LETTER TO THE EDITOR

Carpal tunnel syndrome and oral contraceptive drugs: risk or protective factor?

In view of the prevalence of carpal tunnel syndrome (CTS) in females (prevalence 4 : 1), and other gender-related CTS risk factors (pregnancy and menopause), we hypothesized that hormonal factors could influence the pathogenesis of the syndrome. We thus set out to evaluate the association between the use of oral contraceptive drugs (ORCDs) and CTS as a way to gain insight into the relationship between hormonal factors and CTS.

Some data suggest a positive association between ORCDs and CTS *(Sabour and Fadel, 1970; Vessey et al., 1990)*, but these data lack electromyographic evaluation supporting the CTS diagnosis. In another study in which CTS was diagnosed by electromyography, the authors found a negative association *(De Krom et al., 1990)*.

We recently studied 189 consecutive females (mean age 34.9 ± 7.7 years; range 15–46) who presented with a painful CTS complaint and who were not obese or diabetic (other CTS risk factors). The patients were divided into two groups (group A: women under 35 years of age; group B: women over 35 years) and further divided into three subgroups: 'ORCD' subgroup included women currently taking ORCDs, 'no ORCD' subgroup included those who had never taken them, and 'past ORCD' subgroup included women who had taken ORCDs in the past. All patients underwent electromyography and electroneurography to confirm the diagnosis of CTS.

Our results showed a higher proportion of CTS in group B patients compared with group A patients (58 versus 38%, chi-square test: $p = 0.01$). Mean age of 'ORCD' subgroup was not statistically different from mean age of 'no ORCD' or 'past ORCD' subgroup, either in group A or in group B. Interestingly, in group A patients, the proportion of CTS in the 'ORCD' subgroup and in the 'past ORCD' subgroup was lower when compared with the 'no ORCD' subgroup [34 versus 59.2%, respectively (chi-square test: $p = 0.03$), and 20 versus 59% (chi-square test: $p = 0.02$)]. Conversely, in group B, proportion of CTS was not statistically different, comparing the three subgroups at chi-square test.

Since ORCDs were first introduced in 1966 (Evanor 500 μg of norgestrel and 50 μg of ethynyl estradiol), the total amount of estroprogestin contained in these drugs has been markedly reduced. This would support the idea that some side effects, probably including CTS, as reported in previous studies *(Sabour and Fadel, 1970; Vessey et al., 1990)*, might be attributed to higher hormone dosages. The most recent preparations of third-generation ORCDs, however, contain new types of progestin such as gestodene, norgestemate, and desogestrel, and these preparations have an anti-mineralcorticoid effect, which could be responsible for them playing a protective role in CTS. The activity of these progestins is purely progestational, i.e., they have no androgen activity (which is not needed for contraception and increases side effects and metabolic complications). Recently, there have been claims against makers of third-generation ORCDs regarding the risk of venous thromboembolism *(Dyer, 2002)*. On the other hand, the benefits of the third-generation ORCDs are reflected in a lower incidence of coronary heart disease, reduced hirsutism in hyperandrogenic women, and a reduced risk of stroke. Moreover, other advantages associated with the use of synthetic hormones include a reduced risk of osteoarthritis and increased bone density during estrogen-replacement therapy.

We found a significantly lower incidence ($p = 0.01$) of CTS in the members of our study group who were taking third-generation ORCDs. These results could, reasonably, be explained by the effects of gestodene, whose anti-mineralcorticoid activity seems to translate clinically into fewer premenstrual symptoms, less water retention, less weight gain, and fewer breast symptoms. We might also hypothesize a long-term

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protective effect of ORCDs on the median nerve, given the significantly negative association between ORCDs and CTS also found in the group of previous ORCD users.

In conclusion, we suggest that a reduced dose of estroprogestinic and the preferential use of monophasic rather than triphasic drugs are factors contributing to a reduced risk of CTS in women taking ORCDs, while a possible anti-mineralcorticoid effect of the new-generation ORCDs could also play a protective role.

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