Iraqi Laser Scientists Journal (ILSJ)/ www.ilsj-online.org
Vol .1, Issue 1; Pp;11-16, 2017.

Original article

Role of low energy laser irradiation of the blood on the absorption of the antibiotics

*Rami Ali , **Mohammed S. Mehdi & ***Ihsan, F. Rostum
*Dept. of Laser Engineering- Al- Nahrain University, **Dept. of Applied Sciences -University of Technology.***College of Dentistry , Al - Muthanna University

Abstract

The current work is designed to estimate the effect of Low Level Laser Therapy (L.L.L.T.) administered intravenously on the level of an antibiotic in the blood. It is known that the low level laser irradiation of blood exerts a powerful multiple component effects on quite a number of pathological conditions. It helps in rapid concentration of an administered drug to the blood which assists in treating of overwhelmed cases. Twenty eight adult male New Zealand rabbits were used in this study. They were divided into two equal groups depending on the method of administration of the antibiotic (the 1st. group injected with 10 mg/kg B.W of the antibiotic (Ampicillin) while the 2nd. group given the antibiotic in a form of gelatine capsules, containing 10 mg/kg B.W orally. Then each group was subdivided in to two equal subgroups (control and treated with laser therapy). GaAs diode laser device used for irradiation, it emits at 904 nm, and average power of 1 mW, it contains a connector and optical fiber with fine canula fixed to it's end . Blood of the animals of the treated subgroups was irradiated by introducing the fine needle of the canula into the marginal vein of the ear for 10 minutes. Samples of blood were collected from the animals of both groups at 1, 2, 3, 4, 5 & 6, hours intervals after the injection of the Ampicilline and sent for analysis using High Performance Liquid Chromatography (HPLC). The results of this study revealed a gradual increase in the level of the Ampicillin (ng/ml) in both groups up to the 2nd hours followed with rapid decrees of the drug till the end of the experiment, there was a highly significant increase in the level of the Ampicillin in the treated subgroups of both groups as compared with the control ones for approximately all the given hours $P < 0.01$, while the increase was significant only in the 3rd. hour of the intramuscular group. Irradiation of blood with low level laser increases the concentration of the Ampicilline in the serum whatever was the rout of it's administration, also the irradiation helps in rapid clearance of the blood from the drug.

Key Words: Ampicillin, Laser, Intravascular

To cite this article: Rami Ali , Mohammed S. Mehdi & Ihsan, F. Rostum ; Role of low energy laser irradiation of the blood on the absorption of the antibiotics; Iraqi Laser Scientists Journal. Vol .1, Issue 1; Pp;11-16, 2017.

Introduction

Low power laser has been reported to reduce inflammatory reactions, produce analgesia and promote regeneration and healing. It`s mechanism of action is unknown, one hypothesis is that the light produces free radicals which have beneficial effects at low concentrations, they promote the improvement of microcirculation and activate the mast cells, (1). , it also stimulates the lymphatic system, provides maintenance of high concentrations of drug in blood, lymph and organs for a more prolonged period. This

is important for patients with many diseases conditions (2). Laser light allow it`s transmission through optical fibers, so laser can be introduced in to the blood vessels to be in direct contact with the blood, two types of lasers used in such procedures, the first type is of high energy like Co_2, argon and Nd - YAG, their applications include; recanalization of obstructed atherosclerotic vessels, myocardial and valvular surgery, (3), whereas the second type are those of the low level energy, especially the infrared diode lasers which used widely in recent years for irradiation of blood in ischemic heart diseases, myocardial infarctions and arrhythmias accompany acute conditions which is contributed to be due to the action of the laser on the blood oxygenation level and myocardial blood supply, (4). The therapeutic effect of laser had been identified so that a better knowledge about the mechanism of tissue repair using light energy obtained in the areas of skin, muscle, ligaments, nerves, bones and cartilage which respond to doses of light with wavelengths range between 600-1000nm, but the amount of energy absorbed varied from one tissue to another even when the wave length remain constant , (5). Ampicillin is a semisynthetic penicillin derived from the basic penicillin nucleus, 6 - amino - penicillanic acid, it acts through inhibition of biosynthesis of cell wall mucopeptide. Ampicillin diffuses readily in to all body tissues and fluids. It has a wide spectrum and bactericidal action ,it is administered orally (p/o) , intramuscular (IM) and intravascular (IV) , (6). Due to the importance of optimization of the available drug preparations through preparation of various drug combinations or giving these preparations with other methods of therapy like low level laser which is being widely used during the several past years, (7), the current study planed to estimate the effect of intravascular blood irradiation with the low level laser when applied in combination with administration of Ampicillin (intramuscular or orally) on it`s level in the serum.

