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TUNDA SUTTITUM : NEURO-IMMUNOLOGICAL CHANGES IN THE FUNCTION OF T-LYMPHOCYTES IN HEROIN ADDICTS.
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Conflicting results, both decreased and increased, have been reported concerning the function of T-lymphocytes in heroin addicts. We investigated the alterations of T-lymphocyte proliferative responses and immunophenotypic markers on lymphoid cells in HIV-seronegative heroin addicts, 15-21 day-heroin withdrawal, 6-24 month-heroin withdrawal, 3-5 year-heroin withdrawal and HIV-seropositive heroin addicts. This study has demonstrated a decrease in response of T-lymphocytes to 1.2, 2.5, 5 and 10 μg/ml of phytohemagglutinin (PHA) stimuli in HIV-seronegative heroin addicts and 1-5 day-heroin withdrawal subjects, when compared with controls. Similarly, in an *in vitro* study, 10^{-4}, 10^{-6} and 10^{-8} M concentrations of morphine were shown to suppress 0.6 and 2.5 μg/ml of PHA-stimulated T-lymphocyte obtained from naive subjects. Besides, the inhibition effects of morphine on 2.5 μg/ml of PHA-stimulated T-lymphocyte were blocked by 100 μM naloxone. The immunological parameters: total T-lymphocyte (CD3) cells, T-helper (CD4) cells, T-suppressor (CD8) cells, B cells and natural killer (NK) cells that are the immunophenotypic markers studied by using flow cytometric analysis, were altered in HIV-seronegative heroin addicts, 15-21 day and 6-24 month-heroin withdrawal subjects, when compared with controls. In the HIV-seropositive heroin addicts, we found a profound decrease of immune responses, when compared with controls and HIV-seronegative heroin addicts. These results suggest that HIV-seronegative heroin addicts, short period (15-21 days) of heroin withdrawal and HIV-seropositive heroin addicts have decreases in their immune system functioning and the heroin-withdrawal subjects seem to gradually reverse their immunological parameters to normal levels when withdrawal was sustained more than at least 2 years.

We also investigated whether the immune alteration in heroin addicts is via opioid receptor-mediated or opioid receptor signal tranduction-mediated effect. We failed to detect the normal level of opioid receptors by classical radio-ligand binding. However, we have determined one of the signal transductive systems of the opioid receptor mediated system, the protein kinase C (PKC). This study is also the first report to determine PKC activities on lymphocytes in heroin addicts. In heroin addicts, PKC activities were increased significantly ($p<0.05$), when compared with normal subjects. Stimulatory effects of PKC on immune cells in chronic heroin abusers might be involved in the development of tolerance and dependence.