"Effect of Bone Marrow Derived Mesenchymal Stem Cells infusion Timing on Radiation Induced Oral Mucositis in Albino rat"

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بسم الله الرحمن الرحيم

"وقل ربي زدنى علما"

صدق الله العظيم

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List of Abbreviations

Acronym	Definition
AC	Apoptotic cells
CB	Cord blood
COPD	Chronic obstructive pulmonary disease
CT	Chemotherapy
DSCs	Dental Stem Cells
ES	Embryonic stem
GMSCs	spheroid-derived gingival MSCs
Gy	Gray
H&NRT	Head and neck radiotherapy
HNC	Head and neck patients
HSCs	hematopoietic stem cell
HSCT	hematopoietic stem cell transplantation
IL-1β,	Interleukin 1-beta

Acronym	Definition
IPS cells	Induced pluripotent stem cells
KGF	Keratinocyte growth factor
MMP	Matrix metalloproteinase
NF-KB	Factor-κb
NK	Natural killer
OLP	oral lichen plamus
PARP	Poly (adpribose)polymerase
PCNA	Proliferating cell nuclear antigen
PRP	Platelet rich plasma
PS	Phosphatidylserine
ROS	Reactive oxygen species
RT	Radiotherapy
SLE	Systemic lupus erythematosis
TGF-p3	Transforming growth factor-p3
TNF-α	Tumor necrosis factor-alpha

Acronym	Definition
TUNE	Terminal deoxynucleotidyl transferase end labeling
UC	Umbilical cord
VEGF	vascular endothelial growth factor

Introduction

INRODUCTION

Cancer is defined as uncontrolled proliferation of cell with lack of differentiation and immortality compared to normal cells due to multiple changes in genetic expression which lead to imbalance between cell proliferation and cell death. It is further classified to benign or malignant based on its ability of invading other tissue ***(Zheng, et al. 2009).***

Cancer is one of the leading causes for mortality across the world. Among the various type of cancer, most of the death occurs due to oral cancer and lung cancer. The lancet news report expected that 75% of population will suffer from to cancer in 2030 ***(Makiko, et al., 2012).***

Three kinds of therapy like Chemotherapy (CT), Radiation therapy (RT) and surgical ablation are mainly used for cancer treatment. (CT) and (RT) therapy have many side effects as these therapies are unable to distinguish between normal and cancerous cells due to similar mitotic index. Chemotherapy may lead to bone marrow suppression, anemia, alopecia, cachexia, mucositis, nausea, vomiting, reduced fertility and chances of second cancer ***(Wilkes, 1998).***

Radiotherapy plays an important role in the management of head and neck cancer. The majority of new cases of invasive head and neck cancer need radiotherapy as a primary treatment, as an adjunct to surgery, in combination with chemotherapy, or as palliation The radiation dose needed for the treatment of cancer is based on location and type of malignancy, and whether or not radiotherapy will be used solely or in combination with other modalities ***(Dobbs, et al., 1999).***

Oral mucositis is an inflammatory process of the oral mucosa due to radiation in head and neck cancer patients, chemotherapy or high dose of busulfan and cyclophosphamide used for prevention of graft rejection after bone marrow transplantation. It is characterized by atrophy of squamous epithelial tissue of oral mucosa, vascular damage and an inflammatory infiltrate at the basement membrane region; epithelial atrophy is usually followed by ulceration ***(Sonis, et al. 2004).***

The development of oral mucositis is a complex process. Severe oral mucositis results from injury to rapidly dividing epithelial cells that line the oral cavity. This injury occurs as a consequence of CT and RT regimens, the roles of which are to target and eliminate rapidly dividing cancer cells ***(Sonis, et al. 2004)***

Oral mucositis increases mortality and morbidity and many times contributes to rising health care costs. Because the patient is often neutropenic as well, the soreness may be aggravated by the development of fungal infections in the mouth, most commonly oral candidiases ***(Alkesh, et al. 2013).***

Oral mucositis has a dramatic impact on the patient's quality of life. It also adversely influences the administration of an optimal CT cycle. Frequently, reduction of dose, late treatment and discontinuations of therapy is necessary to allow the oral lesions to heal. Also life-threatening infections with fungus and higher treatment costs are related to the severity of oral mucositis ***(Rubenstein, 2004).***

However, most of current interventions for oral mucositis are palliative, neither specific nor efficient at preventing or treating this complication. Even though recombinant human keratinocyte growth factor