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A survey on stimulatory effects of topical application of radioactive lantern mantle powder on wound healing

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Background: Poorly educated people in some parts of Iran use burned mantles as a wound healing medicine. *Materials and Methods:* To perform surface area measurement, twenty rats were divided randomly into two groups of 10 animals each. The first group received topical burned radioactive lantern mantle powder on the first to third days after making excision wounds. The second group received non-radioactive lantern mantle powder. For histological study, 36 male rats were randomly divided into two groups of 18 animals each. Full thickness excision wound (314 ± 31.4 mm^2) was made on the dorsal neck in all animals after inducing general anesthesia. For the first three days, cases had received topical application of the radioactive lantern mantle powder. Finally, to measure the tensile strength, an incision was made on the dorsal neck of the rats. *Results:* Surface area measurement of the wounds showed a progressive surface reduction in both groups. Histological study showed a significant statistically difference between cases and controls with respect to fibrinoid necrosis and neutrophilic exudate on days 3 and 14. Considering the existence of granulated tissue, a significant difference was observed between case and control groups on days 3 and 7. Tensile strength study showed no significant difference between the cases and controls. *Conclusion:* Topical use of radioactive mantle powder can accelerate the healing process of the wound in rats. **Iran. J. Radiat. Res., 2008; 6 (2): 97-102**

Keywords: *Lantern mantle, wound healing, radioactive, thorium.*

INTRODUCTION

It has been shown that irradiation of skin causes slower healing of open wounds (1). However, in some parts of Iran, poorly educated people use radioactive lantern mantle powder as a therapeutic agent for enhancing wound healing without being aware of its possible dangers. As far as we know, this is the first research which evaluates the stimulatory effects of topical application of radioactive lantern mantel powder on the wound healing. Some lantern mantles which are commonly used for camping contain different levels of thorium compounds (2). Recently, in some developed countries the use of thorium-free mantles has become popular due to the risks associated with the use of a radioactive heavy metal (3). Thorium oxide is a known human carcinogen.

"Hormesis" is a phenomenon in which a harmful substance gives stimulating effects to living organisms when the dose is small. The concept which was initially defined in the field of toxicology was extended to ionizing radiation. It has been shown that living organisms possess the ability to respond to low-dose radiation in very sophisticated ways. The adaptive response is a good example of such responses (4). The induction of the cytogenetic radioadaptive response in human lymphocytes by low doses of ionizing radiation was first reported by Olivieri *et al.* (5). Many articles have demonstrated radioadaptive response in plant cells (6),

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insects [7], Chinese hamster V79 cells [8], cultured human lymphocytes [9-13] including *in vitro* studies on human lymphocytes of the residents of high background radiation areas [14-16], embryonic and HeLa cells [17], occupationally exposed persons [18-19], cultured animal lymphocytes [20], and *in vivo* studies on laboratory animals [21-24]. There has also been reports indicating lack of radioadaptive response in cultured human lymphocytes [25-27]. Further, long-term follow up studies have indicated that lack of radioadaptive response is not a temporary effect and it does not depend on transient physiological factors [28-29]. Many epidemiologic studies with high statistical significance have shown that exposure to low or intermediate levels of radiation may lead to *decreased* mortality or *decreased* incidence of cancer. It has been reported that there was a decreased rate of cancer in people living in the Eastern Urals after radiation exposure from a thermal explosion [30]. Due to lack of published reports on the stimulatory effects of topical application of radioactive lantern mantle powder on wound healing, the present research was conducted.

MATERIALS AND METHODS

Laboratory animals

Twenty Albino NMRI rats which were kept in the animal laboratory center of Rafsanjan University of Medical Sciences (RUMS) were randomly divided into two groups of 10 (experimental and control). The mean weight of the animals was 200 grams (ranged 190-210 g). The rats were kept under standard laboratory conditions (12/12 h dark/light cycle, lights on at 7.00, room temperature set on 21 ± 1 °C, and controlled humidity). All experiments on rats were performed in strict compliance with national and the Rafsanjan University of Medical Sciences' Codes for care and use of laboratory animals. All the animals were kept in identical standard conditions. In order to prevent any bias, each animal was given a code and decoding was performed only after the experiments were done.

