

# TOP Journal Club

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### **RACTS: A Prospective Randomized Antiplatelet Trial of Cilostazol Versus Ticlopidine in Patients Undergoing Coronary Stenting: Long-Term Clinical and Angiographic Outcome.**

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*Aug;46(2):162-166*

We compared the efficacy of cilostazol for the prevention of late restenosis and acute or subacute stent thrombosis with that of ticlopidine. Cilostazol has been used for antiplatelet therapy after coronary stent implantation, but the results are controversial. Patients scheduled for stent implantation were randomly assigned to receive either cilostazol (100 mg twice daily for 6 months, n = 201) or ticlopidine (250 mg twice daily for 1 month, n = 196). All patients also received oral aspirin (100 mg once daily for 6 months). Coronary angiography was performed at baseline and immediately and 6 months after coronary stenting. Clinical follow-up was continued up to 9 months postprocedure. There was no significant difference in the composite incidence of death, myocardial infarction, stroke, and stent thrombosis between the 2 groups [cilostazol (1.5%) versus ticlopidine (3.6%),  $P = 0.216$ ], but the target lesion revascularization rate per patient was significantly lower in the cilostazol group than in the ticlopidine group (22.9% vs 32.7%,  $P = 0.030$ ) 9 months post-coronary stenting. Medication withdrawn because of drug-related side effects tended to be higher in the ticlopidine group than that in the cilostazol group (3.5% vs 8.2%,  $P = 0.054$ ). At follow-up angiography, the minimal luminal diameters (2.31 +/- 1.06 vs 2.10 +/- 1.16,  $P = 0.057$ ) tended to be larger and the restenosis rates lower (23.3% vs 30.9%,  $P = 0.086$ ) in the cilostazol group than in the ticlopidine group. Aspirin plus cilostazol is a comparable antithrombotic regimen to aspirin plus ticlopidine after elective coronary stenting, but the rate of target lesion revascularization was significantly lower in the cilostazol group than in the ticlopidine group.

### **The inhibitory effects of rebamipide on cigarette smoke-induced airway mucin production.**

*Respir Med.* 2005 Jul 20

Cigarette smoke may be the main cause of chronic bronchitis. Exposure of cigarette smoke induces the recruitment of inflammatory cells in the airway epithelium, and release of the tumor necrosis factor alpha (TNFalpha) from airways. Previous reports have shown that cigarette smoke induces goblet cell metaplasia by activating an epidermal growth factor receptor (EGFR) cascade, and that this results in mucin production. Rebamipide (2-(4-chlorobenzoylamino)-3-[2(1H)-quinolino n-4-yl] propionic acid, OPC-12759) directly inhibits the production of superoxide (O(2)(-)) and inhibits proinflammatory cytokines (such as TNFalpha and IL-8). In the present study, we aimed to analyze the inhibitory effects of rebamipide on TNFalpha and EGFR activation after cigarette smoke treatment in vitro and in vivo. NCI-H292 cells and Sprague-Dawley rats were used for in vitro and in vivo studies. In vitro studies, cigarette smoke solution was found to increase TNFalpha secretion, and EGFR-specific tyrosine phosphorylation, and to elevate MUC5AC production. These effects were inhibited dose-dependently by pretreatment with rebamipide (MUC5AC protein levels were inhibited from 44% to 17%,  $P < 0.05$ ). In vivo studies, cigarette smoke was found to cause inflammatory cell recruitment and to increase the secretion of TNFalpha in bronchoalveolar lavage (BAL) fluids (from 198 +/- 78 to 2270 +/- 158 pg/ml,  $P < 0.01$ ). Moreover, the pretreatment of rats with rebamipide inhibited goblet cell metaplasia and TNFalpha secretion, dose-dependently (from 2270 +/- 158 to 1377 +/- 112 pg/ml,  $P < 0.05$ ). In conclusion, the exposure of airway epithelium to cigarette smoke-induced TNFalpha production, neutrophil recruitment, activated EGFR, and caused MUC5AC mucin synthesis. Moreover, rebamipide was found to prevent this cigarette smoke-induced TNFalpha release, and mucin production.

