Journal of Cardiovascular Disease Research
ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 08, 2023

Case series

Role of Prostaglandin (PGE1) in Patients with Nonhealing Ulcers due to Thromboangitis Obliterans (Buergers disease)

Authors: Dr Gaurav Singal [1], Dr Dipesh Goel [2], Dr Harshita Mittal [3]

Dr Gaurav Singal, Associate Professor, Department of General Surgery, Maharishi Markendeshwar Institute of Medical Science and Research, Mullana.

Dr Dipesh Goel, Associate Professor, Department of General Surgery, Maharishi Markendeshwar Institute of Medical Science and Research, Mullana.

Dr Harshita Mittal, Resident, Department of General Surgery, Maharishi Markendeshwar Institute of Medical Science and Research, Mullana.

Corresponding Author: Dr Dipesh Goel, E-mail dipeshsurindergoel@yahoo.com, +918360467511.

Abstract

Introduction PGE1 is effective in treatment of Buergers disease. It reduces pain in limbs, improves wound healing and prevents amputation. PGE1 is a form of prostaglandin which causes peripheral vasodilatation, improvement of microcirculation, anti-inflammatory immune modulation and inhibition of platelet aggregation.

Aim To determine the role of PGE1 in Buergers disease (BD).

Methods A Prospective cohort study was undertaken from April 2022 to March 2023 at a Medical college hospital. 72 patients were included in the study. Improvement in wound size and side effects of PGE1 were studied.

Results The mean of improvement in wound size expressed in percentages at 4 weeks and 8 weeks were 45.7±2.8 % and 85.2±4.3% respectively**.** The mean of ankle brachial pressure index (ABPI) at 0 weeks was 0.5 ±0.37 and at 12 weeks was 0.82±0.03 respectively.

Conclusions PGE1 is very effective in treatment of Buergers Disease with minimal side effects.

Keywords- PGE1 (Prostaglandins), BD (Buergers Disease), ABPI (ankle brachial pressure index)

Introduction

BD is widely prevalent in Indian subcontinent. It is because of a chunk of population smoke or chew tobacco. Smoking cessation is the mainstay of treatment. Pharmacotherapies and surgery have been employed to treat ischaemic pain, chronic limb ulcers and gangrene.

Over the last decades different kind of surgeries have been attempted in patients with critical limb ischaemia with BD. The results are varied. It has been found that revascularization surgery is not effective because of acute inflammatory pathology [1]. This is due to diffuse

inflammation of peripheral arteries. Lumbar sympathectomy (chemical/surgical) till date have been the mainstay of treatment in BD. It ameliorates Raynaud's phenomenon in the feet. But, its effect in upper limb is short lived and there is no effect on the progression of the disease. There is no reliable evidence to support its use in Buerger's disease, intermittent claudication, diabetic vascular disease or ischaemic ulceration or gangrene [2].

In most severe form of BD there is no possibility of improving the condition with surgery, and therefore, drugs (pharmacological agents) are used [3]. Also, there are patients who have improvement from symptoms for limited time after the surgery. They are also the candidates for pharmacotherapy. Prostaglandins and prostacyclin's are used to treat BD. They redirect blood flow and improve the circulation in affected areas. They help to heal ulcers and relieve rest pain. PGE1 (Alprostadil) is effective in treatment of Buergers disease. It reduces pain in limbs, improves wound healing and prevents amputation [4]. PGE1 is a form of prostaglandin which causes peripheral vasodilatation, improvement of microcirculation, anti-inflammatory immune modulation and inhibition of platelet aggregation [5,6,7].

In our Institute PGE1 was to patients with non-healing ulcer, gangrene limited to feet and palm. It was also given to the patients who had already undergone surgery but were still symptomatic. They complained of pain in limbs, non-healing ulcers or gangrene. Good results were noted. So, we decided to undertake the study to know the effect of PGE1 on wound healing of non-healing ulcers in patients with BD. We also will study any untoward effects of PGE1 leading to ill health of patients.

