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Effect of Cilostazol on Ischaemic Wound Size

KEYWORDS: Ischaemic wounds, Cilostazol, Ulcer size, Wound healing.

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ABSTRACT ***Introduction:*** *Ischaemic wounds accounted for a substantial threat to a patient's quality of life. There is a need for agents which would aid in the faster healing of these ulcers and improve the quality of living of these individuals and also reduce the burden on the health care system. As newer drugs are released in the market, interest has grown in the feasibility of use of cilostazol in the treatment of ischaemic wounds and to hasten the healing process. Methods: 3 week administration of tab. Cilostazol 100mg twice daily in patients. Ulcer healing was measured and standardized by marking on tracing sheets. To assess the area on the tracing paper, the major diameter is multiplied by the major orthogonal diameter. Results: The mean duration of ulcer before the treatment with cilostazol was 13 months. We observed changes in the characteristics of ischemic wound when it is responding to cilostazol. Wound becomes redder and appears more vascular in nature, the necrosis starts ceasing and wound begins heal. The mean percentage improvement in the area of ulcer after treatment with cilostazol is 45.95%. Conclusion: Cilostazol was found to have potentiated the wound healing rate of ischemic ulcer. Although cilostazol is somewhat expensive, it appears to be more helpful in alleviating claudication and improving wound healing rate as useful adjunctive therapy.*

INTRODUCTION

Ischaemic wounds are those caused in patients with peripheral vascular diseases and in patients with longstanding diabetes mellitus. These wounds are known for their chronicity and tend to become non-healing ulcers.[1] It was concluded that they accounted for a substantial threat to a patient's quality of life. Thus the burden of ischaemic wounds on the health care system is very high.[2] The etiology of these ulcers varies from vascular diseases like thromboangiitis obliterans, various vasculitides, diabetes mellitus to atherosclerosis. Whatever the cause of these ulcers, if there is a component of ischaemia, healing is definitely delayed and the burden on the health care system increases drastically. Thus there is a need for agents which would aid in the faster healing of these ulcers and improve the quality of living of these individuals and also reduce the burden on the health care system.[3] Cilostazol is is a phosphodiesterase 3 inhibitor, approved by the FDA in 1999 as a treatment option for intermittent claudication. Patients assigned to the cilostazol group had a significantly greater absolute claudication distance.[4] A study to analyse the effect of drug on the healing of ischaemic wounds would prove useful in forming evidence based protocol for the management of such patients.

Importance of the study: As newer drugs are released in the market, interest has grown in the feasibility of use of cilostazol in the treatment of ischaemic wounds and to hasten the healing process.

Objectives

To know the effects of cilostazol of the healing rate of ischaemic wounds.

To assess the adverse effects of cilostazol, if any, on the patients

MATERIALS AND METHODS

Study population: Patients treated in the department of General Surgery at Government Wenlock Hospital, Mangalore and in KMC Hospital Attavar.

Selection of cases: [n=40] the patients who are diagnosed to have ischaemic wound.

Inclusion criteria: Wounds over extremities with absence of at least one distal pulse, presence of claudication, rest pain and gangrene.

Exclusion criteria: Patients with congestive cardiac failure for cilostazol therapy.

All the investigations which were needed for the study were routinely done during the admission period or prior to it. A detailed history regarding the onset of wounds, its progression etc was taken followed by detail local examination.

Treatment protocol: 3 week administration of tab. Cilostazol 100mg twice daily in patients. Along with standard ulcer care with antiseptic dressings, wound debridement and amputation where required. Extensive wound are covered with split skin grafts. Control of diabetes mellitus, hypertension, infection with appropriate therapy.

Ulcer healing was measured and standardized by marking on tracing sheets. To assess the area on the tracing paper, the major diameter is multiplied by the major orthogonal diameter.

