ficient than for an initial diuretic or beta-blocker. In view of the similar (and not better) efficacy for a typically more expensive calcium antagonist, compared to a generally less expensive diuretic or beta-blocker in preventing most cardiovascular events, it is likely that the current large disparity in acquisition costs would support a public policy recommendation for an initial diuretic (or possibly a beta-blocker) as the more cost-effective initial choice.

Key Words: Meta-analysis, Calcium channel blocker controversy, Guidelines for initial therapy

OR-23
POPULATION-WIDE DIURETIC USE IS DIRECTLY ASSOCIATED WITH THE INCIDENCE OF END-STAGE RENAL FAILURE IN THE UNITED STATES
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Treatment of hypertension over the past 3 decades using predominantly diuretic and beta-blocker drug regimens has been promoted as a factor in the reduction of cardiovascular disease related (CVD) and stroke-related mortality. Concurrent long-term measurement of end-stage renal disease (ESRD) morbidity in the US shows an increasing incident population for both hypertensive nephrosclerosis (HT-NS) and all-cause ESRD.

Utilizing the technique of data fusion, where concurrent observations of the same total population using different measurement tools are merged for analysis, we have evaluated available national databases for CVD mortality, stroke mortality, HT-NS incidence and ESRD incidence two years later. A hypothesis can be proposed that ESRD incidence two years later (Y) and annual percentage changes in ESRD incidence (X) are related by a simple linear model that relates annual percentage changes in diuretic supply and annual percentage changes in ESRD incidence (Y = 0.7X + 1.16; r² = 0.568, p = 0.03).

The data from 1990 to 2001 show that changes in US diuretic supply and consumption were directly associated with changes in ESRD incidence in the US two years later. A hypothesis can be proposed that ESRD incidence rates might attenuate if diuretic use is deliberately minimized in the United States as much as possible.

Key Words: ESRD, Diuretics, Data Fusion

OR-24
ANTIHYPERTENSIVE CALCIUM CHANNEL BLOCKERS MAY PROMOTE HUMAN CANCER CELL GROWTH
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It has been suggested that calcium ion (Ca²⁺) channel blocking drugs (CCB), commonly employed as antihypertensive agents, may promote growth of pre-existing cancer cells by inhibition of apoptosis. So far, however, there are no experimental data to support this notion, and results from clinical trials and epidemiological studies have been negative or ambiguous, respectively. Therefore, we examined if vascular type (L-type) Ca²⁺ channels are expressed in human colon cancer cells and if L-type Ca²⁺ channel activators (CCA) and blockers (CCB) influence Ca²⁺ influx and subsequent apoptosis in such cells. Both primary (collected at operation) and commercially available human colon cancer cell lines were used. The cells were incubated with three different CCB (verapamil, diltiazem or nifedipine) and one CCA (Bayk 8644) at clinically relevant concentrations. RNA was determined by reverse-transcription polymerase chain reaction (RT-PCR SuperScript one-Step). Intracellular Ca²⁺ levels were measured by fluorometry (Fluo-4-AM). Apoptosis was quantified by flow cytometry (Annexin V binding). Cells from both lines expressed vascular (L-type) Ca²⁺ channel mRNA but neither N- nor P-type channel mRNA. The L-type Ca²⁺ channels were composed of α1D and β₃ subunits. The selective L-type CCA BayK 8644 markedly increased Ca²⁺ influx and apoptosis in the cells, and CCB pretreatment abolished BayK 8644-induced Ca²⁺ influx and apoptosis. Accordingly, while there is no evidence that CCB induce transformation of normal cells to cancer cells, these drugs may promote growth of pre-existing cancer cells in humans. As this would become clinically relevant only in subjects who already harbor a critical mass of cancer cells, the negative results in clinical trials and the conflicting results of epidemiological studies are not surprising. Until studies have been conducted in appropriate patient groups to substantiate or refute the notion that CCB treatment poses a real cancer threat, it seems prudent to minimize the use of CCB in hypertensive patients.

Key Words: Calcium channel blockers, Cancer, Apoptosis