Aim

To determine the role of PGE1 in Buergers disease (BD).

Objectives of the Study

1. To determine the effect of PGE1 on healing of non-healing limb ulcers.
2. To determine the complications of PGE1 administration.

Research Methodology

A Prospective cohort study was undertaken from April 2022 to March 2023 at a Medical college hospital. 72 patients were included in the study. Institutional ethics committee approval and informed consent was taken.

Inclusion criteria

Patients of age < 45 years, smoker or tobacco chewer, claudication or rest pain in limbs, non-healing ulcers, gangrene.

Exclusion criteria

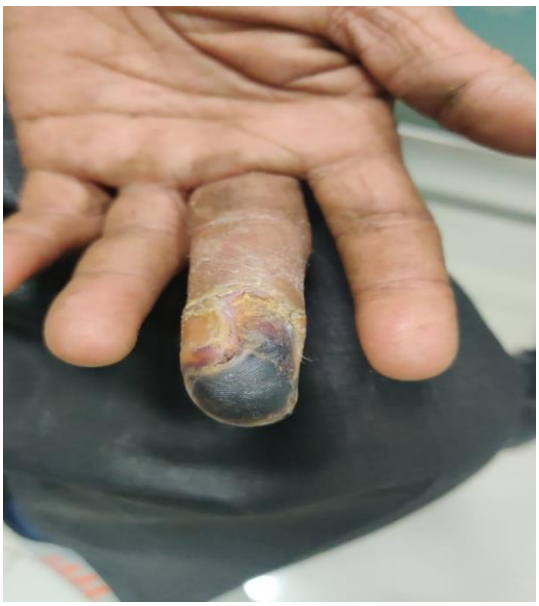
Patients with ejection fraction of <35 % on 2DECHO, no relief of symptoms after first cycle of PGE1 infusion, lost to follow up, autoimmune diseases, hypercoagulable states [8], arrythmias, venous ulcers and diabetes mellitus were excluded**.**

Complete history was taken. History of smoking, chronicity of limb ulcers, amputations or surgery for BD done in past was elicited. Symptoms of limb pain on exertion or on rest was

noted. Clinical examination well performed. All peripheral pulses were examined. Ankle brachial pressure index (ABPI) was measured. Limb amputations, gangrene and previous scars of surgery documented. Special note was made of size of the wound in cm^2 and presence of granulation tissue. All Routine blood investigations (CBC, RBS, RFT, LFT, Lipid profile, quantitative CRP levels, APTT, PT, INR) were done. All patients underwent ECG, 2DECHO, affected peripheral limb doppler and CT Angiography. 3 cycles Intravenous administration of PGE1 were planned with 4 weeks interval. In each cycle a total dose of 500 micrograms was administered. 150 µgm on day 1, 150 µgm on day 2 and 200 µgm on day 3 was given over 6 hours through infusion pump. On 1^{st} day of infusion PGE1 was given in ICU setting. This was done to timely manage any anaphylactic reaction to the drug. Patient was discharged on day 4 in stable condition. Patients followed us after 4 weeks for next cycle. History and clinical examination were repeated. Change in clinical status was determined. Reduction in the size of ulcer and improvement in pain was noted. If there was no improvement in clinical status then next cycle of PGE1 was not given. And, if there is complete healing of ulcer and pain relief then next cycle of PGE1 was not given. Data was tabulated in Microsoft excel and analysis done. Data was expressed in percentages. Our results were discussed with the available literature and conclusions drawn.