OBSERVATIONS AND RESULTS

40 Patients with ischemic ulcers were treated with cilostazol. All were males with a mean age of 52.78 years. The mean duration of ulcer before the treatment with cilostazol was 13 months. On studying the risk factors that predispose to ischemic wounds, 22 patients (55%) accounted for tobacco users, 20 patients (50%) had diabetes and 16(40%) patients were hypertensive. After the treatment the group

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statistics show that there was significant difference in the size of the ulcer, inferring that cilostazol brought about a significant reduction in the ulcer size.

	Frequency	Range	Mean	Standard deviation
Duration of Ulcer(months)	40	1-48	13	
Size before(sqcms)	40	5.98-257.25	52.78	42.22
Size after(sqcms)	40	0-189	31.64	31.19
Improvement(%)	40	17.13- 100	45.95	20.32

DISSCUSSION

We observed changes in the characteristics of ischemic wound when it is responding to cilostazol. Wound becomes redder and appears more vascular in nature, the necrosis starts ceasing and wound begins heal. This was observed as early as 12th day in about 30% of cases. These patients also described decrease in the pain and in those that did not heal there was no decrease in the pain. It is assumed that the cilostazol used here potentiated the wound healing by increasing the blood flow to the affected extremities. At the end of our study the wound healing rate was significantly satisfactory in cilostazol recipients.

In our study the mean percentage improvement in the area of ulcer after treatment with cilostazol is 45.95%. In a study by Stanley N et al on 25 patients 15(60%) patients showed healing progress with 70% of wound epitheliased. Healthy granulation tissue with no necrosis and little exudate was seen within 60 days (30–60 days, average five weeks). 5 patients showed granulation tissue with decreased slough and healed after skin grafting and skin substitutes.[1]

In a study by Yuriy K et al observed that there was reduction in size of ulcer from 4.25 cm^2 to 2.75 cm^2 on 30^{th} day and to 2.13 cm^2 on 60^{th} day in the placebo group. In patients treated with trans-resveratrol (t-RSV) there was reduction from 2.63 cm^2 to 0.75 cm^2 on 30^{th} day and to 0.13 cm^2 on 60^{th} day.[5]

Cilostazole reduces platelet reactivity both in *high on-treatment platelet reactivity* and non-*high on-treatment platelet reactivity* patients, although these pharmacodynamic effects are enhanced in *high on-treatment platelet reactivity* patients with diabetes mellitus. Nevertheless, larger studies are needed to better evaluate possible differential effects of cilostazol on platelet reactivity by diabetes status.[6]

In a study by Dawson DL et al, it was observed that mean percent increase of 54% from baseline in walking distance in cilostazol group when compared to pentoxifylline which was 30%.[7] In a study by Dawson DL, Bruce S, et al the estimated treatment effect by cilostazol showed a 35% increase in ICD (initial claudication distance) and a 41% increase in ACD (absolute claudication distance).[8] In a study by Surjit Singh et al observed that Cilostazole significantly increase ICD (initial claudication distance) by 53.18% and ACD (absolute claudication distance) by 42.41% from baseline at 12 weeks.[9]

In our study the mean age of patients was 52.78 years. In the sex distribution, the ischemic wounds were seen mainly in male sex of study population. On studying the risk factors that predispose to ischemic wounds, 22 patients (55%) accounted for tobacco users and 20 patients (50%) had diabetes. Stanley N et al observed that average age was 63years and there was male predominance in their study. Out of 25 patients, 10(40%) patients were tobacco users and 13(52%) had diabetes.[1]

In our study the side effects of the drug included headache, diarrhea, abnormal stools and palpitations. Dawson DL et al observed that the side effects headache, palpitations, and diarrhea were more common in the cilostazol-treated patients, but withdrawal rates were similar in the cilostazol and pentoxifylline groups.[7]

CONCLUSION

Cilostazol was found to have potentiated the wound healing rate of ischemic ulcer. The most common adverse effect of cilostazol was headache followed by diarrhoea and palpitations. The side effects of cilostazol were self-limiting. Although cilostazol is somewhat expensive, it appears to be more helpful in alleviating claudication and improving wound healing rate as useful adjunctive therapy.

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