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# Adverse Effects of Dopamine Category Drugs on cancer Risk: A Retrospective Cohort Study

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**Abstract**
The dopamine D2 receptor (D2R) family has been found to be upregulated in various cancers and is associated with stemness characteristics. Interestingly, a lower risk of cancer has been linked to conditions such as schizophrenia and Parkinson's disease, where dopaminergic medications are utilized. Research indicates that D2R antagonists exhibit anticancer properties in both cell cultures and animal studies, demonstrating effects such as reduced tumor growth, induction of autophagy, alterations in lipid metabolism, and triggering of apoptosis, among others. This has led to several hypotheses, with the most prominent suggesting that D2R ligands could represent a novel strategy for cancer chemotherapy. This notion is particularly attractive due to the availability of numerous approved and experimental drugs within this class that may be repurposed. We examine the existing literature and the supporting and opposing evidence regarding this hypothesis. A notable observation from a pharmacological perspective is that the concentrations required for the cytotoxic effects of D2R antagonists are significantly higher than their binding affinity for the receptor. While further definitive studies are necessary for greater understanding, we propose that targeting D2-like dopamine receptors may only occasionally yield effective ligands for cancer chemotherapy.

**Keyword:** PD Parkinson disease, SCZ Schizophrenia, $D_2R$ Dopaminergic receptor

## I. Introduction

- **Dopamine**

Dopamine is classified as a monoamine neurotransmitter. It is produced in the brain and functions as a chemical messenger, facilitating communication between nerve cells within the brain as well as between the brain and other parts of the body. Additionally, dopamine serves as a hormone that influences various bodily functions, including movement, emotional responses, and the reward system.

- **Dopaminergic neuron**

Dopaminergic neurons of the midbrain are the main cause of dopamine (DA) in the mammalian central nervous system. Their loss is linked with one of the most prominent human neurological disorders, Parkinson's disease (PD).

- **Dopaminergic Drug**

Dopaminergic drugs are medications that affect dopamine levels in the brain and body. Its also mostly used in Parkinson disease and neurotransmitter disorder.

**Reasons behind dopamine drug that causing carcinogenetic effects**

Dopamine, a neurotransmitter, has been linked to cancer development and progression through various mechanisms. Here are some reasons behind dopamine's potential carcinogenic effects:

Mechanisms:

1. Oxidative stress: Dopamine can undergo autoxidation, producing reactive oxygen species (ROS) that damage DNA, proteins, and lipids.
2. DNA damage: Dopamine's oxidative metabolites can bind to DNA, causing mutations and epigenetic changes.
3. Cell proliferation: Dopamine stimulates cell growth and division, potentially leading to uncontrolled proliferation and tumor formation.
4. Angiogenesis: Dopamine promotes blood vessel formation, supporting tumor growth and metastasis.
5. Immune system modulation: Dopamine can suppress immune responses, allowing cancer cells to evade detection.
6. Hormonal imbalance: Dopamine affects hormone regulation, potentially leading to hormonal cancers (e.g., breast, prostate).
7. Receptor-mediated signalling: Dopamine binds to receptors, activating signalling pathways that promote cell survival and proliferation.

**Specific cancers linked to dopamine:**

1. Melanoma: Dopamine's oxidative metabolites may contribute to melanoma development.
2. Breast cancer: Dopamine receptor expression is associated with breast cancer progression.
3. Prostate cancer: Dopamine's hormonal effects may contribute to prostate cancer development.
4. Glioblastoma: Dopamine receptors are overexpressed in glioblastoma, promoting tumour growth.

**Factors Influencing Dopamine Carcinogenic Potential :**

1. Dose and Duration : Prolonged exposure to high dopamine level increases cancer Risk.

2. Individual Susceptibility : genetic predisposition , Environmental factors and lifestyle choices can modulate dopamine carcinogenic effects.
3. Interactions with other Neurotransmitters: Dopamine interactions with other neurotransmitters (e.g. Serotonin ) may Influence Cancer Risk .

