多次胸腔穿刺引流對惡性肋膜積水的性質、細胞激素及纖維蛋白分解活性之影響

Effect of Repeated Thoracenteses on Fluid Characteristics, Cytokines, and Fibrinolytic Activity in Malignant Pleural Effusion

中文摘要

一. 研究目的：

本研究在了解惡性肋膜積水經多次胸腔穿刺引流後，對肋膜積水的性質、各種細胞激素(包括 TNF-α、IL-1β、IL-5、IL-6、 IL-8)、與纖維蛋白分解相關酵素（PAI-1，tPA）所產生的影響及其臨床上的意義。

二. 實驗材料和方法：

本研究共收集 26 位具有大量自由流動之惡性肋膜積水且有呼吸困難症狀的病患，作胸腔穿刺引流，每次引流 500 mL，連作三天(days 1 to 3)，收集肋膜積水，檢測比較此連續三天肋膜積水的性質、細胞激素及纖維蛋白分解活性之變化。於第六天(day 6) 時，以胸腔超音波檢測肋膜腔內有無纖維蛋白形成，將病人分成兩組，施予肋膜沾粘術，並評估其成效。

三. 結果:

此 26 位病人之肋膜積水，經連續三天胸腔穿刺引流後，肋膜積水中的 TNF-α、PAI-1、IL-8 濃度及 neutrophil count 呈現有意義增加。

在連續穿刺引流過程中，正向關連(positive correlation)可見於肋膜積水內的 IL-8 濃度及 neutrophil count (day 1, $r = 0.43$, $p < 0.05$; day 2, $r = 0.51$, $p < 0.01$; day 3, $r = 0.68$, $p < 0.001$)以及 TNF-α與 PAI-1 (day 2, $r = 0.49$, $p < 0.05$; day 3, $r = 0.41$, $p < 0.05$)之間。

在 day 6 以胸腔超音波追蹤病人肋膜積水情形，有 11 位產生纖維蛋白沉積(42%,fibrinous group)，其他 15 位則否(nonfibrinous group)。在連續穿刺引流過程中， fibrinous group 病人肋膜積水中的 TNF-α與 PAI-1 濃度呈現有意義增加，且在 day 2 及 day 3 時其數值有意義地高於 nonfibrinous group。肋膜沾粘術之成功率，fibrinous group(11/11, 100%)高於 nonfibrinous group (8/12, 67%)。

四. 結論：

惡性肋膜積水經多次胸腔穿刺引流後，會引起肋膜發炎及促發炎細胞激素 TNF-α的分泌，之後促成 PAI-1 的釋放，形成纖維蛋白。此纖維蛋白的存在與否，或許可用來預測惡性肋膜積水施予肋膜沾粘術的成效。

英文摘要
--Objective:
To evaluate the effect of repeated thoracenteses on the fluid characteristics and the levels of various cytokines, including tumor necrosis factor (TNF)-α, interleukin (IL)-1β, IL-5, IL-6 and IL-8, and of plasminogen activator inhibitor type 1 (PAI-1) and tissue type plasminogen activator (tPA) in malignant pleural effusion and its clinical significance.
--Design: A prospective study.
--Patients and methods:
Twenty-six patients with symptomatic and large amount of free-flow malignant pleural effusions were studied. Thoracentesis with drainage of 500 mL pleural fluid per day was performed for 3 continuous days (days 1 to 3). The effusion samples were collected to evaluate the changes of fluid characteristics, cytokine levels and fibrinolytic activity. Chest ultrasonography was done on day 6 to observe the presence of fibrin strands. The result of pleurodesis was evaluated in the patients classified into groups based on chest ultrasonographic findings.
--Results:
The values of TNF-α, PAI-1, IL-8 and neutrophil count in pleural fluid increased significantly during repeated thoracenteses in 26 patients studied.
A positive correlation was found between the concentrations of TNF-αand PAI-1 and between the values of IL-8 and neutrophils.
On day 6, fibrin strands were observed in the pleural effusion on chest ultrasonography in 11 patients (42%, fibrinous group) but were absent in the remaining 15 patients (nonfibrinous group). During repeated thoracenteses, a significant increase of effusion PAI-1 and TNF-α was observed in the fibrinous but not in nonfibrinous groups. In addition, the levels of effusion PAI-1 and TNF-α obtained from days 2 and 3 were significantly higher in the fibrinous group than in nonfibrinous groups.
The success rate of pleurodesis was significantly higher in the fibrinous group (11 of 11 patients, 100%) than in non-fibrinous group (8 of 12 patients, 67%).
--Conclusions:
Repeated thoracenteses may cause pleural inflammation and induce local release of proinflammatory cytokine as TNF-α, which may subsequently enhance the release of PAI-1 and lead to fibrin formation in malignant effusion. The presence of fibrin strands after repeated thoracenteses may be of considerable value in predicting the success of subsequent pleurodesis in patients with malignant pleural effusions.
--Key words: fibrinolysis; malignancy; pleural effusion; proinflammatory cytokines; thoracentesis

--Abbreviations: IL = interleukin; LDH = lactate dehydrogenase; PAI = plasminogen activator inhibitor; PAI-1= plasminogen activator inhibitor type 1; TNF-α= tumor necrosis factor-α; tPA = tissue type plasminogen activator