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Analysis of Potentiality and Anti-Tumour activity of Cap in cancer treatment

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ABSTRACT: Oral Cancer is one of the paramount cause of death in India to be a little specific it showed an adverse effect especially in Northern and eastern region in India. India holds about one third cases of the total oral cancer in the worked. According to a report based on 2018 data, India hath an approx. 19999 new cases of oral cancer and approx. 80 deaths. We all know well that all clinical approaches in cancer treatment mainly include aciurgy, radiation therapy& chemotherapy. These treatments often give a morbid outcome and reduce the survivality rate. It's due to their non-selective nature of tumour cells along with the normal cells that they kill or, hampers the ling of another cells. Recently the potential or ColdAtmospheric Plasma (CAP) in cancer therapy is gathering a great interest among scientists and researchers.

Over the past decade, Cold Atmospheric Plasma (CAP) near room temperature an ionized gas has shown it's application in cancer therapy. Two CAP devices, namely dielectric barrier discharge and another one is plasma jet; which showsremarkablyanti-cancer capacity over millions of cancer cell lines in vitro and several hypodermic xenograft tumours in vivo treatment. In contrast to conventional anti-cancer approaches and drugs CAP is a selective anti-cancer treatment procedure. Thus as far as establishing the chemical and molecular mechanism of the anti-cancer capacity of CAP is far from complete. This review is based on a comprehensive introduction of the basics of CAP, state of the skill of invention in this field, the primary challenges, and future directions to the cancer biologists.

Keywords: Cold plasma, cancer treatment, reactive species, selectivity

I. INTRODUCTION:

Cancer is one of the main cause of death in India. Although Oral cancer is distributed globally, this cancer type is more widespreadin Southern and Central Asia. India contributes to about 1/3rdof the total global cases. The death-toll of the disease in 2018 was 72,616. Statistically, this is a very devastating number to deal with. The term "oral cancer" often tends to get replaced with Oral Squamous Cell Carcinoma (OSCC) which is most frequent among all other oral neoplasms. It is reported that around >90% of all oral neoplasms are OSCC Plasma is the fourth state of matter Non-thermal plasma (NTP) has gained much popularity in recent times in the domain of cancer therapy by using cold plasma due to its selective nature to kill tumour cells.

This is mainly due to the enhanced selective nature of the CAP in targeting and killing the tumour cells without affecting the surrounding tissue and causing minimal side effects. Reactive Oxygen and Nitrogen species (RONS) are the main contributors to the efficacy of CAP in killing cancer cells. Although many attempts have been made to understand the underlying mechanism of CAP in cancer treatment, there is still a lack of detailed study with respect to different treatment conditions. The use of CAP can be a potential innovative therapy in the upcoming days and more clinical trials should be encouraged to prove its efficacy and relevance in clinical purpose.

NTP/ CAP:

The Cold Atmospheric Plasma (CAP) technology is being proposed for application in combination therapy to enhance the effect of TMZ. CAP can be artificially produced in laboratory settings by applying a high alternating electric current through a gas which results in a plasma glow discharge.

NTPs are actually a cocktail of ionized gas with electrons, ions, neutral atoms, radicals, and UV photons. NTPs mainly work by inducing apoptosis via the signalling pathway, inhibiting cell invasion and migration, or by arresting the cell cycle Devices such as plasma jets are used to treat the tumour cells effectively. A plasma jet consists of a wire electrode, a glass confinement tube with 8mm inner diameter and 10mm approx. outer dimeter, a Teflon fitting and a pen shaped nozzle having 2mm

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inner diameter at the exit. A sharp tipped tungsten pin wireis placed on the tube axis and the nozzle is attached to the glass tube end.

CAP and Oral Cancer:

Arecent study showed that the cancer type and culture conditions influences CAP treatment and hence need to be considered when selective activity of CAP is checked. These are considered as water channels that often facilitate the transport of free oxygen and nitrogen species, such as hydrogen peroxide as well as other small molecules including CO2, NO etc. Aquaporin 1.3 and 8 are known to play role in transport of H_2O_2 in mammalian cells. Studies show that over-expression of aquaporins to increases oxidative stress due to rising intracellular ROS concentration. Furthermore, monitoring the intracellular hydrogen peroxide content shows that the tumour cells accumulate H202 faster than the non-malignant ones CAPis composed of RONS, charged particles, LUV radiation and electromagnetic fields. All these synergistically act on the tumour cells.

But the main factor that contributes to cell death in oral cancer cells upon CAPtreatment is the ROS and RNS. In many studies primarily DSB have been assessed by detection of □H2AX, a phosphorylated form of the histone H2AX.Bishop et al. (2019)

CAP in tumour microenvironment and Immunology:

The effects of CAP have been observed on different parts of the tumour microenvironment, which is majorly composed of malignant cells, immune cells, endothelial cells, fibroblasts tumour vasculature and the extracellular matrix, which are in constant communication with each other. In vitro studies have shown that CAP is able to destroy collagen. It is also reported that high doses of CAP prevent extracellular matrix interactions with cells and bone formation.

As the plasma treatment is a local therapy that possibly modulates the tumour microenvironment, various reports claim the possibility of plasma to stimulate immunity to support anticancer treatment. Recently, two lines of research are going on in parallel to disentangle the effect of plasma treatment in anticancer immunity. One is the ability of plasma to affect immune cells directly, which leads to their activated ion or selection of specific subpopulations of immune cells, while the other is an indirect activation of immune cells via plasma- mediated tumour cell death and pro-inflammatory signals in the microenvironment.

II. CONCLUSION:

Reactive oxygen and nitrogen species (RONS) have been identified as the main contributors for the efficacy of CAP in killing oral cancer cells. However, many studies indicate a selective effect on CAP towards malignant cells compared to their healthy counterparts, the experimental settings in many of these studies may have influenced this finding. Furthermore, several factors have been 1dentified that often differ between healthy and malignant cells and hence, may contribute to an increased sensitivity of cancer cells to CAP. Factors such as expression of aquaporins, cholesterol or the ability to protect against oxidative stress by the anti-0xidative system determine how many RONS can enter the cell and interfere with intracellular signalling pathways. CAP treatment often results in reduced adhesion, migration and invasion and may contribute to a successful cancer treatment by reducing the ability of the cells to spread and form metastasis.

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