**Dopaminergic drugs with their possible Unintended Consequences :**

Dopa category drugs , primarily used to treat Parkinsons Diseases , can have adverse effect . some studies suggest Potential carcinogenic risk associated with long term use. Here are some dopa category drugs and their possible cancer related adverse effects .

❖ **Drugs:**

1) Levodopa ( L- DOPA )
2) Dopamine Agonists (e.g. , Ropinirole , Pramipexole )
3) COMT inhibitors ( e.g. , Entacapone , Tolcapone )
4) MAO- inhibitors ( e.g. , Selegiline , Rasagiline )

❖ **Possible cancer - Related Adverse Effects:**

1) Levodopa :
- Increased risk of melanoma
- Potential risk of Prostate Cancer

2) Dopamine agonists :
- Possible increased risk of breast cancer
- Potential risk of prostate cancer

3) COMT inhibitors :
- No conclusive evidence of Carcinogenic effects

4) MAO - B Inhibitors :
- Potential Risk of Skin Cancer ( e.g. , basal cell Carcinoma )

❖ **Mechanisms:**

1. Oxidative Stress And DNA Damage .
2. Increased cell proliferation and tumor growth.
3. Hormonal Imbalance And Receptor Modulation.

**Treatment**

Dopamine as an antagonist in cancer treatment:

❖ **Mechanism:**

Dopamine receptors are expressed on various cancer cells, including:

1. Breast cancer
2. Prostate cancer
3. Melanoma
4. Glioblastoma

❖ **Dopamine antagonists can:**

1. Block dopamine receptors, inhibiting cancer cell growth
2. Reduce angiogenesis (tumor blood vessel formation)
3. Enhance apoptosis (cancer cell death)
4. Inhibit cancer cell migration and invasion

❖ **Dopamine Antagonists in Cancer Treatment:**

1. Metoclopramide: Blocks dopamine D2 receptors, inhibiting cancer cell growth.
2. Haloperidol: Blocks dopamine D2 receptors, inducing apoptosis in cancer cells.
3. Chlorpromazine: Blocks dopamine D2 receptors, inhibiting cancer cell proliferation.
4. Sulpiride: Blocks dopamine D2 receptors, enhancing apoptosis in cancer cells.

❖ **Cancer-Specific Dopamine Antagonists:**

1. Cabergoline: Blocks dopamine D2 receptors, used in treatment of prolactinomas and breast cancer.
2. Bromocriptine: Blocks dopamine D2 receptors, used in treatment of pituitary tumors and prostate cancer.

❖ **Combination Therapies:**

1. Dopamine antagonists + chemotherapy
2. Dopamine antagonists + targeted therapy
3. Dopamine antagonists + immunotherapy

❖ **Clinical Trials:**

1. Phase I/II trials: evaluating dopamine antagonists in various cancer types.
2. Phase III trials: comparing dopamine antagonists with standard treatments.

