PLEURODESIS IN CHRONIC EFFUSIONS
Studies on inflammatory mediators, respiratory function, predictability of treatment outcome, drug efficiency and survival after treatment.

av

Valiant Ukale

AKADEMISK AVHANDLING

som för avläggande av medicine doktorsexamen vid Karolinska institutet, offentligen försvaras på svenska språket i Thoraxklinikernas föreläsningsal N2:U1, Karolinska universitetssjukhuset fredagen den 8 oktober 2004 kl 09.00

Handledare:
Docent Olle Widström
Institutionen för medicin
Enheden för lungmedicin
Karolinska institutet
Karolinska universitetssjukhuset, Solna

Bihandledare:
Docent Gunnar Hillerdal
Institutionen för medicin
Enheden för lungmedicin
Karolinska institutet
Karolinska universitetssjukhuset, Solna

Fakultetsopponent:
Docent Rune Lundgren
Institutionen för folkhälsa och klinisk medicin
Avdelningen för lungmedicin
Umeå universitet

Betygsnämnd:
Docent Jan-Olof Fernberg, Karolinska institutet
Docent Björn Mossberg, Karolinska institutet
Docent Christer Jansson, Uppsala universitet

Stockholm 2004
ABSTRACT

Metastatic or primary (mesothelioma) malignancy of the pleura often generates major pleural effusion, giving respiratory distress and low quality of life to the patients. Evacuation of fluid by thoracocentesis gives only temporary relief, therefore pleurodesis is generally regarded the best way to give palliation. The principle of pleurodesis is to cause a severe inflammation with desquamation of the mesothelial cells, resulting in a fibrosis that obliterates the pleural space. The aims of this thesis were to study various aspects of chemical pleurodesis: the inflammatory response in the pleura and the systemic inflammatory reaction during such treatment and also to investigate if the reaction had predictive value on pleurodesis outcome; the impact of pleurodesis on respiratory function; to compare the efficacy and side effects of two drugs used for pleurodesis; and the long-term survival after pleurodesis in different malignancies.

It was found that the cytokine IL-1β was present in the pleural fluid before and during chest tube drainage and increased after quinacrine instillation. However high concentrations of IL-1β values after instillation were related to the need for longer treatment duration. Successful pleurodesis leads to fibrous adhesions between the lung and costal pleura, which might restrict lung mobility. Ten patients without radiological signs of tumour infiltration and without visible signs of tumour growth in the pleural space at thoracoscopy were investigated after pleurodesis with static and dynamic spirometry, exercise testing with blood gas determination, and radiospirometry. The study showed that pleurodesis in malignant pleurisy has very limited influence on respiratory function.

Quinacrine has been used for pleurodesis with good results in our clinic for decades and talc, which has gradually during recent years become the most commonly used drug for this purpose world-wide. The comparative study between talc and quinacrine in 110 patients showed that both drugs were effective for pleurodesis. Fluid accumulation was stopped within six days in 96% of the talc group and 89% of the quinacrine group.

All 89 prospective patients had verified malignant effusion. The markers investigated for the systemic inflammatory reaction were erythrocyte sedimentation rate, C-reactive protein, and leukocyte count from venous blood samples, and fever reaction. Cessation of fluid accumulation was achieved in 82 patients (92%) and all had a prominent transitional elevation of the inflammatory parameters. The unsuccessful attempts (8%) caused negligible or very small elevations, but due to the small number, only the degree of fever after 8 and 48 hours showed a statistically significant difference. Pleurodesis causes a systemic inflammation and there is a tendency to a correlation between the success of pleurodesis and the degree of inflammation caused by the procedure.

Altogether 197 patients with malignant effusion were discharged from our clinic between January 1, 1991 to September 30, 1994 after a successful pleurodesis. The four most common primary tumours were lung, breast, lymphoma and ovarian malignancies. The overall median survival from pleurodesis was 135 days. Patients with breast cancer had the best prognosis (median survival 216 days). In lung cancer patients, this figure was 28 days and in lymphomas 168 days. The longer the time from diagnosis of primary tumour to effusion, the better the prognosis.

ISBN: 91-7140-031-1