SESSION 3

BLOCKING OF OPIOID RECEPTORS AGGRAVATES INFLAMMATION IN EXPERIMENTAL FORMALINE-INACTIVATED RESPIRATORY SYNCYTIAL VIRUS (FI-RSV) IMMUNOPATHOGENESIS.

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BACKGROUND

Opioids and their receptors have received remarkable attention since they affects viral infection course. The aim of this study was to investigate the effect of opioid receptors on the immunopathogenesis of RSV vaccine-mediated illness in a widely used mouse model. We studied mice previously immunized with FI-RSV vaccine alone or FI-RSV vaccine in combination with nalmefene (blocker of opioid receptors). We also assessed the adjuvant effect of nalmefene in this model.

METHOD

Female BALB/c mice were divided into 6 groups: PBS-PBS, PBS-RSV, FIRSV-RSV, FIRSV/nal-RSV, FIRSV/nal-RSV/nal, FIRSV-RSV/nal. Mice were injected intramuscularly (days -42 and -21) and infected intranasaly with RSV-A2 (day 0). 1mg/kg of nalmefene was administered during viral infection. At day 5 after infection mice were sacrificed. BAL fluid was collected, and differential cell counts were performed. T cell subtypes (CD4 and CD8) were evaluated by felow cytometry. Cytokines and chemokines were determined using ELISA kits. Viral titers were determined by plaque assay. The histology slides were prepared from the lungs and analyzed.

RESULTS

Administration of nalmefene in combination with FI-RSV vaccine (FIRSV/nal-RSV) results in the reduction of the immune cells infiltrated to the BAL fluid, decreases the eosinophil and monocyte infiltration, decreases the ratio of CD4/CD8 T lymphocyte, decreases the level of IL-5, IL-10, MIP-1 alpha, and lung pathology and had no effect on viral infection in compared to FIRSV-RSV and FIRSV/nal- RSV/nal groups. In contrary, blocking of opioid receptors during RSV infection in vaccinated mice (FIRSV/nal- RSV/nal and FIRSV- RSV/nal) result in an increased influx of neutrophils, eosinophil and lymphocytes, increases the level of IL-5, IFN-gama, MIP-1 alpha, and lung pathology in compared to FIRSV-RSV and FIRSV/nal-RSV groups.

INTERPRETATION

Nalmefene administration as a new adjuvant candidate in unfavorable FI-RSV vaccine inhibits the shift of immune response toward Th2. In addition, opioid receptor blocking during RSV infection aggravated the host inflammatory response to RSV infection. Targeting of opioid system is potentially attractive to develop effective therapies. However opioids are frequently used in infant during mechanical ventilation for severe RSV infection therefore caution is required due to beneficial/ harmful functions of opioid systems. the CD103lo DC population in neonates during vaccination may promote more adult-like T cell responses and be important for effective immunization during early life.