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The Regenerative Role of Vitamins B1, B6, B12 in Treatment of Peripheral Neuropathy

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Abstract: ***The peripheral neuropathy is one of the common complications of various types of diseases, trauma and vitamins deficiency. Till now the C.N.S has no ability to regeneration, while peripheral nervous systems can be regenerate following trauma or disease, So many medication had been used to relieve neurological pain or to regenerate the peripheral nerve. One of the most commonly drugs used is vitamins B. However which one of vitamins B is more effective in regeneration of nerve damage is still obscure. Aim of study: Study the effect of various types of vitamins B on regeneration of damage nerve through morphometrical and histological study. Materials and methods: 60 albino rats had been conducted in this study. Each rat exposed to sciatic crush injury. Those animals had been divided into 4 groups, group A consider as a control experimental group, group B received vitamin B1, group C received vitamin B6, while the last group treated with vitamin B12. Each rat examined macroscopically and histologically. Result: The results obtained illustrated regeneration of all groups treated with various types of Vitamins B. However the degree of regeneration had been differed according to the type of vitamin B. Vitamin B12 treated animals revealed best regeneration, followed by B1 treated animals and the least effect could be observed in animals treated with B6. Conclusion: This variable response to regenerative role of vitamins B could be attributed to the mechanism of action of each types of vitamins B.***

1. Introduction

The nervous system could be classified into central and peripheral nervous system. The peripheral nervous system involved cranial and spinal nerves which represent the neuronal processes (axons and dendrites). Accordingly, the peripheral nerves could have sensory, motor or mixed function[(1)(2)]. Many diseases or trauma could affect peripheral nervous system causing what is called peripheral neuropathy. The most common disease that causes peripheral neuropathy are diabetes mellitus, alcohol consumption, tumor and vitamins deficiency[(3)]. So many medications have been used to induce regeneration of the nerve or to reduce pain following peripheral neuropathy. Among these medication is systemic steroid [(4)(5)(6)], gabaptin or carbamazepine could also be used[(7)].Other drugs, that accelerate the regeneration of damaged nerve are vitamins, such as Vitamin D[(8)],Vitamin C[(9)] and Vitamins B[(10)(11)(12)(13)]. Among these medications[(14)(15)(16)(17)], had been proved that Vitamins B, especificallyB1, B6 and B12 are most important therapy used for regeneration of injured peripheral nerve. Many researches had been performed to illustrate the role of vitamin B, either individually or as a cocktail, intreating peripheral neuropathy. Some researches revealed improvement in nerve conduction, other relived pain sensation. However non of these studies discussed which of these vitamins (B1, B6, B12) is more efficacious than the other in regeneration of damaged nerve fibers.

2. The Aim of the Study

Is to recognized which types of the various vitamins B is the best drug of choice in treating peripheral neuropathy.

3. Materials and Methods

60 albino rats, of both sexes, weighting 200-250 gm, had been included in this study. All the animals involved in this study had been exposed to the following procedure. After anaesthetization, the animals had been kept in prone position, alongitudinal incision along the upper posterior aspect of right hind limb, exploration of sciatic nerve had been performed. Using Kocher hemostatic forceps (8mm size),the sciatic nerve had been crushed for 20 seconds. The animals involved in this study, had been divided into 4 groups and as the following in table 1:-

Table 1: Grouping of animals, the treatment received

Grouping of animals	Control group	Experimental groups		
	A	B	C	D
Number of animals	15	15	15	15
Treatment received by animals	1ml of normal saline intramusclar injection daily	i.m. injection of 180 mg / kg body weight of vitamin B1[(18)] (Zhongshan Co.,LTD)	i.m. injection of 180 mg / kg bodyweight of vitamin B6[(18)] (ZhongshanCo.,LTD).	i.m. injection of 1 mg / kg bodyweight of vitamin B12[(19)] (Bushu pharmaceuticals Ltd. For Eisai Co., Ltd).
Duration of treatment	45 days	45 days	45 days	45 days

Five animals of each group had been sacrified at 15th,30th,45thday following the beginning of the experiment.

