

Waterpipe Smoking and Women's Health: From Pregnancy to Breast Cancer

Abstract

Today, smoking tobacco in waterpipes has increased in popularity worldwide; this is largely based on the belief that waterpipe smoking (WPS) is less harmful than cigarette smoking. On the other hand, it was recently pointed out that WPS can have a dramatic effect on women's health from pregnancy to breast cancer initiation and/or progression through targeting two important members of cadherin genes, cadherin-6 type 2 and E-cadherin, which are important regulators of cell migration and invasion. More significantly, it is noted that the deregulation of these two genes as well as others can occur through the Erk1/Erk2 and PI3K/Akt signaling pathways. Herein, we discuss, for the first time, the outcome of WPS and its mechanism on the embryo, at the early stage of its development, as well as breast cancer progression.

Keywords: Breast cancer, cancer progression, embryo, toxicity, waterpipe smoking

Introduction

Tobacco smoking, although easily preventable, is considered a major cause of morbidity and mortality worldwide, accounting for 6 million deaths each year (World Health Organization).^[1] Tobacco smoking today has different forms including cigarette, cigar smoking, e-cigarettes as well as waterpipe.^[2] Waterpipe smoking (WPS) is the most common tobacco use in the Middle East region, and its popularity worldwide is rapidly increasing.^[2] Waterpipe provides a variety of flower-flavored tobacco in addition to various spices and fruits with some regional and cultural differences.^[3] In general, WPS has gained a certain degree of public acceptability that allowed it to be integrated into local cafe and restaurant culture, especially in the absence of waterpipe specific regulatory policies.^[2,3] In some cases, common misconceptions that consider WPS less harmful than cigarettes exist, which are pointed out in several studies.^[4-6] Nevertheless, recent investigations stressed the obvious harmful outcomes of WPS on human health, which is comparable, and maybe even worse than that of cigarette smoking.^[7-11] These harmful factors combine the effect of the

common toxic elements between WPS and cigarette smoking such as high levels of nicotine, heavy metals, particulate matter, and various carcinogens with the additional harmful effect of the charcoal used to heat the tobacco;^[9-11] this raises health risks by producing high levels of carbon monoxide, metals, and cancer-causing chemicals. On the other hand, secondhand smoke from WPS can also cause serious risk of respiratory diseases in addition to other health disorders and probably cancers in exposed nonsmokers.^[7-9]

To date, it has been well established that cigarette smoking causes multiple adverse effects on human health including cardiovascular and lung diseases in addition to several types of cancers including breast.^[12-15] In addition, the toxic effect of cigarette smoke or exposure to smoke in the case of secondhand smokers during pregnancy has been recognized to cause numerous poor birth outcomes, such as low birth weight and preterm birth, as well as lifelong health and developmental problems.^[16] Thus, it is evident that smoking in different forms can cause serious effects on human health. However, the impact of WPS on women's health, especially during pregnancy as well as breast cancer development, has not been clarified yet. Thus, in our laboratory, we investigated, for the first time, the outcome of WPS on

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the early stage of embryonic development using chicken embryo as a model. In parallel, we investigated the effect of WPS on human breast cancer progression using two noninvasive breast cancer cell lines. Our data revealed that WPS inhibits angiogenesis of the chorioallantoic membrane in the embryos; in addition, WPS-exposed embryos show a slight reduction in their sizes. We reported that around 80% of WPS-exposed embryos die before 10 days of incubation. More significantly, we found that WPS induces upregulations of several key regulator genes related to cell apoptosis, proliferation, and migration.^[17] Among these genes, we noted that cadherin-6 type 2 (CDH6 type 2) is upregulated in brain and heart tissues from WPS-exposed embryos in comparison with unexposed ones. As other cadherin protein members, CDH6 type 2 is involved in embryogenesis as well as cancer progression through the initiation of epithelial-to-mesenchymal transition (EMT) in which epithelial cells shed their differentiated characteristics to undergo changes in morphology, architecture, adhesion, and motility.^[18,19] Thus, our study revealed for the first time that WPS can deregulate CDH6 type 2 gene in the embryo which can dramatically affect its normal development.

Nowadays, it is well known that breast cancer is the most common malignancy in women worldwide and its metastatic form is the major cause of morbidity and mortality in breast cancer patients.^[20,21] On the other hand, it has been reported that cigarette smoking can enhance breast and lung cancer progression through the initiation of EMT.^[22,23] However, the outcome of WPS on human breast cancer has not been investigated yet; thus, we recently explored the effect of WPS on two noninvasive breast cancer cell lines, MCF7 and BT20. Our data revealed, for the first time, that WPS enhances cell motility and invasion of these two cell lines; this is accompanied by a down- and upregulation of E-cadherin and focal adhesion kinase (FAK) protein, respectively, which are important key controllers of cancer progression genes and EMT biomarkers.^[15,24] More significantly, our data pointed out that WPS can activate Erk1/Erk2 and PI3K/Akt signaling pathways which could be the main mechanism behind E-cadherin and FAK deregulation and consequently the enhancement of cell motility and invasion of breast cancer cells [Figure 1].^[15]

Therefore, these data clearly suggest that WPS can enhance cancer progression including breast, at least in part, by the downregulation of E-cadherin in addition to the upregulation of FAK and CDH6 type 2 genes through Erk1/Erk2 and PI3K/Akt signaling pathways.

In conclusion, our embryonic study implies that WPS and/or secondhand smoking from WPS can have a dramatic effect on the embryo at the early stage of pregnancy. Meanwhile, our investigation concerning the outcome of WPS on breast cancer indicates that exposure

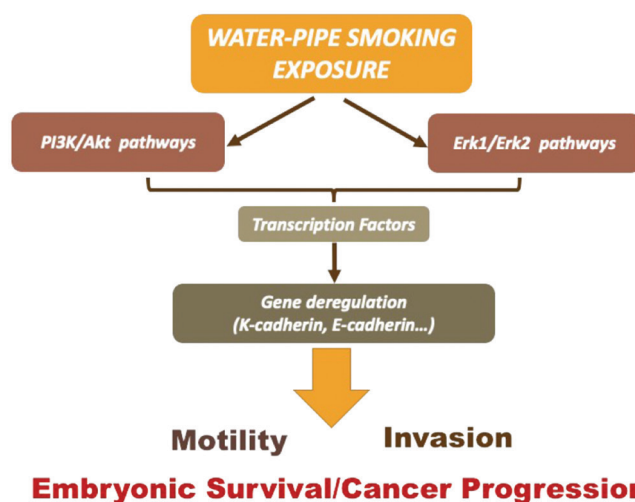


Figure 1: Schematic outline showing the potential signaling pathways of waterpipe smoking exposure in the embryo and breast cancer progression. We believe that waterpipe smoking can affect the normal development of the embryo as well as breast cancer progression through Erk1/Erk2 and PI3K/Akt pathways which can deregulate several genes related to cell migration and invasion and consequently embryonic survival and cancer progression

to WPS can enhance breast cancer progression; these two events could take place through Erk1/Erk2 and PI3K/Akt signaling pathways [Figure 1]. Thus, we herein provide evidence, for the first time, that WPS can harm women's health, especially during the early stage of pregnancy in addition to breast cancer development and/or progression. Accordingly, we believe that additional studies are required to elucidate the pathogenic effect of WPS on other aspects of women's health.

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Conflicts of interest

There are no conflicts of interest.

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