Experimental procedure

Animal preparation : Twenty eight male adult New Zealand rabbits were used in this study. They were divided in to two equal groups, the first group treated with Ampicillin (10 mg / kg B.W.) administered IM[1] while the second one received the same dose administered as small capsules per oss[2].Each group was further subdivided in to two subgroups (control & treated with laser). Fine canula fixed inside marginal vein of the ear to obtain blood samples from the animals sent for estimation of the level of Ampicillin using HPLC[3].

HPLC is a sensitive and selective chromatographic method with UV detector used for determination of the Ampicillin C-component ratio, (8).

Laser treatment : A semiconductor GaAs diode laser device constructed locally , it emits at 904 nm, and average power of 1 mW with an optical package which contain a connector and optical fiber with fine canula fixed to it`s end.

The blood of the animals of the treated subgroups irradiated once using the device after the administration of the antibiotic immediately. Time of irradiation was 10 minutes.

Method of irradiation of the blood was by transmitting of the laser energy through a fine fiber optic[4] [4]passed in to the femoral vein across a fine cannula[5] fixed to it`s end.

[1] Holland Medicines Company - Netherlands. hollandmc@europe.com
[2] Ajanta pharma limited, Ajanta house, 98, Govt. Indl. Area, charkop, kandivili, (W) Mumbai 400 067, India
[3] Schmsu Analytical Laboratory, Japan, 45 J-4002
[4] Light guide probe with outer diameter of (0.8 mm).
5 20 G1 ¼ “mm, B, Braun Melsungen AG, D-34209, Vasofix-Germany

Sample's collection : Samples of blood collected from the animals of all subgroups after 1, 2, 3, 4, 5 & 6 hours from the time of injecting the antibiotic.

Statistical estimations : Values from blood samples examination estimated statistically using analysis of variations, ANOVA to compare the responses of all subgroups; control and laser treated throughout the entire period of the study, (9).

Results

Concentration - time relationship of the Ampicillin is shown in tables, 1 & 2 , there is a gradual increase in the readings of the samples at all the given times in both the groups (intramuscular & oral) and all the subgroups (control & treated) beginning from the 1st. hour and reach the peak at the end of the 2nd. hour, then they lessens gradually by time till the end of the experiment.

In the 1st. group, in which the Ampicillin is administered IM, there was highly significant $P < 0.01$ differences in the readings of the treated subgroup when compared with the control one at all the given times except the 2nd. hour in which the readings showed very highly significant $P < 0.001$ differences in reference to the control subgroup.

In the 2nd. group in which the Ampicillin is administered per oss, the readings of all the given hours in the treated subgroup showed highly significant $P < 0.01$ differences when compared with those of the control one.

Table 1: Concentrations of the Ampicillin in the intramuscular group.

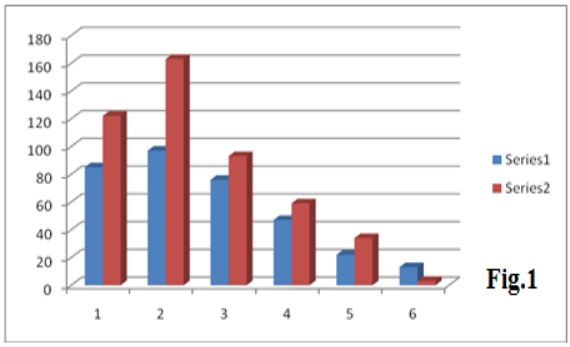
Oral							
Time (hr)	Control (ng/ml)			Laser (ng/ml)			
	Mean	SD	SE	Mean	SD	SE	Degree of Significance
1	65	±4.4	0.87	98	±3.2	0.74	*
2	81	±4	0.83	142	±3.7	0.8	*
3	62	±2.7	1.0	73	±1.41	0.53	*
4	48	±2.71	1.0	54.1	±1.35	0.51	*
5	39	±2.31	0.87	24	±2.16	0.82	*
6	15	±1.41	0.53	7	±0.81	0.31	*

Table 2: Concentrations of the Ampicillin in the oral group.

