再発性心膜炎の予防薬としてのコルヒチン

CORP：コルヒチンは再発性心膜炎の予防薬として安全かつ有効であることが証明された

CORP: Colchicine proves safe and effective in the prevention of recurrent pericarditis

コルヒチンを従来の治療法に追加するとプラセボを追加するよりも再発および症状持続率軽減の上でより有効であるとの無作為化コントロールトライアルの結果が、2011年European Society of Cardiology学会で発表され、Annals of Internal Medicineに掲載された。心膜炎の再発エピソードを予防するコルヒチンの効果が今回初めて二重盲検多施設無作為化トライアルで示された。このコルヒチンによる心膜炎二次予防（CORP）トライアルでは、再発性心膜炎の初回エピソードを有する連続120人の患者を組み入れた。その結果、コルヒチンはプラセボと比較し18ヵ月後の再発率を有意に低下させた（24%対55%、p<0.001）。さらに、72時間後の症状持続率はコルヒチン群においてプラセボ群より有意に低く（23.3%対53.3%、p=0.001）、平均再発エピソード数も少なかった。1週間後の寛解率はコルヒチン投与群においてプラセボ投与群よりも高く（82%対48%、p<0.001）、次の再発までの時間も長かった。副作用発現率はコルヒチンとプラセボとで同等であった（7%対7%、p>0.99）。

Full Text

Colchicine, when given in addition to conventional therapy, was more effective than placebo in reducing the incidence of recurrence and the persistence of symptoms of pericarditis in a randomized controlled trial presented at the European Society of Cardiology 2011 conference. This is the first time that the efficacy of colchicine in preventing recurrent episodes of pericarditis has been demonstrated in a double blind multicenter randomized trial.

"Recurrence," said investigator Dr. Massimo Imazio from the Maria Vittoria Hospital in Turin, Italy," is the most common complication of pericarditis, affecting between 20 and 50% of patients. Recurrences can be frequent and may seriously affect quality of life, cause hospital readmission, and increase management costs. There has been some preliminary data from non-randomised observational studies and two single-center open-label randomised studies suggesting that colchicine may be a safe and useful drug for preventing these recurrences. Our aim was to test these suggestions in a multicenter double-blind randomised placebo-controlled trial."

Indeed, it was on the basis of such non-randomised observational findings (as well as expert opinion) that colchicine was recommended for the treatment of recurrent pericarditis (class I recommendation) in the 2004 guidelines on pericardial diseases of the European Society of Cardiology.

The CORP trial, an independent non-sponsored study and the first multicenter double-blind randomised trial of colchicine in the secondary prevention of pericarditis, was performed in four centers in Italy and recruited 120 consecutive patients with a first episode of recurrent pericarditis. The primary endpoint of the study was the recurrence rate at 18 months; the secondary endpoints were symptom persistence at 72 hours, remission rate at one week, the number of recurrences, time to first recurrence, disease-related hospitalization, cardiac tamponade, and constrictive pericarditis rates.

Colchicine was given as adjunctive therapy at an initial dose of 1.0-2.0 mg for the first day and a maintenance dose of 0.5-1.0 mg daily for the following six months. The lower dose (initial dose: 0.5 mg every 12 hours and maintenance dose 0.5 mg daily) was given to patients under 70 kg in weight or intolerant of the highest dose (initial dose 1.0 mg every 12 hours and maintenance dose of 0.5 mg every 12 hours).

Results showed that colchicine significantly reduced the incidence of recurrences at 18 months when compared to placebo (24% vs. 55%, p<0.001). In addition, symptom persistence at 72 hours was significantly lower in the colchicine group than in the placebo group (23.3% vs. 53.3%, p=0.001) as were the mean number of recurring episodes. The rate of remission at one week was higher in those patients given colchicine than placebo (82% vs. 48%; p<0.001), as was the time to a subsequent recurrence. The rate of side effects was similar in the colchicine and placebo groups (7% vs. 7%; p>0.99).

Commenting on the results, Dr. Imazio said: "When added to empiric anti-inflammatory therapy, colchicine appears to be a safe low-cost drug for rapid symptom relief, improved remission rates at one week, and reduced recurrence after an initial episode of recurrent pericarditis.

"However, our findings might not be generalizable to other settings or other patient populations. This trial only addressed the use of colchicine following a first recurrence of pericarditis, and not in patients with multiple recurrences. We recruited only adult patients, and thus cannot apply our results to pediatric populations. We excluded patients with bacterial or neoplastic pericarditis, patients with transaminases elevation or severe liver disease, elevated creatinine, patients with myopathy, blood dyscrasias or gastrointestinal disease, pregnant and lactating women, as well as women of childbearing potential and not using contraception.

"It should also be noted that colchicine is not registered for the prevention of pericarditis and its use for this indication is off-label."

A full report of this study will be published simultaneously online by the Annals of Internal Medicine.

Conference News