Before sacrificing the animals, tail flick test had been performed using water bath of 50±2 C,into which the tip of tail of each rats of the 4 groups,had been dipped[(20)].

To evaluate the changes in muscles bulk of thigh and leg ,tap measure had been used to measure the circumference of mid thigh and mid leg 0f both affected side (right hind limb) and normal side (left hind limb). Then 5-10mm of crushed area of sciatic nerve and area distal to it had been excised. The paraffinized sciatic nerve piece had been sectioned, then some of these sections had been stained by eosin and haematoxylin[21] to examin the general histology of the crushed nerve. While the other group of tissue sections had been stained by special stain using Van Giesons stain.

4. Results

All the animals involved in this study appeared in good general condition and healthy apart from limbing in the right hind limb and impairment of response to painful stimuli. The bulk of muscles of the right thigh and leg elicited wasting, Yet animals of group D (which received B12) showed less wasting of these muscles than the other groups.

Tail flick test demonstrated delayed in response to the painful stimuli. The time needed, to pull away of the tip of the rat tail, was longer in all 4 groups. However rats received B12 injection revealed shorter time in response to thermal stimulus in comparison with other groups.(Fig 1)

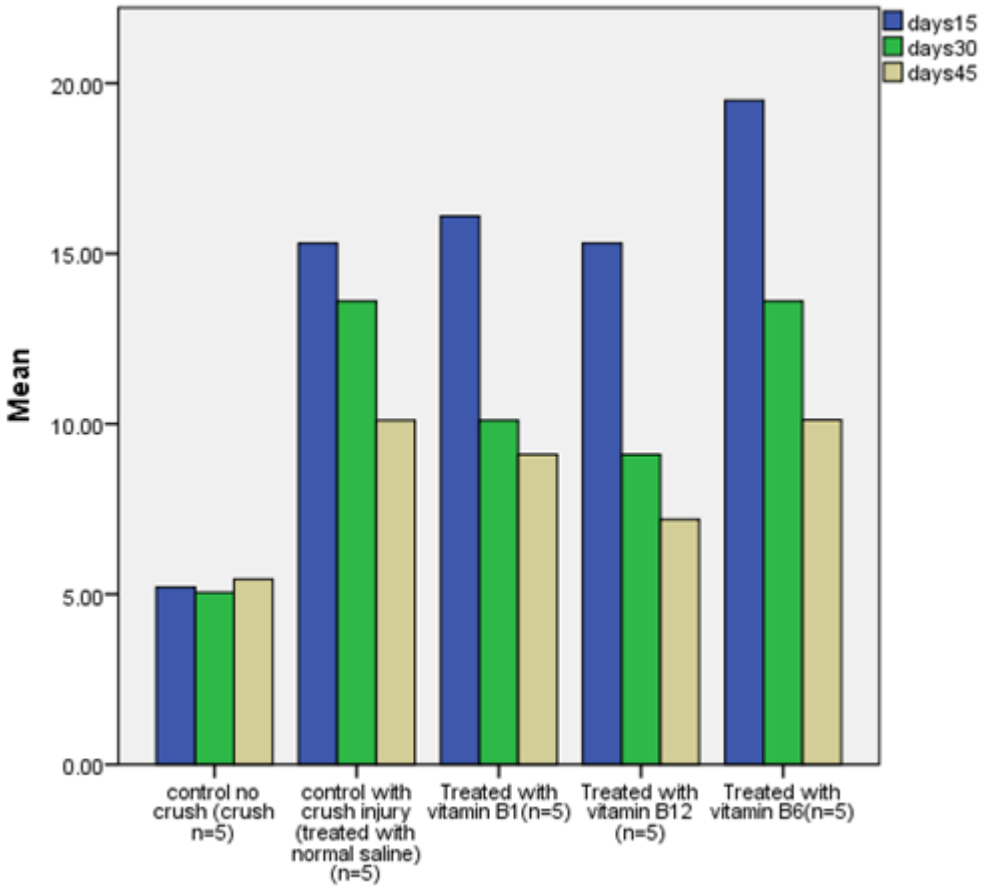
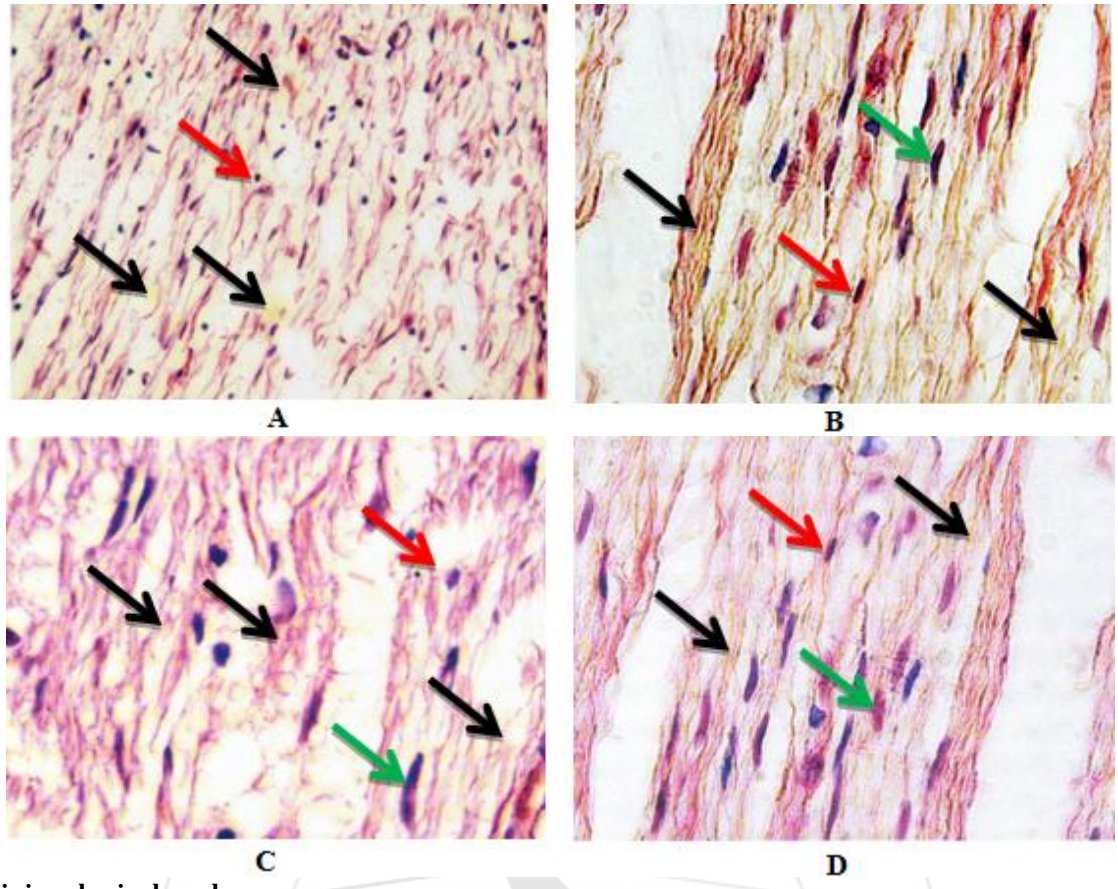


Figure 1

Microscopical examination of nerve tissue sections demonstrate the following pictures. Regarding longitudinal section of crushed nerve fibers microscopical examination showed degeneration of nerve fibers, disturbance of parallel arrangement of nerve fibers within crushed nerve. Besides the sciatic nerve section appeared foamy and cloudy. The regeneration process that affect crushed sciatic nerve appeared to be more clear and faster in group of rats that received B12 vitamin. To a lesser extent, animals of group C elicited regeneration lesser than that of group D and less than that of group B.