Area measurement

To perform surface area measurement, twenty rats were divided randomly into two groups of 10 animals each. After inducing general anesthesia, full thickness excision wound was made on the dorsal neck in all animals. The first group received topical burned radioactive lantern mantle (Butterfly, China) powder at the first to third days after making excision wounds. The activity of each mantle was about 0.8 kBq. The second group received non-radioactive lantern mantle powder at the same days. Accurate blind surface measurement of the wounds by transparency tracing was used for assessment of the wounds healing at 1st, 3rd, 7th, 10th and 15th days after making the wounds. The following equation was used to determine the percentage of wound area:

$$\text{Wound area } (\%) = \frac{\text{Wound area}_{DayX}}{\text{Wound area}_{Day\ 0}} \times 100$$

In this equation, day_x is the day of wound area measurement (days 3, 5, 7, 10, 15 after wounding) and day_0 is the day wounding had done. On the other hand, the percentage of healing was measured as:

Wound area percentage – 100 = Healing

Relevant statistical tests (Student's *t-test*, and ANOVA) were performed using SPSS software (version 15) at $p<0.05$ as the significant level.

Histological study

For histological study, 36 male rats were randomly divided into two groups of 18 animals each. Full thickness excision wound (314 ± 31.4 mm^2) was made on the dorsal neck in all animals after inducing general anesthesia. For the first 3 days, the cases were receiving topical application of the radioactive lantern mantle powder, while the controls received non-radioactive lantern mantle powder. Six rats were randomly selected in each group for wound sampling, three, seven and fourteen days after wounding. The four criteria used for histological investigation were 1) fibrinoid necrosis and neutrophilic exudate, 2) granulation tissue, 3) superficial epithelization and 4) collagen fiber synthesis. The minimum and maximum scores for each criterion were 1 (or minus) and 5 (or 4+) respectively. Data analysis was performed using Mann-Whitney statistical test at p<0.05 as the significant level.

Tensile strength

Thirty six rats were randomly divided into two groups of case and control (each group consisted of 18 animals). For the first 3 days, the cases were receiving topical application of the radioactive lantern mantle powder while controls received non-radioactive lantern mantle powder. To measure the tensile strength, a full thickness incision (20 mm length) was made on the dorsal part of the rats. The samples were obtained at 14th, 21st and 30th days after making incisions. Tensile strength was measured by using a Tensiometer. Student's *t-test* and ANOVA were used for data analysis at p<0.05 as the significant level.

RESULTS

Area measurement

Surface area measurement of the wounds showed a progressive surface reduction in both groups. However, for thorium treated group, the rate of recovery was significantly enhanced in comparison with that of the control group. Although the wound area in the thorium group was not significantly different from that of the control group at the 3rd and 5th days after wounding, a statistically significant difference was observed between the thorium and the control groups on the day7, day10 and day 15. The mean wound surface in thorium and control groups were 150±15.87 and 186±12.68 mm^2 on day7 (P<0.001), 93±15.97 and 134±14.19 mm^2 on day 10 (P<0.001), 1±0.41 and 9±2.04 mm^2 on day15 after wounding, respectively (P<0.01), (tables 1 and 2).

Histological findings

The histological study showed a significant statistical difference between case and control groups with respect to fibrinoid necrosis and neutrophilic exudate on the days 3 and 14. Considering the existence of granulated tissue, a significant difference was observed between case and control groups on days 3 and 7. No difference was observed in superficial

Table 1. Wound area changes in control and test groups at different times.

Time of Investigation (after wounding)	Wound Area in Controls * [Vehicle Group] (mm^2)	Wound Area in Cases* (mm^2)	P-Value
Day 0 (wounding)	314 ± 31.40	314 ± 31.40	NA
3 Days	258 ± 20.65	255 ± 17.20	NS
5 Days	224 ± 11.38	218 ± 8.95	NS
7 Days	186 ± 12.68	150 ± 15.87	P < 0.001
10 Days	134 ± 14.19	93 ± 15.97	P < 0.001
15 Days	9 ± 5.76	1 ± 1.29	P < 0.01

*Mean ± SD NA: Not applicable NS: Non Significant

Table 2. Healing percentages in control and test groups at different times.

Time of Investigation (after wounding)	Healing Percentage in Controls [Vehicle Group]	Healing Percentage in Cases [Radioactive Group]
Day 0 (wounding)	0	0
3 Days	17.8	18.8
5 Days	28.6	30.5
7 Days	40.6	52.2
10 Days	57.3	70.4
15 Days	97.3	99.5

epithelization and collagen fiber synthesis at all days. (figures 1 and 2).

Tensile strength

Tensile strength study showed no statistically significant difference between the case and control groups on days 14 and 21; however, a significant difference was observed on day 30 (P<0.001), (table 3 and 4).

