Long-term follow-up for EBUS-TBNA negative mediastinal lesions

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M Wong, D Lam, J Lam, J Wang, M Ip, J Ho
Department of Medicine, The University of Hong Kong, Queen Mary Hospital, Hong Kong

Introduction: Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TNBA) is recognised as an accurate diagnostic and staging technique in patients having abnormal mediastinal lesions. Negative results of EBUS-TBNA could be resulted from true negative lymph node involvement in patients having malignancy, or from other benign conditions. Prevalence of tuberculosis was 80 per 100 000 population in Hong Kong during the study period. This study aimed to evaluate the results of these negative lymph nodes upon follow-up for at least 1 year.

Methods: A prospective study on patients having EBUS-TBNA for mediastinal lymphadenopathy by thoracic CT scan from July 2007 to April 2009 was conducted in a tertiary referral centre in Hong Kong where tuberculosis is endemic. Rapid on-site pathological examination was not available. Demographic data and occupational dust exposure were recorded. Negative results were defined as cases without specific diagnoses from the EBUS-TBNA results. Patients having negative results of EBUS-TBNA would pursue surgery, further investigation or clinical follow-up for at least 1 year as necessary.

Results: A total of 122 patients (malignancy in 84.4%) underwent EBUS-TBNA. The sensitivity was 90.4%, with a negative predictive value of 70%. Thirty-seven patients (30%) had negative EBUS-TBNA results. The mean size of lymph nodes was 1.21±0.56 cm and mean number of needle pass per lymph node was 2.80±1.05. One patient defaulted follow-up and 36 patients were analysed. Seventeen patients (47%) had subsequent surgery and same number of patients decided for clinical follow-up. Repeat EBUS-TBNA or CT-FNA was performed in the remaining two patients and both confirmed non–small-cell lung cancer (NSCLC). Among 24 patients confirmed malignancy (23 NSCLC, 1 nasopharyngeal carcinoma), 14 patients confirmed true negative lymph node involvement, seven had false-negative lymph node (19% of all negative results) and three refused surgery. Three patients (8%) were confirmed tuberculosis. Seven patients (19%) had no definitive diagnosis likely due to inflammatory changes including three patients with background of silicosis. After 1 year of follow-up, five patients were clinically and radiologically stable, while one patient had mediastinal lesions resolved spontaneously.

Conclusion: Negative results from EBUS-TBNA lymph nodes should be pursued for further investigations, as up to 19% patients had false-negative lymph nodes and 8% had tuberculosis.

Use-dependent block of hKv1.5 channels and the molecular determinant by the natural flavone acacetin

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HJ Wu[1], W Wu[1], CP Lau[1], PM Vanhoutte[2], GR Li[1]
[1]Department of Medicine, The University of Hong Kong, Hong Kong
[2]Department of Pharmacology and Pharmacy, The University of Hong Kong, Hong Kong

Introduction: We have recently demonstrated that the natural flavone acacetin is an atrial-selective compound that inhibits ultra-rapid delayed rectifier potassium current (IKur) and transient outward potassium current (Ito) in human atrial myocytes, and also acetylcholine-activated potassium current (IK.ACh). It increased atrial effective refractory period and effectively prevented atrial fibrillation (AF) in anaesthetised dogs without prolonging QT interval of ECG. The present study was designed to determine whether the IKur block of acacetin is rate- and/or use-dependent, and the molecular determinant of the channel block in HEK 293 cells expressing hKv1.5 channels (coding IKur in human atrial myocytes).

Method and Results: It was found acacetin was an open channel blocker of hKv1.5 channels and inhibited hKv1.5 current in use- and frequency-dependent manner. The IC50 of acacetin for inhibiting hKv1.5 was reduced from 3.7 μM at 0.2 Hz to 3.1 μM at 0.5Hz, 2.9 μM at 1Hz, 2.1 μM at 3 Hz, and 1.7 μM at 4 Hz. The mutagenesis study showed that the hKv1.5 mutant I508A in the S6-segment exhibited a significant reduction of the channel block by acacetin (IC50, 19.4 μM, 5.2- fold of WT). MCAb BI was significantly higher for SLE patients compared.

Conclusion: These results demonstrate that acacetin is an open channel blocker by binding to the S6 domain of hKv1.5 channels. The use- and rate-dependent blocking property of hKv1.5 by acacetin indicates that this natural compound could exert a strong suppressive effect on atrial fibrillation in man.