## **Relationship Between HbA1c Level and Peripheral Arterial Disease.**

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**OBJECTIVE:** Homeostatic glucose control may play an important role in the development of peripheral arterial disease among individuals without diabetes. We sought to evaluate the association of HbA(1c) (A1C) with peripheral arterial disease in a representative sample of the U.S. population with and without diabetes. **RESEARCH DESIGN AND METHODS:** A cross-sectional study was conducted among 4,526 National Health and Nutrition Examination Survey 1999-2002 participants  $\geq 40$  years of age. Peripheral arterial disease was defined as an ankle-brachial index  $< 0.9$  ( $n = 327$ ). **RESULTS:** Among nondiabetic subjects, the age-standardized prevalence of peripheral arterial disease was 3.1, 4.8, 4.7, and 6.4% for participants with an A1C  $< 5.3$ , 5.3-5.4, 5.5-5.6, and 5.7-6.0%, respectively ( $P$  trend  $< 0.001$ ). The prevalence of peripheral arterial disease was 7.5 and 8.8% for diabetic participants with A1C  $< 7$  and  $\geq 7\%$ , respectively. After multivariable adjustment and compared with nondiabetic participants with A1C  $< 5.3\%$ , the odds ratio (95% CI) of peripheral arterial disease for nondiabetic participants with an A1C of 5.3-5.4, 5.5-5.6, and 5.7-6.0% was 1.41 (0.85-2.32), 1.39 (0.70-2.75), and 1.57 (1.02-2.47), respectively, and it was 2.33 (1.15-4.70) and 2.74 (1.25-6.02) for diabetic participants with A1C  $< 7$  and  $\geq 7\%$ , respectively. **CONCLUSIONS:** An association exists between higher levels of A1C and peripheral arterial disease, even among patients without diabetes. Individuals with A1C levels  $\geq 5.3\%$  should be targeted for aggressive risk factor reduction, which may reduce the burden of subclinical cardiovascular disease even among those without diabetes

## **CINP 2000 - Collegium Internationale Neuro-Psychopharmacologicum 22nd Congress.**

*IDrugs*. 2000 Sep;3(9):1023-5.

At this large and varied meeting on neuropharmacotherapy, progress was reported

on the newer more selective antipsychotics. The selective D(2) dopamine receptor partial agonist, aripiprazole (Otsuka Pharmaceutical Co Ltd) was recently proved effective over the medium term. The atypical antipsychotics generally, such as clozapine, have a good side effect profile and better patient compliance, even in Parkinson's disease (PD). Reboxetine (Pharmacia & Upjohn AB), having a far greater selectivity for norepinephrine reuptake inhibition than for serotonin or dopamine reuptake, is of particular value in treating depression. Paroxetine (Novo Nordisk A/S), a selective serotonin reuptake inhibitor (SSRI), has just completed a multicenter clinical trial, being effective in about 50% of cases of post-traumatic stress disorder. A meta-analysis of trials of other uptake inhibitors showed that ability to block serotonin (rather than norepinephrine) uptake correlated well with efficacy. Bipolar and other disorders were hoped to benefit from more selective agents in the future, the potential for which has been revealed through basic neurobiology, with, for example, only non- $\alpha 7$  nicotinic receptor subunits being expressed by those interneurons mediating nicotinic responses. An open label, 30-day study of a pyrrolopyrimidine, the corticotrophin releasing factor (CRF) type 1 receptor inhibitor, NBI-30775 (Neurocrine Biosciences Inc/Janssen Pharmaceutica NV) produced good antidepressant effects, but has had to be abandoned as a product due to indications of potential liver damage. Similarly, although glial-derived neurotrophic factor (GDNF) had proved ineffective in a 1999 trial for PD, due to failure to access the striatum, there was however much evidence to suggest that small molecule agonists of the TRK-B receptor should be effective. Of these, quinones such as L-783281 (Merck Research Laboratories) appear to activate all TRK subtypes by a common intracellular, rather than receptor-mediated action, which may limit their usefulness. Although such agents would have many potential applications, it is likely that highly selective receptor activation will be needed.

<http://www.thai-otsuka.co.th/pxnews/index.html>  
Opinions and suggestions are welcomed  
Dr. Shwe Win, [shwewin@thai-otsuka.co.th](mailto:shwewin@thai-otsuka.co.th)