Intramuscular							
Time (hr)	Control (ng/ml)			Laser (ng/ml)			
	Mean	SD	SE	Mean	SD	SE	Degree of Significance
1	85	±2.8	0.66	122	±2.3	0.62	*
2	97	±2.3	0.62	163	±2.3	0.62	**
3	76	±2.5	0.65	93	±2.3	0.62	*
4	47	±2.6	0.66	59	±2.3	0.59	*
5	22	±2.3	0.62	34	±2.5	0.65	*
6	13	±2.3	0.62	3	±1.2	0.41	*

* Highly Significant: P< 0.01

**Very Highly Significant: P< 0.001



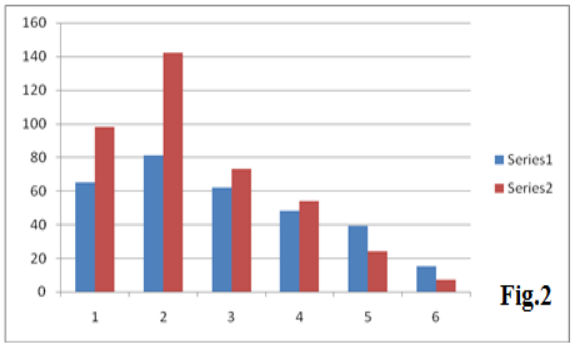


Fig 1: Concentrations of the Ampicillin in the intramuscular group
Fig 2: Concentrations of the Ampicillin in the oral group.

Comments

The increase in the concentration of the Ampicillin in the blood of the treated subgroup which administered the antibiotic intramuscular was highly significant as compared with the control subgroup , this fact is attributed to the laser light which increases the formation of new capillaries, promotes the healing process and accelerates the angiogenesis, leading to a temporary vasodilatation, and increase in the diameter of blood vessels, the vasodilatation is considered as an important factor increase the bioavailability of the drug, ,(10). The values obtained from the treated subgroups which received the drug per oss, is an increment contributed to the blood irradiation with the laser which activates erythrogenesis and anti-hypoxic activity on tissues , activation of microcirculation are detected , in vitro studies have shown increase production of prostaglandins E&F following L.L.L.T., these products known to work at the cellular membrane levels and act as synaptic modulator in afferent stimuli transfer , (11). The action of laser therapy is attributed to the ability of the cell to absorb the photon and transform the energy into adenosine triphosphate - ATP. ATP is a type of energy used by the cell to carry out it`s functions, so the cell must absorb the light energy for this process to occur. Certain cells have the capacity to absorb light energy, as in the skin reacting to sunlight. These light-absorbing components of the cells are termed chromophores or photoacceptors and are contained within the mitochondria and cell membrane. Cell components such as cytochrome c, porphyrins, and flavins also have a light absorbing capability. Normally ATP is produced by the mitochondria, using oxygen as the primary fuel. Laser stimulation has been shown to enhance the production of ATP by forming singlet oxygen, reactive oxygen species - ROS, or nitric oxide, all of which influence the normal formation of ATP. The increased ATP prompts homeostatic function of the cells to resume,(12). The increase in the level of the antibiotic was highly significant in both groups for the $1^{st.}$ and 2^{nd} hours and then began decrease by time till reach to clearance approximately, medications such as procaine, certain antibiotics, and copper-based local substances may enhance the effectiveness of laser energy by enhancing the receptor sites, (12 & 13). The results of the current study agreed with those got by Jin Woong Lee et. al. , who investigated the efficacy of methyl 5-aminolevulinic acid (MAL)-PDT for the treatment of recalcitrant Malassezia folliculitis, they founded after three sessions of MAL-PDT, that the inflammatory lesions had decreased and improved obviously, they concluded that laser therapy improve and increase the rule of the drug in the treatment of the disease , (14) . The results obtained from the present study should be attributed to the improvement of rheological properties of blood, and an increase in the capillary's blood flow, in addition to reduced

vascular resistance and vascular tone which lead to increase the motion and out flow of fluids from the interstitial spaces in to the lymphatic system , thus blood irradiation with laser combined with intramuscular injection of Ampicillin allows to obtain higher drug saturation in blood in comparison with the intramuscular or oral administration of the antibiotic alone.

Conclusions

The stimulating effect of L.L.L.I. on the antibiotic activity is the key point of its therapeutic value. Laser irradiation of blood combined with antibiotic p/o or IM injection allows obtaining also higher drug saturation in the blood, in comparison with p/o or IM injection alone.

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