The Role of PDE5 Inhibitors and the NO/cGMP Pathway in Cancer.

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INTRODUCTION: Phosphodiesterase 5 (PDE5) inhibitors (PDE5i) have been used clinically for the treatment of erectile dysfunction, acting on the nitric oxide/cyclic guanosine monophosphate (NO/cGMP) signaling pathway. Simultaneously, researchers have elucidated the roles that this pathway plays in the regulation of cell proliferation, tumor development, and progression. As a result, our knowledge of PDE5i and cancer biology has expanded and provides an integration that holds great promise for some, but concern for others.

This review evaluates the role of PDE5i and the NO/cGMP signaling pathway in the pathogenesis and prevention of various malignancies.

METHODS: A literature review was performed with regard to the role of NO/cGMP pathway in tumor formation and prevention in preclinical and clinical studies. Studies that utilized PDE5i to further explore the involvement of this pathway also were included.

MAIN OUTCOME MEASURES: To evaluate whether PDE5i provide a potential benefit for treating and/or preventing malignancies; or if they create potential harm leading to the development of these malignancies.

RESULTS: The best available data suggest that the interactions between PDE5i and cancer are tumor- and tissue-specific. Currently, the effect of PDE5i use on melanoma development is being debated. Further clinical controversy lies in PDE5i use for penile rehabilitation after nerve-sparing prostate cancer surgery. Preclinical studies suggest that PDE5 inhibition could lead to a decreased risk of developing colorectal and breast cancer, leukemia, and myeloma. PDE5i also may provide an additional antitumor immune response. Finally, researchers have demonstrated a synergistic effect from combining PDE5i with current chemotherapeutic regimens.

CONCLUSION: Currently, there are inadequate data to make any conclusive statements regarding the role of PDE5i in cancer pathogenesis and how to alter clinical management. In order to create appropriate clinical guidelines, further experimental and clinical evidence is required.