❖ **Potential Benefits:**

1. Improved treatment outcomes
2. Reduced side effects
3. Enhanced quality of life

❖ **Challenges and Limitations:**

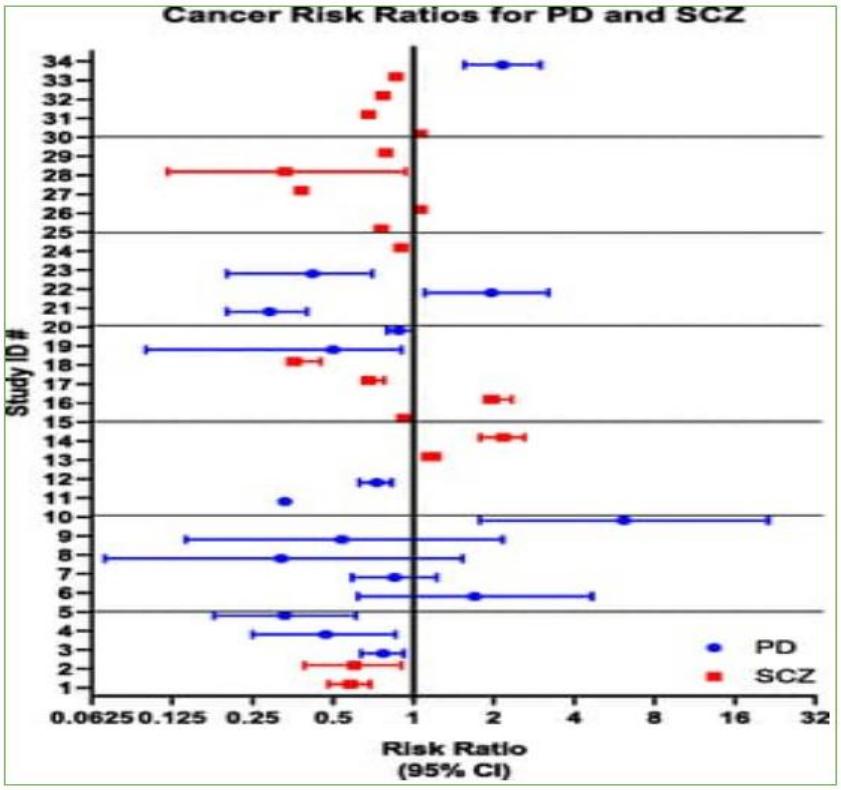
1. Dopamine receptor expression variability in cancer cells
2. Potential psychiatric side effects (e.g., depression, anxiety)
3. Interactions with other medications

❖ **Future Directions:**

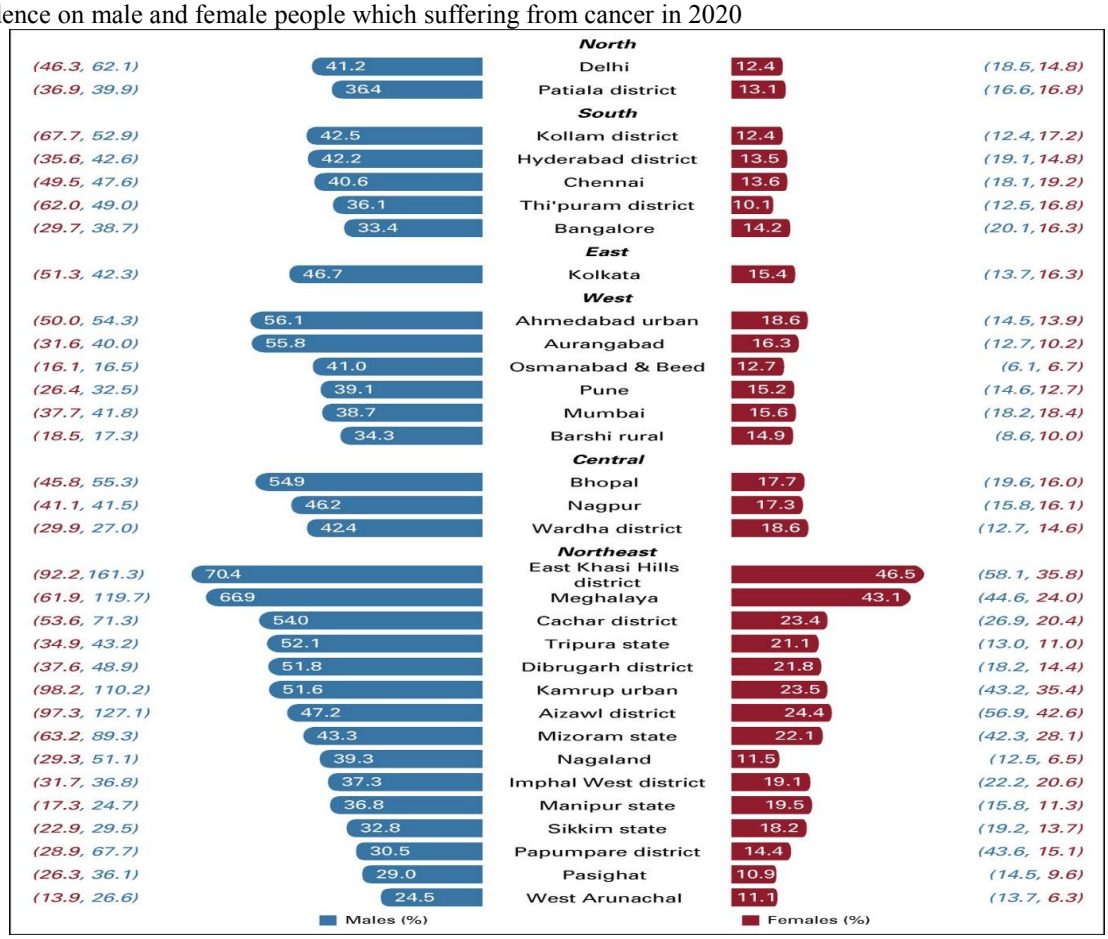
1. Investigating dopamine antagonists in combination with other therapies.
2. Developing targeted dopamine antagonists for specific cancer types.
3. Exploring dopamine antagonist-based immunotherapies.

