86 Exposure to environmental tobacco smoke in childhood and incidence for selected cancers in adulthood: an analysis in the European prospective investigation into cancer and nutrition

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Introduction: Exposure to environmental tobacco smoke (ETS) during childhood has been linked to childhood respiratory illness and childhood cancers. Some studies claimed that exposure during childhood, when the target organs are still growing, is important for health later in life. However, observations on adulthood cancers in previous studies were not consistent. Here we explore the association between childhood ETS exposure and adulthood cancer development among never smokers in a large cohort.
Material and Methods: We examined the association between childhood ETS exposure and the most frequent cancers within the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort. We selected the sites that accumulated at least 500 cases by 2004: upper aero-digestive tract, stomach and esophageal, colorectal, pancreas, lung, breast, cervix, endometrial, ovary, prostate, bladder, kidney, brain, thyroid cancers, and lymphoma. The analyses were restricted to never smokers (N = 112,430). Hazard ratios (HR) and 95% confidence intervals (CI) were estimated by Cox proportional hazard model stratified by age, sex, and center. Models were adjusted for education, body mass index, physical activity, total energy intake, vegetable intake, and fruit intake. Whenever applicable, models were further adjusted for or stratified by adulthood ETS exposure, previous respiratory illness, or family history (for breast and colorectal cancers).
Results: Higher risks were observed for lung (HR = 2.87, 95% CI = 1.20–6.91) and pancreatic cancers (HR = 3.18, 95% CI = 1.30–7.76) comparing childhood ETS exposure daily for many hours to never or seldom. A higher risk for brain cancer (HR = 1.98, 95% CI = 1.06–3.71) was also observed for those exposed a few times during a week, albeit non-significant for those exposed many hours daily (N = 4, HR = 1.75, 95% CI = 0.60–5.10).
Conclusions: We observed a higher risk of adulthood lung, pancreatic, and brain cancers for those who self-reported childhood ETS exposure in never-smokers, after adjusting for well-known confounders, such as education (as a proxy for socio-economical status) or adulthood ETS exposure. Further work includes examining whether other lifestyle risk factors, such as diet and physical activity, and reproductive factors (for female cancers) would modify the observed associations.

87 NTX and VEGF in cancer patients with bone metastases treated with zoledronic acid

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Background: Patients with breast, lung, and prostate cancer frequently develop bone metastases (BM), which are responsible for high morbidity and reduced quality of life. Zoledronic acid (Zometa®, Zol), routinely used to treat patients with BM, inhibits bone resorption and has antitumour properties. It has also been reported to have an antiangiogenic effect.
Material and Methods: The study prospectively evaluated serum levels of vascular endothelial growth factor (VEGF) and cross-linked N-telopeptide of type I collagen (NTX) in 45 consecutive patients with advanced breast, lung, or prostate cancer. Patients were eligible if they were at first diagnosis of bone metastases and if they had not previously undergone bisphosphonate treatment. All patients received the standard Zol schedule of a 4 mg infusion every 28 days. Patients were monitored for about 9 months and blood samples were collected before the first infusion of Zol and every 3 months thereafter.
Results: The baseline VEGF median value was 318.9 pg/ml (interquartile [IQ] 182.4–656.1). Median value at 3 months was 345.2 pg/ml (IQ 182.8–656.1), 329.5 pg/ml (IQ 183.7–568.8) at 6 months and 395.4 pg/ml (IQ 253.2–702.9) at 9 months, none of which reached statistical difference. Interestingly, when only patients with prostate and lung cancer were considered, VEGF levels had decreased by 35% at 3 months. NTX median values significantly decreased with respect to baseline (median value 15.9, range 129–22.9 nm BCE) at 3 (10.2 nm BCE, range 7.0–12.7) and 6 months (10.3 nm BCE, range 6.8–13.3) ($p < 0.001$), but not at 9 months (12.0 nm BCE, range 11.1–14.2). Serum NTX median values at 3 months were 35% less than those of baseline values. Blood samples at 6 and 9 months showed a decrease of 39% and 26% with respect to baseline, respectively. There was no correlation between VEGF and NTX values.
Conclusions: The present prospective study focused on serum markers that are potentially associated with bone metastases. Our results show that standard monthly treatment with zoledronic acid induced a rapid and long-lasting decrease in NTX levels in the majority of our patients. Conversely, conclusions on the VEGF analysis cannot be drawn perhaps because of the small number of cases involved.

