(VHA) is organized into 21 administrative regions called Veterans Integrated Service Networks (VISN). VISN 16 provides health care treatment to >1.4 million veterans in an eight state region in south central United States. The network, an integrated health care system, includes ten medical centers, 33 community-based outpatient clinics, seven nursing homes, and two domiciliary. The data was queried from Oct 1998 to June 2004, using a retrospective case control design. Statistical analysis was performed using SAS software version 9.0 (Chicago, IL). Multiple logistic regression analysis was used with calculation of odds ratios and 95% confidence intervals. The data was adjusted for age, race, gender, BMI, smoking, alcohol use, diabetes and statin use. Patients were placed in the ACE inhibitor user group if they were using ACE inhibitors prior to the diagnosis of pancreatic cancer. RESULTS: A total of 483,733 patients were included in the analysis. 185,852 (38.43%) of those were using ACE inhibitors. Pancreatic cancer (ICD-9 code 157) was seen in 475 (0.1%). ACE inhibitor users were 48% less likely to develop pancreatic cancer (Odds ratio 0.484; 95% CI 0.386-0.607, $p < 0.01$). The dose, duration and type of ACE inhibitor used were not factored into the analysis. The protective effect of ACE inhibitors was independent of statin use.

Conclusion: ACE inhibitors are associated with a 48% reduced incidence of pancreatic cancer. The limitations of our data are the Veteran population, the database and the fact that this is a case control study.

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Apoptosis induction by sulforaphane is a consequence of G2/M cell cycle arrest in cultured 40-16 human colon carcinoma cells

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Sulforaphane (SFN) [CH3S(O)(CH2)4-N=C=S)] is a naturally occurring cancer chemopreventive isothiocyanate found as its glucosinolate precursor in cruciferous vegetables like broccoli. Apart from its ability to modulate carcinogen metabolism SFN also acts by antiproliferative and apoptosis-inducing activities. As an example, treatment of the human colon carcinoma cell line 40-16 with SFN at a 15 μM concentration led to the cleavage of PARP [poly (ADP-ribose) polymerase] as a marker of apoptosis induction, mediated by the activation of caspase-3, -7, -8 and -9, detected by Western Blotting experiments. To analyze whether cytotoxic activity was accompanied by inhibitory effects on cell cycle progression, unsynchronized SFN-treated 40-16 cells were stained with propidium iodide and analyzed by flow cytometry. Treatment with 15 μM SFN for 12 h induced a marked G2/M phase arrest, which persisted until 24 h. After 48 h incubation, a sub-G1 peak was detected, indicating apoptosis induction. To further characterize time-dependent cell cycle changes by SFN we performed kinetic experiments. After a pre-incubation phase of 24 h, cells were treated with 15 μM SFN for 3, 6, 12 and 24 h, respectively, and allowed to recover with SFN-free medium for up to 12, 24 and 48 h. Treatment for 3 and 6 h resulted in a transient G2/M arrest, which was detectable after 12 h. During prolonged incubation under SFN-free conditions, the cell cycle arrest was reversible and cells recovered from SFN treatment. In contrast, incubation with SFN for 12 h led to an irreversible G2/M phase arrest after 24 h and apoptosis induction after 48 h. In order to investigate whether activation of the caspase cascade is essential for the induction of apoptosis by SFN in 40-16 cells, we treated the cells simultaneously with 15 μM SFN and the pan caspase inhibitor z-VAD-fmk. Importantly, SFN-mediated apoptosis induction, detected by PARP cleavage and the occurrence of a sub-G1 peak in flow cytometry after 48 h, was completely inhibited by co-treatment with z-VAD-fmk. Instead, a marked G2/M arrest could be observed. Based on these data we conclude that the primary antiproliferative mechanism of SFN is a cell cycle arrest in G2/M, which is reversible after short term incubation for 3 to 6 h. After longer incubation times, the cell cycle arrest becomes irreversible and is followed by caspase-dependent apoptosis induction.

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The effect of the dyes used in sentinel lymph node biopsy localization on immunocytochemical determination of hormonal receptors in MCF-7 breast cancer cell line

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Introduction: Sentinel Lymph Node Biopsy (SLNB) is the procedure of choice for staging the axilla in breast cancer patients who are clinically and radiologically node negative. Node localization is achieved with the use of injected dye, radioactive tracer or both. The biological effect of using these materials has not been fully investigated.

Aims: To determine the effect of the added dyes (Patent Blue V(PBV), Methylene Blue (MB) and Indigocarmine (IDC)) on the immunocytochemical expression (ICC) of estrogen receptor (ERα) and progesterone receptor (PR) in monolayer cultures of breast cancer cells.

Methods: MCF-7 cells (a malignant breast cell line which is known to be positive for both ERα and PR) were cultured and treated with the above dyes. The dyes were 2.5% PBV, 1% MB and 0.4% IDC and were diluted further using RPMI-1640 media with 5% Fetal Calf serum in three dilutions, 1 in 10, 1 in 100 and 1 in 1000. The cells were treated with the dyes for 4hours and 24hours. Formalin fixed paraffin embedded blocks were prepared and ICC for both ERα and PR performed. The slides were scored blindly using the Alred quick score by two breast histopathologists.

Results: The results of the scoring showed decrease of both ERα and PR scores with higher concentration of MB dye (1 in 10 dilution of the 1%MB preparation) particularly if exposed for 24hrs. PBV and IDC did not show a significant reduction.

Conclusion: The addition of MB can interfere in vitro with the results of ER and PR receptor assessment by ICC. If the effect occurs in vivo it could lead to inappropriate antihormonal treatment ch