Results

72 patients were included in the study. 12 patients met the exclusion criteria, of them 8 had no effect on wound healing or pain, 2 were diabetic and 2 had ejection fraction <35% (n=60). The mean age of the patients with BD in our study was 44.2 years. There were 46 males and 14 females. All the patients in our study had pain in the affect limb. 49 patients had intermittent claudication and 11 had rest pain. 48 patients had non healing ulcers and 12 had gangrene of the limb or digits. (Fig 1 & 2 showing gangrene of the limbs / digits)



ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 08, 2023

Fig 1. Painful gangrene of the left middle finger distal phalanx in 30 years old male

Fig 2 Painful left great toe gangrene in 28-year male

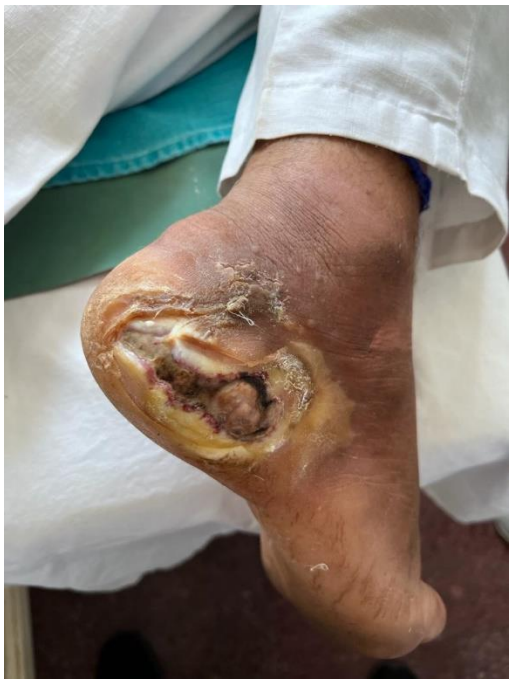


Fig 3 shows painful ulcer with gangrene in left heel. He was started on PGE1 infusion. His results can be seen (fig 4) after 4 weeks.

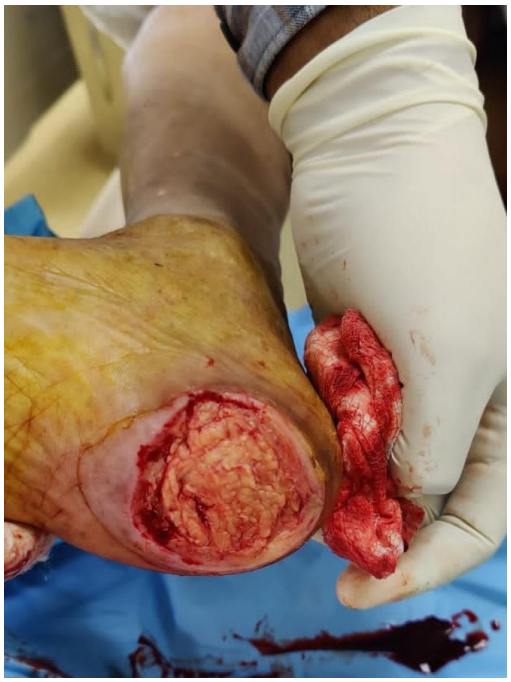
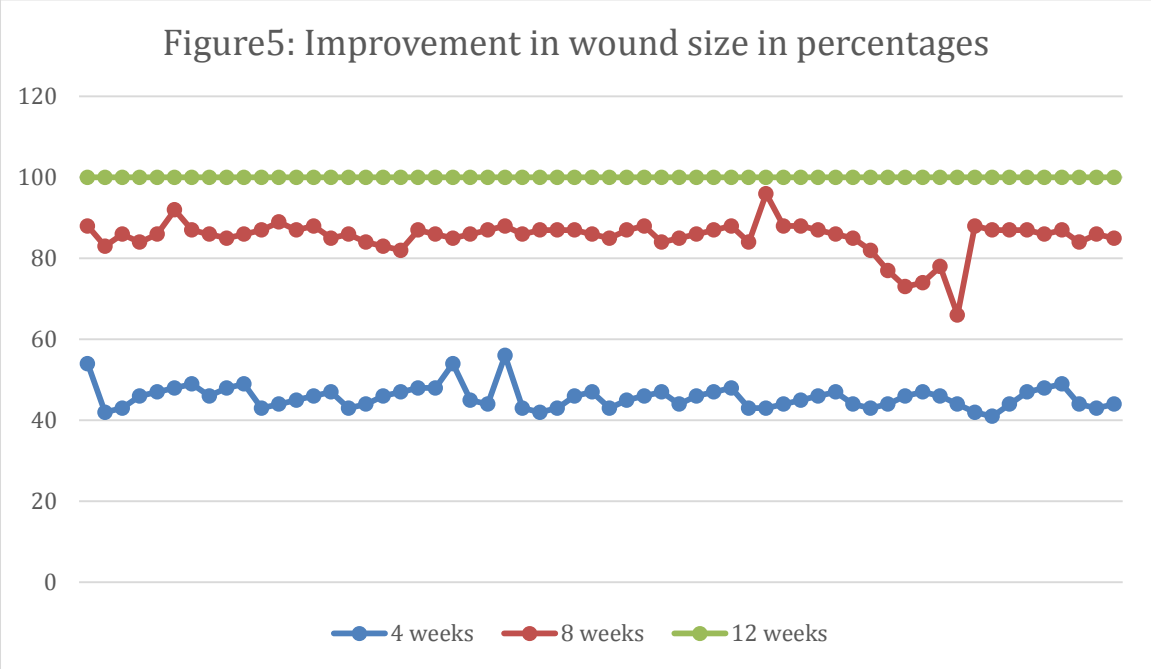