Cross sections of injured sciatic nerve demonstrated degeneration of nerve fibers with their myelin sheath, the section field filled with tissue debris with abundant of macrophages, vacuoles could be detected with the field especially tissue sections of groups A, B, C and to a lesser extend tissue sections of group D (Figure 1).

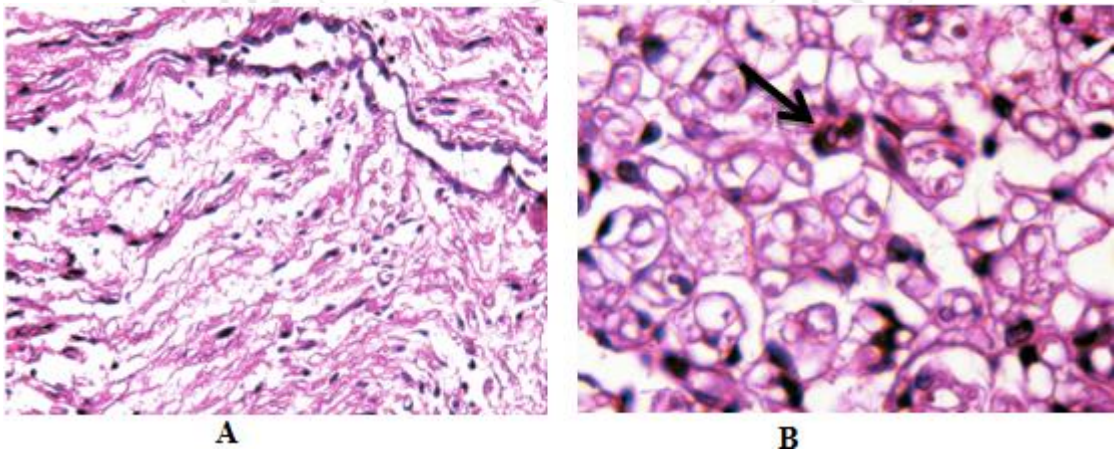
Following 45 day of experiment, tissue section of group D (which received B12 therapy) showed regeneration of nerve fibers with their myelin sheath, Yet macrophage and tissue debris could diffusely seen. The same pictures could be illustrated in animals received vitamin B1 but to lesser extend and then group C rats which received vitamin B6 showed minimal regenerative activity (Figure 2).



Section of injured spinal cord.
A- Control experimental,
B- Treated with Vit. B1,
C- Received Vit. B6 therapy
D- Treated with Vit. B12.

Black arrows indicate collagen fibers, green arrow represent schwann nuclei while red arrow pointed to macrophage

Group D demonstrates well organized fiber, with little collagen fiber & abundant of schwann cells.



