Investigation of the Effect of Pentoxifylline on HIF-1Alpha Gene Expression and Serum HIF-1Alpha Levels in Irradiated Rats

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INTRODUCTION and AIM

Head and neck cancer is the seventh most common cancer worldwide and is treated with surgery, radiotherapy and chemotherapy or combinations. Radiotherapy, which is still one of the most commonly used treatments, brings with it acute and chronic side effects. Radiation-induced fibrosis is one of these side effects, causing trismus and negatively affecting the patient's quality of life.
Fibrosis is a pathological process in which normal tissue components are replaced by matrix and various irregular collagen fibrils, leading to loss of organ function and/or significant impairment in quality of life.

In our study, it was planned to evaluate the preventive/therapeutic efficacy of pentoxifylline against hypoxic damage in tissues in rats with irradiation-induced fibrosis model, based on HIF-1α gene expression level and accompanying histopathological findings.

METHODS AND MATERIALS

17 male Sprague Dawley rats used in our study were divided into 3 groups. The first group is the experimental group (R) that only received radiotherapy, and the second group is the experimental group (PR), which is administered oral pentoxifylline for 24 days after radiotherapy. The third group is the control group (K) consisting of 5 completely healthy rats.Oral pentoxifylline was given to 3 rats randomly selected from the control group for 24 days (K(+)). A single dose of 90Gy equivalent radiotherapy was administered to the experimental groups under anesthesia. Oral pentoxifylline was given to the PR and K(+) groups for prophylactic purposes, while we expected fibrosis to develop following radiotherapy.At the end of the 24th day, the groups were sacrificed and tissue samples were taken from M.rectus femoris muscles exposed to radiation along with blood samples. ELISA was studied for HIF-1 gene expression in blood samples; Histopathological findings and Real-Time PCR findings were also evaluated in tissue samples.

RESULTS

Real Time PCR results

	Ort±S.S.	Medyan (IQR)
R	3,72±3,80	2,14 (1,14-5,41)
PR	1,12±,51	1,23 (0,76-1,57)
K+	1,16±,99	0,97 (0,27-2,23)
K-	1,00±,13	1,00 (,91-1,10)
P	0,317	

ELISA results

	Ort±S.S.	Medyan (IQR)
R	20,448±2,453	19,607 (18,526-23,210)
PR	20,013±2,595	19,733 (18,272-21,318)
K+	17,823±1,806	17,188 (16,421-19,861)
K-	22,200±1,606	22,200 (21,065-23,336)
P	0,264	

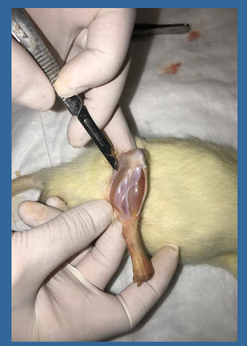

Figure 1. Sacrification and sampling of the muscles

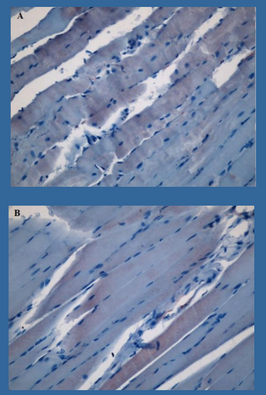

Figure 2. Focal punctate accumulation of HIF-1α in the cytoplasm of muscle cells. A) R group. B) PR group (x400).

Hematoxylin-Eosin vs Masson Trichrome Histochemical Staining

GROUP R

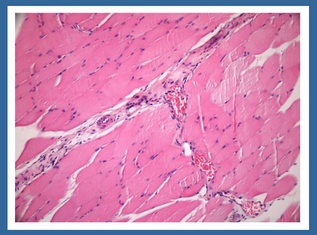

Figure 3. Fibrotic bands and vascular sections between muscle bundles (H&E x200).

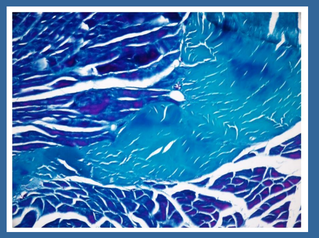

Figure 4. Collagen bands stained green between muscle cells (Masson Trichrome x200).

GROUP PR

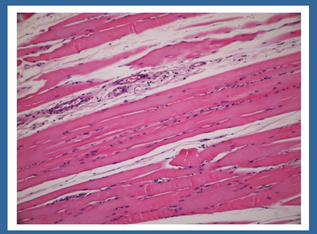

Figure 5. Muscle bundles separated by mildly fibrotic bands(H&E x200).

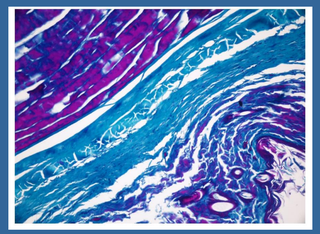

Figure 6. Collagen fibers stained green with Masson Trichrome stain (Masson Trichrome x100).

CONCLUSIONS

When the R and PR groups are compared with the control groups, we can say that the RBF process can be induced in 24 days based on the differences observed in histopathological examinations. Collagen bands and focal punctate cytoplasmic accumulation of HIF-1α in the experimental groups may be evidence for this. - Currently, RBF treatment is mainly symptomatic and a treatment option that provides definitive remission has not yet been defined. Therefore, more detailed research on pentoxifylline, a promising therapeutic option, should be conducted.

ACKNOWLEGEMENT

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