Fig 4 Same patient as in fig 3 after PGE1 infusion showing increased vascularity and good wound healing.



The mean of improvement in wound size expressed in percentages at 4 weeks and 8 weeks were 45.7±2.8 % and 85.2±4.3% respectively (Fig5). The mean of ankle brachial pressure index (ABPI) at 0 weeks was 0.5 ±0.37 and at 12 weeks was 0.82±0.03 respectively. Only one patient developed anaphylactic reaction. No other adverse effect was seen.

Discussion

The mean age of the patients with BD in our study was 44.2 years. It was on the higher side of the normal value because in our study those patients were also included who underwent sympathectomy or amputations. Since surgeries for BD are done in later age group from presentation, mean age of 44.2 years is explained. It is nearly the same as described in literature [8]. The male to female ratio in our study was is 3.2:1. Similar findings have been observed in literature with males being more predisposed to the disease [8]. Women also suffer from BD due to habit of smoking tobacco leaves in Indian subcontinent.

All the patients in our study had pain in the affected limb. 48 patients had non healing ulcers with rest pain and 12 had gangrene of the limb or digits. In the literature symptoms were almost the same. There were reports of ischemic pain of the arms, legs, hands and foot. There was rare involvement of large arteries[9]. Patients presented with claudication of the foot, legs, hands and arms. As the disease progressed, typical calf claudication, ischemic pain at rest and ischemic ulcerations on the toes, feet or fingers developed.[10].

In our study all the ulcers healed completely within 12 weeks. The mean of improvement in wound size expressed in percentages at 4 weeks and 8 weeks were 45.7±2.8 % and 85.2±4.3% respectively. When compared with other pharmacological agents following findings were observed. When comparing prostacyclin with prostaglandin analogues, ulcer healing was similar as was the eradication of rest pain after 28 days [3]. Similar findings were observed in our study.

In our study there is gradual improvement of ABPI at 12 weeks. The mean of ankle brachial pressure index (ABPI) at 0 weeks was 0.5 ±0.37 and at 12 weeks was 0.82±0.03 respectively. Literature suggested that patients with BD will usually have a reduced ankle brachial index with a further reduction following exercise. Which was consistent with our study.

