Effect of Mesenchymal Stem Cells Injection on Induced Stomatitis in Chemotherapy Treated Rats

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By

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Abbreviation	Meaning
5-FU	5-Fluorouracil
FUMP	5-fluourouridine monophosphate
GIT	gastrointestinal tract
OM	oral mucositis
Gy	Gray: is the unit of absorbed dose, which represents the amount of radiation required to deposit one joule of energy in one kilogram of any kind of matter
NCI-CTC	National Cancer Institute–Common Toxicity Criteria
WHO	World Health Organization
IA	intra-artery
IV	Intravenous
IP	intraperitoneal
MSCs	mesenchymal stem cells
BM-MSCs	bone marrow mesenchymal stem cells
FGF	fibroblast growth factor
VEGF	vascular endothelial growth factor
BMSCs	bone marrow stem cells
hMSCs	Human mesenchymal stem cells
OMS	oral mucositis scoring system
H&E	Haematoxylin and Eosin
PCNA	Proliferating Cell Nuclear Antigen
IR	Infrared
GMSCs	gingival mesenchymal stem cells
hGMSC	human gingival mesenchymal stem cells
hASCs	human adipose stem cells
GvHD	graft-versus-host disease

1. Introduction

With their tremendous clinical utility, there are many classes of chemotherapeutic agents in the market that are used effectively as anti-neoplastic treatment **(Jaime et al., 2003)**.

The effective treatment of malignancies is usually limited by its harmful effect on normal, healthy cells. Mucosal cells in the gastro-intestinal tract (from the mouth to anus) are highly susceptible to the toxic effects of cancer treatment. These toxicities (including mucositis and stomatitis) are some of the most significant unavoidable effect associated with cancer treatment. So, Stomatitis (the mucositis of oral mucosa) is the best-characterized manifestation because it results in symptoms in an area accessible to routine examination **(Denham et al., 1991)**

The goals of mucositis management are to prevent or reduce the severity of the drug toxicity and to manage the associated symptoms. Mucositis management allows the continued delivery of treatment without interruption or dose reduction leading to improvement of overall prognosis. But unfortunately there is no standard protocol that is used to completely cure or prevent oral mucositis **(Clarkson et al., 2010; Lalla et al., 2014).**

Stem cells are a subject of interest as a potentially revolutionary new way to treat diseases and injuries, with wide-ranging medical benefits as wound healing, ulcer treatment and management of side effects of chemotherapy **(Aboushady et al., 2012).**

2. Review of literature

2.1. Chemotherapy:

2.1.1 Mechanism of action:

Chemotherapeutic drugs cause damage to cells so, they are termed cytotoxic drugs. Most chemotherapeutic drugs work by impairing mitosis (cell division) (specially targeting fast-dividing cells). They prevent mitosis by various mechanisms including damaging DNA and inhibition of the cellular organelles involved in cell division. One theory explaining why these drugs kill cancer cells is that they induce a programmed cell death known as apoptosis **(Makin and Hickman, 2000; Malhotra and Perry, 2003)**

The process of cell division, whether normal or cancerous, passes through the cell cycle. The cell cycle goes from the resting phase, active growing phases, and then to mitosis. Chemotherapeutic drugs that affect cells only when they are dividing are called cell-cycle specific. While those affect cells when they are at rest are called cell-cycle non-specific. The scheduling of chemotherapy is set based on the type of cells, rate of cell division, and the time at which the given drug is likely to be effective. This is why chemotherapy (cell cycle spescific) is typically given in cycles. The main action of these drugs works against cells in a specific phase of the cell cycle; For example, the drug Cyclophosphamide acts upon cells in the DNA replication phase of the cycle, while other drugs, such as Taxol, more effectively influence cells in the division phase. These types of drugs do not affect cells in the