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Short Communication

Why E-Cigarettes and Vaping Probably Increase Risk for Lung Diseases, Heart Attacks, Coronary Artery Disease, Stroke and Death: Potential Roles of Marijuana, Thiocyanate and Unrecognized Magnesium Deficiency; A Hypothesis

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It is now estimated that 1 out of 20 Americans may indulge in using E-cigarettes and vaping [1]. New research obtained by the CDC and published in several very recent editions of Morbidity and Mortality Weekly Reports links E-cigarette-vaping to high risks for heart attacks (>50%), coronary artery disease (>60%), lung diseases (>60%), strokes (>70%) and death [1-6]. This scourge now appears to be focused, primarily (i.e., more than 65% of all subjects), on youths 16-24 years of age. These multistate USA outbreaks, in particular with lung diseases have appeared, so far as of this writing, in almost 1,300 people with almost 30 deaths. Although the specific chemical (s) responsible for these outbreaks are not as yet known, we believe the focus should be on nicotine, marijuana-cannabis products, thiocyanate, and hypomagnesemia. Below, we posit why we think marijuana products (particularly delta-9 tetrahydrocannabinol), thiocyanate and hypomagnesemia should be centers of focus.

Recent findings on almost twenty people suggest that vaping results in lungs which seem like they have been exposed to toxic chemicals

Workers at The Mayo Clinic have reported that the lungs of almost 20 vapers (two of which had died) had lung tissues that resembled chemical burns [7]. They have suggested these lung tissues looked very similar to what has been observed in industrial accidents [7].

Recent Evidence Demonstrates that Marijuana-cannabis Products and Thiocyanates Cause Vasospasm and Inflammation of Coronary, Pulmonary and Cerebral Blood Vessels and Deplete Vascular Smooth Muscle Cells of Magnesium Ions.

Several studies (since 1990), using isolated blood vessels (including peripheral, coronary, pulmonary and cerebral), have now shown that sodium and potassium thiocyanates [8-13], as well as marijuana products (e.g., delta-9 tetrahydrocannabinol) [14], cause vascular smooth muscle cells to contract (and often spasm) when exposed to these substances. Moreover, when primary cells from these diverse vessels are cultured in-vitro (using techniques developed in our labs), for several days they: 1. Lose free intracellular magnesium ions ($[Mg^{2+}]I$ [15], and 2. Demonstrate an increase in TNF-alpha, IL-1, and IL-6 as well as activation of cellular NF-kB [18], signs characteristic of the beginnings of an inflammatory response.

Potential significance of vascular and inflammatory actions of marijuana-cannabis products and thiocyanates to risks for heart attacks, lung diseases, coronary artery disease, strokes and death

Approximately 50 years ago, we first demonstrated that when isolated macro- and micro-blood vessels (including peripheral, coronary, pulmonary, umbilical-placental and cerebral) are exposed to low extracellular Mg^{2+}, the vascular smooth muscle cells undergo contractions and vasospasm with changes in their geometrical shapes and calcium overload [16-24]. We suggested that such findings, if verified in human subjects might portend a rationale for ischemic heart disease (IHD), angina, pulmonary artery and lung diseases, coronary artery diseases CAD), strokes, hypertension, preeclampsia, and sudden-death ischemic heart disease (SDIHD) [20-22,24-27]. Several lines of evidence have now been brought forth in numerous experimental and human studies from different parts of the globe which support our hypothesis [28-33].

At the turn of the 20th century, people in North America and Europe were ingesting about 450-550 mg of Mg/day, whereas now people living in these areas are now only ingesting about 165-238 mg of Mg/day [24,26,34,35]. Thus, more than 75% of most North Americans and Europeans are Mg deficient.

If vaping causes depletion of intracellular Mg^{2+} in pulmonary, cerebral and coronary blood vessels, as we suspect, and additional depletion of $[Mg^{2+}]I$ from inhaling thiocyanates and marijuana-cannabis products takes place, again as we suspect, then a constellation of pathological effects would take place, over time, as indicated above. It should be pointed out, here, that many of the blood vessels and cardiac tissues from the victims of vaping-induced deaths appear to exhibit muscle cells in various stages of cell death. Recently, we have reported results from Mg-deficient animals which indicate coronary vascular smooth and cardiac muscle cells are found in different stages of programmed cell death (i.e., apoptosis; necroptosis; pyroptosis; or ferroptosis) [36-39]. Whether or not any of these forms of programmed cell death are present in users of e-cigarettes remains to be determined. It is, however, possible if our hypothesis is correct, that intravenous administration of Mg salts, followed by oral dosing, might be therapeutically-helpful in prophylactic and therapeutic treatment against the pathological actions of vaping.

Conclusions and Future Thoughts

As of this writing almost 1,300 people (with approximately 30 deaths), in the USA, have presented with various cardiovascular and lung ailments after using E-cigarettes and "vaping". More than 65% of the subjects are youths between 18-25 years of age. Why vaping causes high risks for development of lung diseases, coronary artery disease, heart attacks, strokes, and death is not known. Most all of the victims were found to have high levels of delta 9-tetrahydrocannabinol and had to have had elevated levels of thiocyanate. Based on our findings with diverse vascular smooth muscles, and primary cell cultures, we have posited a new hypothesis that marijuana-cannabis products and thiocyanates, by depleting blood vessels of Mg along with nicotine, found in many E-cigarettes, are probably instrumental in causing some or all of the pathological effects of vaping. As most North Americans and Europeans (particularly youths) have diets deficient in Mg, such a situation would tend to exacerbate the pathological effects of vaping.

In view of our findings, and suggestions, we believe clinical trials and investigative studies should be undertaken to determine whether: 1. Pulmonary and coronary tissues of e-cigarette smokers have decreased levels of intracellular free Mg; and 2. Intravenous Mg compounds given to E-cigarette -vapor users would yield potential prophylactic and therapeutic effects.

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Volume 2 Issue 11 November 2019