In our study one patient developed anaphylactic reaction. No other side effects were noted. Following side effects of I.V. infusion were seen in literature. Flushing, apnoea, fever, bradycardia/tachycardia, cardiac episode, oedema, hypertension/hypotension, seizure, headache, dizziness, diarrhoea, disseminated intravascular coagulation (DIC), sepsis, local pain not at the injection site, back pain, upper respiratory tract infection, [11]. This is because of our strict exclusion criteria.

Conclusions

Cessation of smoking is the mainstay of the treatment in BD. PGE1 is very effective in healing of limb ulcer. It increases vascularity, microcirculation and perfusion by vasodilatory effect. There is improvement in ABPI of the affected limb. It has made patient pain free after single dose of infusion, thus improving quality of life. It is well tolerated with minimal side effects. Results of PGE1 infusion in BD is so promising that it motivated us to investigate its role as primary treatment modality in BD even before surgery in further studies. Owing to its less invasive and cost effectiveness, we hope that it will replace surgical intervention in near future.

Limitations In our study the short-term outcome is satisfactory. The follow up period was less (mean follow up 6 months). In order to find long term effectiveness of PGE1 infusion in patients with Buergers disease a long follow up is required.

Conflict of interest: None

References

1. Vijayakumar A, Tiwari R, Kumar Prabhuswamy V. Thromboangiitis Obliterans (Buerger's Disease)-Current Practices. Int J Inflam. 2013;2013:156905. doi: 10.1155/2013/156905. Epub 2013 Sep 11. PMID: 24102033; PMCID: PMC3786473.
2. Andrew Gordon, Katalin Zechmeister, Jack Collin, The role of sympathectomy in current surgical practice, European Journal of Vascular Surgery, Volume 8, Issue 2, 1994, Pages 129-137.
3. Cacione DG, Macedo CR, Baptista-Silva JC. Pharmacological treatment for Buerger's disease. Cochrane Database Syst Rev. 2016 Mar 11;3(3):CD011033. doi: 10.1002/14651858.CD011033.pub3. Update in: Cochrane Database Syst Rev. 2020 May 4;5:CD011033. PMID: 26967103; PMCID: PMC7104255.
4. Meimeti Evangelia, Lykoudi Elissavet, Provatopoulou Xeni, Moisoglou Ioannis, Galanis Petros, Galanis Ioannis. (2022). Buerger's disease and intravenous administration of prostaglandins: A case report and review of the literature. Surgical Chronicles. 27. 240-242.
5. Gruss JD, Vargas-Montano H, Bartels D, et al. Use of prostaglandins in arterial occlusive disease. Inter Angio. 1984;3, supplement:7–17.
6. De Sanctis MT, Incandela L, Iacobitti P. 'Responders and non-responders' to PGE1 and alpha-cyclodextrin. Minerva Cardioangiologica. 1998;10, supplement:31–36. (Ita).
7. Fantone JC, Marasco WA, Elgas LJ, Ward PA. Anti-inflammatory effects of prostaglandin E1: in vivo modulation of the formyl peptide chemotactic receptor on the rat neutrophil. J Immunol. 1983 Apr;130(4):1495-7. PMID: 6300229.
8. Arkkila PE. Thromboangiitis obliterans (Buerger's disease). Orphanet J Rare Dis. 2006 Apr 27; 1:14. doi: 10.1186/1750-1172-1-14. PMID: 16722538; PMCID: PMC1523324.
9. Shionoya S, Ban I, Nakata Y, Matsubara J, Hirai M, Kawai S: Involvement of the iliac artery in Buerger's disease (pathogenesis and arterial reconstruction). J Cardiovasc Surg (Torino). 1978, 19: 69-76.
10. Olin JW: Thromboangiitis obliterans (Buerger's disease). N Engl J Med. 2000, 343: 864-869.
11. Costabile RA, Mammen T, Hwang K. An overview and expert opinion on the use of alprostadil in the treatment of sexual dysfunction. Expert Opin Pharmacother. 2008 Jun;9(8):1421-9