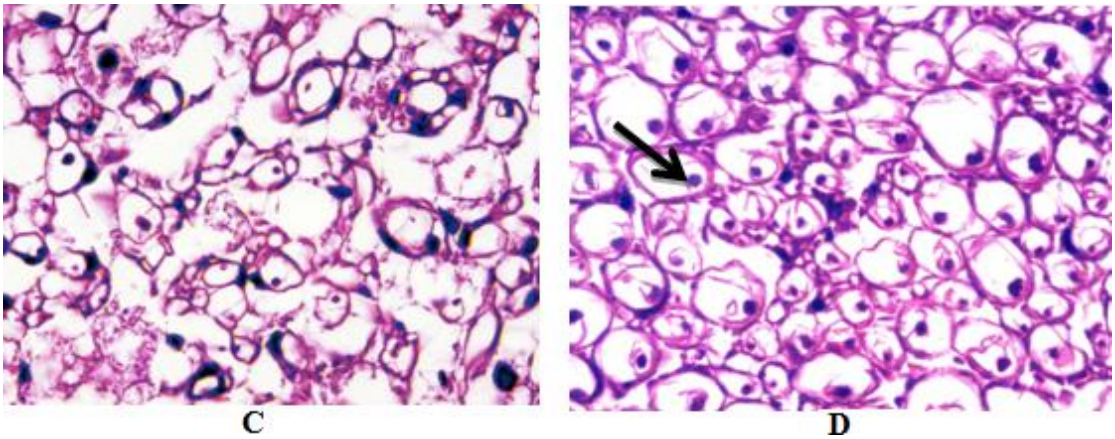


Figure 3

Tissue section of injured spinal cord after 45 days of experiment.
A- Control experimental,
B- Treated with Vit. B1,
C- Received Vit. B6 therapy
D- Treated with Vit. B12.

Group A revealed damaged nerve fiber, with slight improvement in Group C. Group B illustrated newly formed nerve fiber with schwann cell.

Group D demonstrated well organized myelinated nerve fibers with abundant of schwann nuclei.

5. Discussion

Peripheral neuropathy is one of common pathological problem that occurs following many diseases[22]. Since sciatic nerve carries both sensory and motor component (Grayes last) therefore any pathological damage to this nerve could cause motor and sensory deficient. Tail flick test was considered be adequate parameter to examine the sensory component of sciatic nerve. The result of this study revealed reduction In latency period needed by the rats to feel painful stimulus and pull their tails away from noxious stimuli. This result was clearly obtained in rat treated by vitamin B12.In addition to that, the bulk of thigh and leg demonstrated less wasting, following crushing of sciatic nerve, in group D(treated with vitamin B12). This picture was less obvious in rat treated with Vitamin B1 which in turn less clear in animals treated with vitamin B1. Regarding histology of the damage nerve tissue section treated by vitamin B12 demonstrated better recovery of nerve fibers than those treated with vitamin B1 and vitamin B6. Yet animals treated with last two vitamin revealed improvement in their nerve cytoarchiture but less than B12 treated one. Following treatment with vitamins B1, B6, B12regeneration of damaged nerve fiber could be elicited,with promotion of myelinsheath regeneration. Yet, this picture was so obvious in animals treated with B12 than those with B1 and to a lesser extend with these received B6 therapy.

This variation in regenerative response to treatment with vitamin B could be attributed to the mechanism of action of various types of vitamins B. Vitamin B1 regenerative effect on the neuron was related to its role in supplement the tissue with energy which is essential for neuronal conduction[23][24]. Besides it has limited role in production of neurotransmitter and myelin sheath[24]. Regarding vitamin B6 action on nervous tissue, was related to its action as a co-enzyme in various metabolic process, besides its role in decarboxylation and transmission of nerve impulses[24][25]. Although the recovery action of vitamin B12 is still obscure, however many scientists attributed its regenerative effect to the following mechanism:-

1) Vitamin B12 has essential role in myelination of nervous system, which in turn lead to strong communication between different part of nervous system[26].
2) It play an important factor in production of neurotransmitter, through its action together with a compound called SAMe (S-Adenosylmethionine)[25][26].

Accordingly, all types of vitamin B (B1, B6, B12) has a principle role in regeneration of neuropathy. However according to the result obtained from the current study, Vitamin B12 elicited better regenerative process on peripheral neuropathy and appeared to be superior to other vitamins B. Following its activity, vitamin B1 showed less regenerative effect while the least regenerative effect could be illustrated on treatment with B6.

6. Conclusion

Although vitamin B12 therapy reported to have the most effective regenerative activity among vitamins B. However B1 and B6, play important role in regeneration of damage nerve tissue. Therefore it is better to use a cocktail of vitamin B complex to get an optimum regenerative effect in peripheral neuropathy.

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