Smoking, Estrogen, and Membrane Microviscosity in Women

To the Editor:

We read with great interest the recent article by Dr. Kurth et al.1 dealing with the relationship between smoking and hemorrhagic stroke in women. The results of their prospective study demonstrated that the risk of total hemorrhagic stroke, such as intracerebral hemorrhage and subarachnoid hemorrhage, was increased in women who are current cigarette smokers. The authors proposed that smoking may cause structural damage to the arterial wall and be a risk factor for both ischemic and hemorrhagic stroke in women.

Numerous studies have shown that estrogen may protect the brain from experimental stroke, such as global brain ischemia and subarachnoidal hemorrhage.2 One of the mechanisms underlying the protective effect of estrogen may be the enhancement of nitric oxide (NO) production. There is evidence showing that vascular endothelial function is markedly influenced by estrogen, and is improved by hormone replacement therapy in postmenopausal women.3 In an in vitro study presented earlier, we demonstrated that 17β-estradiol increased membrane fluidity (a reciprocal value of membrane microviscosity) of erythrocytes and improved the rigidity of cell membranes in postmenopausal women via the NO- and cGMP-dependent mechanisms.4 In a separate series of experiments, we showed that hormone replacement therapy restored the membrane microviscosity in elderly women with a concomitant increase in plasma NO metabolite level.5 These findings suggest that, because abnormalities in membrane microviscosity could cause a disturbance in rheological behavior and microcirculation, estrogen-deficiency might be involved in the pathogenesis of vascular complications in women. In this context, it can be speculated that changes in plasma estrogen level might modify the onset and outcome of stroke in women. Mueck and Seeger6 proposed that smoking can reduce the efficacy of orally administered estrogen in women. Although the authors mentioned that use of hormone replacement therapy and postmenopausal status did not substantially change the effect of estimates of the association between smoking and hemorrhagic stroke, we would like to know whether the endogenous sex hormones might be different between smokers and non-smokers in women. It would be important to assess more precisely the relationship between estrogen status and vascular complications in women.

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Response

Tsuda and Nishio postulate a potential beneficial effect of estradiol on the arterial wall, although the effect of estradiol on the vascular system in the brain remains controversial.1

In addition, recent randomized trial data provided evidence that postmenopausal hormone therapy increases the risk of ischemic stroke.2 Plasma estradiol levels were only measured in a small case-control study3 from participants of the Women’s Health Study. Preliminary results did not show statistically significant differences of plasma estradiol levels according to smoking status among users and non-users of postmenopausal hormone therapy. With respect to exogenous hormones, we showed that current smokers were less likely to utilize postmenopausal hormone therapy (see Table 1 in Reference 4). In our data, although based on a small number of cases, postmenopausal hormone use did not significantly modify the association between smoking and total hemorrhagic stroke.

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