 50 mg/kg) or the vehicle was given as a single intraperitoneal (IP) injection at 0.5 hour before the 3-hour MCAO. Another group of rats received an IP injection of Melatonin (5 mg/kg) at 0.5 hour before permanent MCAO. Body temperature was maintained constant, and haemodynamic parameters were continuously monitored during the anaesthesia. The rats were decapitated on day 3, and their brains were cut into 2 mm coronal slices before being stained with 2% triphenyltetrazolium chloride for determination of infarction volume.

Results: After MCAO for 3 hours, the relative infarction volumes were 32.1± 3.9% (mean ± SEM; 11 rats) in the vehicle-treated group and 27.7± 3.8% (10 rats), 17.3± 3.4% (9 rats), 24.6± 4.5% (9 rats), or 27.7± 3.2% (9 rats) in the groups treated with Melatonin at 1.5, 5, 15, or 50 mg/kg, respectively. The relative infarct volume was 17.0± 6.5% (8 rats) after the permanent MCAO and an IP dose of Melatonin at 5 mg/kg. In both 3-hour and permanent MCAO, the reduction in infarction volume was statistically significantly with an IP dose of Melatonin at 5 mg/kg ($P < 0.05$, 2-tailed student's t test). There was no significant difference in the haemodynamic parameters among all the groups.

Conclusions: Exogenous Melatonin at 5 mg/kg protects against both transient (3 hours) and permanent focal cerebral ischaemia in the rat, when given as a single IP dose at 0.5 hour before the MCAO. Both the non-receptor mediated (such as antioxidant effects) and receptor-mediated actions of Melatonin may influence the infarction volume of focal cerebral ischaemia. Melatonin at the present doses does not produce any significant haemodynamic effect.