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Ultrastructural Study of the Pulmonary Lesions Induced by Bleomycin in Rats

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The purpose of this study was to investigate the modifying effects of verapamil (a calcium antagonist) and to clarify the cellular events in bronchoalveolar lavage (BAL) on the bleomycin-induced pulmonary lesions in rats. A total of 132 Sprague-Dawley male rats were divided into three groups : control group, bleomycin alone group (BLM), and bleomycin and verapamil combination group (BLM+VERA). The rats of 2 test groups (BLM and BLM+VERA) were given a single intratracheal dose of bleomycin (1.5 mg/rat), and the rats of control group were given sterile isotonic saline (0.2 ml/rat). The rats of group 3 (BLM+VERA) were daily intraperitoneally injected with verapamil (15 mg/kg/day) for 7 or 14 days after bleomycin treatment. And then the rats of Experiment I were sacrificed at day 7 or 14 after bleomycin treatment. Excised lung tissues were examined histopathologically and electron microscopically. Bronchoalveolar lavage (BAL) was analyzed using cell culture techniques.

The relative lung weight to final body weight of both treatment groups (BLM and BLM+VERA) was significantly increased compared with those of the relative control groups at each period. However, those data of bleomycin and verapamil combination group (BLM+VERA) were significantly decreased compared with those of the bleomycin alone group (BLM) at day 7. The quantitative lung inflammatory area scores

(%) of the rat consecutively daily injected with verapamil after bleomycin dose were significantly decreased at each period ($p<0.05$). Verapamil mildly reduced the cellularity in the fibrotic tissues using the histopathological evaluation.

The differntial cell counts were revealed that the predominant cell type in bronchoalveolar lavage (BAL) of bleomycin-treated animals was neutrophils in the initial stage. However, lymphocytes were the predominant cell type in the final stage, and followed by macrophages at day 7.

The values of total white blood cell count of bleomycin-treated animals were rapidly increased from day 7 after bleomycin treatment. The values of lymphocytes in the peripheral bloods of bleomycin-treated animals were increased from day 7 after bleomycin treatment. Treatment of verapamil moderately reduced the cellularity (fibroblasts, alveolar type 2 cells, and lymphocytes) in the fibrotic tissues and the cellular infiltration including neutrophils and lymphocytes.

Therefore verapamil may act as an inhibitor in the lung inflammatory reaction, and this compound could mildly or moderately decrease the pulmonary lesions induced by bleomycin in rats.