News in Brief

TREATMENT-EMERGENT ENDOCRINE SYMPTOMS AND THE RISK OF BREAST CANCER RECURRENCE: A RETROSPECTIVE ANALYSIS OF THE ATAC TRIAL

A retrospective study reported the incidence of vasomotor or joint symptoms and breast cancer recurrence in women undergoing endocrine treatment with anastrazole or tamoxifen in the Arimidex, Tamosifen, Alone or in Combination (ATAC) trial. It was hypothesised that when the mechanism of action behind treatment toxicity reflects the intended effect on the treatment target, the toxicity might be a useful marker for efficacy.

Women with hormone-receptor-positive tumours who reported vasomotor or joint symptoms – both linked to oestrogen depletion or oestrogen blockade – at the first follow-up visit (3 months) in the ATAC trial, (which assessed anastrozole or tamoxifen for adjuvant treatment of postmenopausal breast cancer), were compared with women without these symptoms to see if there was a relation between these symptoms and subsequent recurrence. It was reported that 1486 of 3964 (37.5%) women indicated newly emergent vasomotor symptoms at the 3-month follow-up visit and had lower subsequent recurrence than those who did not report these symptoms (223 during 10 752 women-years of follow-up versus 366 during 11 573 woman-years of follow-up, respectively; hazard ratio [HR] 0.84 [95% CI 0.71—1.00], p=0.04; adjusted for age, body-mass index, previous hormone-replacement therapy, nodal status, tumour size, and tumour grade). There was a greater decrease in breast cancer recurrence in 1245 of 3964 (31.4%) women who reported new joint symptoms at the 3-month follow-up visit as compared to those not reporting these symptoms (158 during 9242 women-years of follow-up versus 366 during 11 573 women-years of follow-up; adjusted HR 0.60 [0.50—0.72], p<0.0001).

The authors suggest that the appearance of new vasomotor symptoms or joint symptoms within the first 3 months of treatment is a useful biomarker, and may suggest a greater response to endocrine treatment compared with women without these symptoms. It was opined that with awareness of the relation between early treatment-emergent symptoms and beneficial response to therapy, it might be useful when reassuring patients who present with them, and might help to improve long-term treatment adherence. The authors also cautioned that this relation needs to be confirmed prospectively.

Source: Cuzick J, et al. Treatment-emergent endocrine symptoms and the risk of breast cancer recurrence: a retrospective analysis of the ATAC trial. The Lancet Oncology: DOI: 10.1016/S1470-2045(08)70259-6

PATERNAL AGE AND ADVERSE BIRTH OUTCOMES: TEENAGER OR 40+, WHO IS AT RISK?

The effect of paternal age on pregnancy and birth outcomes was examined in a retrospective cohort study restricted to live singletons born to married, nulliparous women 20–29 years of age. This is due to missing information on paternal age being more prevalent in unmarried women than in married women, parity and multiple births being important risk factors for birth, as well as the age group having the lowest incidence of sub-fecundity. It was hypothesised that paternal effects have biological plausibility, as the placenta is largely dependent on the expression of genes of paternal origins and potentially harmful mutations may be more frequent among immature men and older men, leading to adverse birth outcomes.

The National Centre for Health Statistics (NCHS) database of the USA categorised paternal age into seven groups: <20, 20–29, 30–34, 35–39, 40–44, 45–49 and >50 years of age. Rates of adverse birth outcomes were calculated for each paternal age group. Adverse birth outcomes considered in this study included very pre-term delivery (live

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infant delivered at less than 32 weeks' gestation), pre-term delivery (live infant delivered at less than 37 weeks' gestation), very low birth weight (live infant weighing less than 1500g at birth), low birth weight (live infant weighing less than 2500g at birth), small-for-gestational-age birth (live infants with birth weights below the 10th percentile for gestational age and sex), very low Apgar score at 5 min (<4), low Apgar score at 5 min (<7), foetal distress, neonatal death (death of a live birth within 28 days) and post-neonatal death (death of a live birth between 28–364 days of age).

There were 23 654 785 births in the 1995–2000 linked birth and infant death data set, out of which 2 614 966 were suitable subjects for analysis. It was found that after adjustment for paternal race, maternal age, race, education, tobacco smoking and alcohol drinking during pregnancy, adequacy of prenatal care and infant sex, there was an increased risk of very pre-term births, pre-term births, low birth weight, small-for-gestational-age births, low Apgar score, neonatal mortality and post-neonatal mortality among children born to teenage fathers, when compared with fathers 20–29 years of age. Advanced paternal age was not associated with an increased risk of adverse birth outcomes. Restricting the analysis to subjects without birth defects yielded similar results.

The study indicated that advanced paternal age is not an independent risk factor for adverse birth outcomes, and this was consistent with most other previous studies. The authors caution that gestational age was based on self-report, which is presumably subject to measurement error. Information on the socio-economic status and lifestyle factors of the fathers, which might be important confounding variables in the observed association, was unavailable.

The authors hypothesised that possible explanations could include immature sperm being associated with an increased risk of adverse birth outcomes, young fathers being more likely to come from economically disadvantaged families and to have lower educational attainment as socio-economic factors are known to be associated with a number of health outcomes. Lastly, it is possible that the social environment, including lifestyle factors such as illicit drug use, smoking and alcohol drinking are more prevalent in teenage fathers, and is suspected to play a role in the occurrence of adverse birth outcomes. ■

Source: Chen XK, et al. Paternal age and adverse birth outcomes: teenager or 40+, who is at risk? Human Reprod 2008, DOI: 10.1093/humrep/den403.