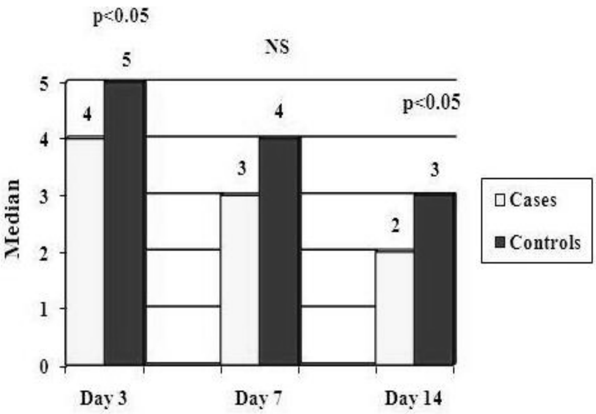

Figure 1. Median score of fibrinoid necrosis and neutrophilic exudate at days 3, 7 and 14 in control and case groups.

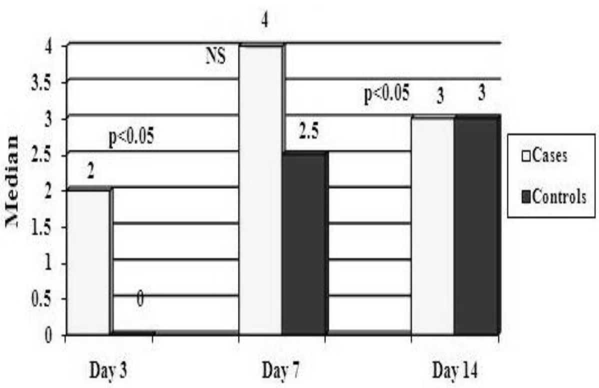

Figure 2. Median score of granulated tissue at days 3, 7 and 14 in control and case groups.

DISCUSSION

The results of the current study clearly indicate that topical use of radioactive mantle powder could accelerate the healing process of the wound in rats. As table 1 indicates, surface area measurement of the wounds on day 7, day 10 and day 15 showed a statistically significant difference

Table 3. Tensile strength in case and control groups at days 14, 21 and 30.

Day	Group	No	Tensile strength (N/mm²) (Mean ±SD)	*P-value* (t-test)
14	Case	6	2.62±2.29	Non Significant
	Control	6	4.26±2.82	
21	Case	6	2.23±1.07	Non Significant
	Control	6	2.07±0.62	
30	Case	4	4.39±2.58	P<0.001
	Control	6	11.52±1.99	

Table 4. Comparison of the means of tensile strengths at days 14, 21 and 30 in case and control groups .

	Tensile strength (N/mm²) (Mean ±SD)	
	Case	Control
Day 14	2.62±2.29 (n=6)	4.26±2.82 (n=6)
Day 21	2.23±1.07 (n=6)	2.07±0.62 (n=6)
Day 30	4.39±2.58 (n=4)	11.52±1.99 (n=6)
P-value (ANOVA)	Non Significant	P<0.001

between the case and control groups ($P<0.01$, $P<0.001$ and $P<0.01$, respectively). Based on these data, it could be concluded that as the radioactive thorium is absorbed through the surface area of the wound and when a threshold of radiation is acquired, the process of wound healing will be accelerated. These results are consistent with the results of numerous studies including the recent studies of Mortazavi (and his colleagues) *et al.* (31-33) who showed the appearance of adaptive response in the people living in high background radiation areas above a threshold of dose.

Identification of the bio-positive effects of low doses of ionizing radiation may change the public perception of the occupational, medical and even environmental dangers of radiation (34). Considering the possible mechanisms of the effects of radioactive powder on the wound healing, the important role of low dose ionizing radiations in the stimulation of the body's defense mechanisms would be proved. Body's defense system, especially granulocytes and macrophages, has a considerable role in the healing of the acute wounds. On the other hand, the factors which could cause the weakness of the defense system could also show their final effect as a disturbance in the wound healing. In some cases this disturbance is so strong that it causes the prolonging of the healing and takes it into the persistent phase (35). The reaction of the defense system to the ionizing radiation depends on some determining factors such as radiation dose and the dose rate (36-37). The stimulating effect of ionizing radiation on the defense system has become an important measurement in the evaluation and identification of the bio positive effects of low dose radiation (38) as well. It seems that low levels of radioactive materials, by inducing a kind of stimulation on the defense system, could accelerate the healing process.

This study indicated that people who have used lantern mantle powder, without being aware of its possible dangers, have known the healing power of this radioactive material and have used it through out the years. Needless to say, the results of this study should not be considered as an approval for using lantern mantle powders as a wound healing agent. In medicine all decisions for the use of any chemical or physical therapeutic method should always be based on the evaluation of the possible risks and benefits. Considering the known risk of alpha emitting radioactive materials (internal radiation), this study was not concerned with evaluation of the dangers of such an internal irradiation. In this light, further studies are needed to clarify whether low level radioactivity can be used as a therapeutic agent for enhancing the process of wound healing.

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