۳۰ درصد تخفیف نوروزی ویژه کارگاه‌ها و فیلم‌های آموزشی

اصول تنظیم قراردادها

پروریزال نویسی

آموزش مهارت های کاربردی در تدوین و چاپ مقاله
EFFICACY OF FOLIC ACID THERAPY FOR PREVENTION OF IN-STENT RESTENOSIS: A RANDOMIZED CLINICAL TRIAL

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Background: It is known that there is an association between elevated total plasma homocysteine level and restenosis after percutaneous coronary angioplasty.

Objective: To evaluate the effect of lowering plasma homocysteine levels on the rate of restenosis after stent-percutaneous coronary angioplasty.

Methods: Folic acid (1 mg) or placebo was administered to 200 patients (mean ± SD age of 54 ± 9 years) for 3 months, after successful coronary angioplasty in a double-blind randomized clinical trial. The primary end point was restenosis within six months, as assessed by quantitative coronary angiography after positive exercise tolerance test. The secondary end point was a composite of major cardiac events.

Results: Base line characteristics and initial angiographic results after stent-percutaneous coronary angioplasty were similar in the two study groups. The rate of restenosis showed no significant difference in the two groups (5% in placebo vs. 10% in folic acid groups; \( P = 0.141 \)), as there was the need for revascularization of the target lesion (4% in both groups; \( P = 0.766 \)).

Conclusion: Treatment with folic acid does not decrease the rate of restenosis and need for revascularization of the target lesion after stent-percutaneous coronary angioplasty.

Keywords: Folic acid • homocysteinemia • in-stent restenosis • percutaneous coronary angioplasty (PTCA) • stent

Introduction

The occurrence of restenosis after percutaneous coronary angioplasty (PTCA) remains an important limitation of the procedure, and effective pharmacotherapy has been elusive. The observation that the total plasma homocysteine level is an important predictor of cardiovascular risk, and that it correlates with the severity of coronary artery disease, has led to interest in its potential role in restenosis.1 – 5 Although the mechanism of homocysteine-induced vascular damage is not still known, a number of potential links have been suggested. Since plasma homocysteine can be reliably lowered by 25 – 30% with a daily dose of at least 500 µg of folic acid, we hypothesized that lowering of homocysteine levels would decrease the rate of restenosis after PTCA.1, 6 – 8

Clinical, anatomical, and some variables such as diabetes, male sex, smoking, old age etc, appear to be associated with increased rate of restenosis.1

Patients and Methods

Study design

We conducted a double-blind randomized clinical trial, enrolling 200 consecutive patients who had undergone successful angioplasty of at least one coronary artery with ≥50% stenosis. Patients who had unstable angina, myocardial infarction (MI) within the previous two weeks, clinically significant disease of the left main...
coronary artery, angioplasty of a bypass vessel with a patent graft, renal dysfunction (defined as a serum creatinine level of >1.8 mg/dL), or those who were taking multivitamins, were excluded from the study. Patients were randomly assigned to receive either folic acid (1 mg) or placebo (100 cases and 100 controls). The number of patients who took part in this study was selected on the basis of other similar studies.

PTCA
PTCA was performed with standard guide wires and stents. The adjunctive drug therapy (heparin, aspirin, ticlopidine, or clopidogrel) was left to the discretion of operator. Successful PTCA was defined as residual stenosis of <35%, with a normal (thrombolysis in MI grade 3) flow pattern. Clinical and angiographic follow-ups were performed at six months or earlier, if symptoms recurred regarding exercise tolerance test (ETT) performed at three months that was denoted as a positive high risk and/or thallium scan showed ischemia in target vessel territory.

Study end points
The primary end point with respect to efficacy was the presence or absence of restenosis of 50% or more at follow-up examination. The secondary end point was a composite of major adverse cardiac events defined as death from cardiac causes, Q-wave and non-Q-wave MI, or revascularization of the target lesion. We followed up the patients with ETT and clinical symptoms for evaluation of clinically significant restenosis and confirmed it with coronary angiography.

Results
A total of 200 patients were randomly assigned to either folic acid treatment (n = 100) or placebo (n = 100) groups. No side effect was reported. The two study groups were similar in terms of sex, age, and cardiovascular risk factors (Table 1). Thirty-three percent of the patients were women. The base line demographic characteristics and the severity of coronary artery disease (CAD) were not significantly different between the two study groups. There was no significant difference between the two study groups with regards to the size of the vessels involved, the minimal luminal diameter, and the degree of stenosis immediately after PTCA.

Patients’ compliance in the two groups showed no significant difference (98% in the folic acid vs. 96% in the placebo group).

End point
In the group assigned to folic acid treatment, 10% reached the primary end point of restenosis as compared with 5% in the control group (P = not-significant). No difference was seen between the two groups in terms of mortality from cardiac causes (0% in both groups) and rehospitalization due to Q-wave or non-Q-wave MI and unstable angina (4% in folic acid group vs. 5% in control group), as was the need for revascularization (4% in both groups) (Table 2).

Discussion
The pathogenesis of homocysteine-induced vascular damage and its possible role in restenosis are not clearly understood. Nevertheless, several hypotheses have been suggested. Elevated homocysteine levels stimulate proliferation of vascular smooth muscle cells, increase collagen deposition, impair endothelium-dependent vasodilation, promote intimal thickening, and increase the production of extracellular superoxide dismutase. There is also a clear association between elevated homocysteine level and increased thrombogenicity through interaction with coagulation factor V, protein C, tissue plasminogen activator, and tissue factor activity.1, 7, 9 Other antioxidants, such as β-carotene, vitamin E, and vitamin C have failed to reduce the rate of restenosis after PTCA.1

The size of the vessel involved (<3 mm), the postprocedural minimal luminal diameter, and the location of the target lesion have been shown to influence the rate of restenosis, but these variables were equally distributed between the two study groups.1, 7, 9

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UA = unstable angina; MI = myocardial infarction; TLR = target lesion revascularization.
Folic acid treatment showed no significant effect on in-stent restenosis after PTCA that might be attributed to multifactorial causes of in-stent restenosis. In contrast to recoil, which is the mechanism of restenosis in native vessels, stent restenosis is accounted for primarily by neointimal proliferation through the stent. The maximum relationship was observed between smoking and hyperlipidemia with in-stent restenosis that shows the importance of life style modification and statin therapy after stent PTCA.

References

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اصول تنظیم قراردادها

پروپوزال نویسی

آموزش مهارت‌های کاربردی در ندوین و چاب مقاوم