88 Genetic polymorphisms in the MMP2 and MMP9 genes decreased lung cancer risk

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Background: Lung cancer constitutes one of the leading causes of death in worldwide, approximately one million people per year, 850.000 men and 330.000 women. Matrix metalloproteinases (MMPs) are a family of proteolytic enzymes involved in process of tumour progression due to its ability to degrade components of the extracellular matrix. However, recent studies have shown that they are involved in all stages of cancer progression not only in process of tumour invasion and metastasis, but also in cancer development processes such as proliferation, adhesion, migration, differentiation, angiogenesis, senescence, autophagy, apoptosis and evasion of the immune system. Unexpectedly, recent studies based on the generation of loss-of-function animal models have provided definitive evidence of the existence of MMPs with anti-tumour properties. These results support an emerging and paradoxical role of MMPs in tumour progression. Genetic variants in the MMP genes may influence the biological function of these enzymes and change their role in carcinogenesis and progression. We have investigated the association between three polymorphisms (−735 C/T, −1562 C/T and 5A/6A) in two human gellatinases (MMP2 and MMP9) and one human stromelysin (MMP3) and the association with development or progression of lung cancer.
Material and Methods: The CAPUA (Lung cancer in Asturias) study is a hospital-based case-control study was designed including 762 lung cancer patients and 649 controls. Genotypes were determined by PCR-RFLP. Results were analyzed using unconditional logistic regression and the Kaplan–Meier method.
Results: The *MMP2* and *MMP9* promoter polymorphisms were associated with lung cancer risk. The *MMP9* T/T genotype was associated with a statistically significant decreased risk of developing lung cancer (ORadj = 0.29; 95% CI = 0.10–0.85) while *MMP2* T/T genotype was associated with a no statistically significant decreased risk (ORadj = 0.52; 95% CI = 0.22–1.26). No association was identified between *MMP3* promoter polymorphism and lung cancer risk (ORadj = 0.98; 95% CI = 0.68–1.41). The Kaplan–Meier analysis showed that the polymorphisms in *MMP9*, *MMP2* and *MMP3* not seem to modify the overall survival.
Conclusions: This study confirms that polymorphism in MMP9 have a protector effect on lung cancer risk, which can be used as a prognostic marker in lung cancer and also lead to more effective cancer therapeutics.

89 Influence of functional genetic variants of TGFβ1/TGFβR2 pathway in prostate cancer development

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Background: The transforming growth factor beta 1 (TGFβ1)/TGFβ type 1 and 2 receptors (TGFβR1−2) signaling pathway play an important role in prostate cancer (PC) development and progression through the regulation of cell proliferation and differentiation. The functional polymorphisms TGFB1 +869T>C and TGFBR2 −875G>A, have been associated with higher circulating levels of TGFβ1 and modified TGFBR2 transcriptional activity. Different levels of these molecules can modulate cellular microenvironment influencing TGFβ1/TGFβR1−2 pathway activation, with impact in PC oncobiology. Our purpose was to investigate the role of *TGFB1 +869T>C* and *TGFBR2 −875G>A* functional polymorphisms in PC risk.
Material and Methods: We conducted a case-control study in histopathologically individuals with confirmed PC (n = 688) and benign prostate disease (n = 378). *TGFB1 +869T>C and TGFBR2 −875G>A* polymorphisms were detected by allelic discrimination using Real-Time PCR with TaqMan® SNP Genotyping Assay.
Results: Frequencies of CC/CT genotypes for *TGFB1+869T>C* polymorphism were significantly lower in PC patients compared with control group (62% and 71%, respectively), carriers of C allele had a protective effect for PC development (age adjusted Odds Ratio (aOR) = 0.68, 95% Confidence Interval