**Evidence**

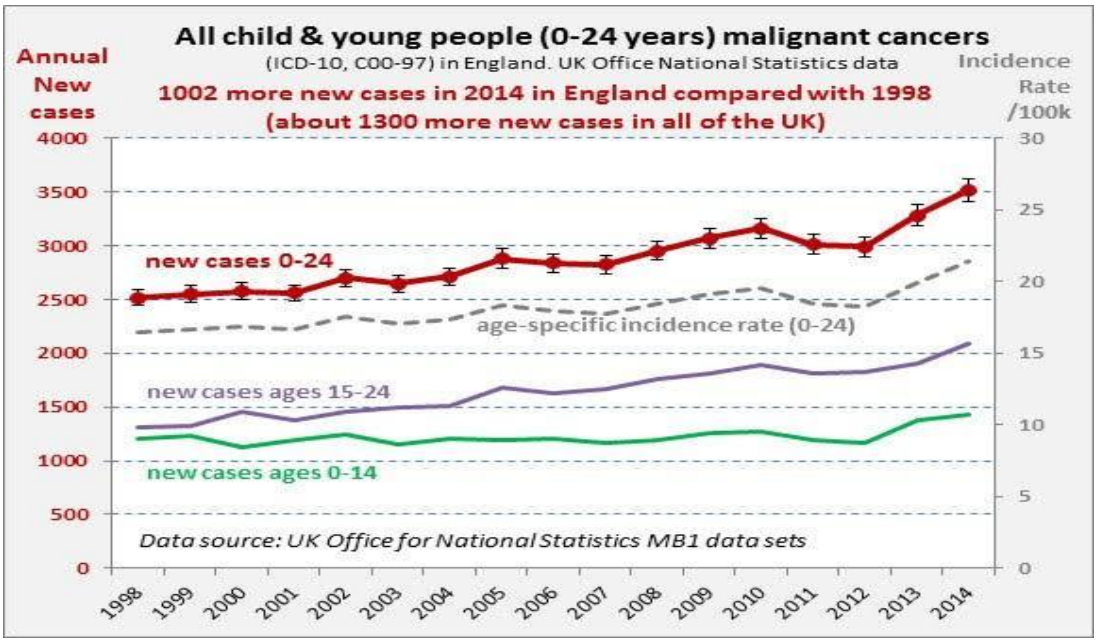
Evidence on cancer cause from dopa category drug in treatment of PD and SCZ




Evidence on male and female people which suffering from cancer in 2020




Evidence of cancer which suffering people in UK




## II. Conclusion

In this research, we are conclude that when even patients taking dopaminergic agonist drug in PD or SCZ. That case the drug increases or releases dopaminergic hormone, so that misbalancing body growth hormone. So that increase cell of body in which defective cell also releases, its defective cell cause cancer or tumor. So that we can treat with dopaminergic antagonist drug or chemotherapy or combination of both. The association between dopamine receptor agonists and increased cancer risk suggests a potential link between dopamine signalling and tumorigenesis. Dopamine antagonists may offer a novel approach to cancer treatment by blocking dopamine receptors and inhibiting cancer cell growth.

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