

**OBSERVATION OF CLINICAL RESPONSE OF XANTHINOL NICOTINATE IN INOPERABLE CASES OF PERIPHERAL VASCULAR DISEASE**Lukram Sidartha<sup>1</sup>, Mohit Sharma<sup>2</sup>, Ramchandra Sherawat<sup>3</sup>, Amit Sharan<sup>4</sup>, Sunil Dixit<sup>5</sup>, Anil Sharma<sup>6</sup>**HOW TO CITE THIS ARTICLE:**

Lukram Sidartha, Mohit Sharma, Ramchandra Sherawat, Amit Sharan, Sunil Dixit, Anil Sharma. "Observation of Clinical Response of Xanthinol Nicotinate in Inoperable Cases of Peripheral Vascular Disease". Journal of Evolution of Medical and Dental Sciences 2014; Vol. 3, Issue 29, July 21; Page: 8227-8232, DOI: 10.14260/jemds/2014/3035

**ABSTRACT: OBJECTIVE:** The therapeutic role of Xanthinolnicotinate was studied in 120 patients with inoperable peripheral vascular disease who completed a 4 weeks regimen of intravenous continuous infusion. **METHODS:** This is a prospective study of 120 patients with inoperable progressive peripheral obliterative vascular disease admitted in the Department of Cardiothoracic & Vascular Surgery, Sawai Man Singh Medical College, Jaipur, Rajasthan. The clinical response like limb temperature, peripheral pulses, skin colour and capillary filling time along with patient response on relief of rest pain and claudication pain are recorded in a simple manner. **RESULTS:** This response is observed during and just after follow up. Long term usage is still questionable. Out of the 120 patients, 117 cases (97.5%) had claudication pain which after treatment, 106 cases (87.9%) had some relief and sense of well-being. 74 cases (61.7%) presented with rest pain out of which 60 cases (49.8%) got relief and had decreased analgesic usage. Rise in limb temperature with regained pulse and increased capillary filling was clinically observed in 27 cases (22.4%). There was a case of reappearance of pulsation in an acute case where the blockage was post intra-arterial annulation. Reversion of pre-gangrenous cyanotic changes was found in 15 cases (12.5%) but out of which 3 cases ultimately went to amputation on follow up. **CONCLUSION:** Overall Xanthinolnicotinate has been found a useful drug for peripheral vascular disease patients in whom vascular surgery is not indicated or contraindicated.

**KEYWORDS:** Xanthinolnicotinate, Peripheral vascular disease, Infusion therapy.

**INTRODUCTION:** The treatment of Peripheral Vascular Disease (PVD) is not satisfactory. Surgical treatment is indicated in acute conditions to save life and limb. But the therapeutic use of any drug, with its potent action on the peripheral circulation, in ameliorating symptoms of inoperable cases of PVD, when added to conservative measures was dismal.

Prophylactic therapy with drugs inhibiting platelet aggregation and vasodilatory effects is thought to reduce thrombo-embolic disease and delay the development of atherosclerosis.<sup>1</sup> It would seem unlikely that drugs would influence arteriosclerotic plaques already existing although they may conceivably prevent or slow down plaque formation and improve overall circulation. The ideal therapeutic drug does not exist and it seems improbable that it will ever be found.

In a preliminary trial, Xanthinolnicotinate helped a significant number of patients whose peripheral obliterative vascular disease had been resistant to previous treatment (Davis and Rozov, 1973)<sup>2</sup>. Musil (1973) among others also reported encouraging results with this preparation.<sup>3</sup>

**AIM:** Xanthinolnicotinate which has a potent action on peripheral circulation<sup>4</sup> was chosen in order to assess its potent therapeutic role in helping patients with inoperable peripheral vascular disease.

**MATERIAL AND METHODS:**

**Study Design:** This is a prospective study for a period of one year from Feb 2013 to Jan 2014 of 120 patients treated in the Vascular Surgery Department of SMS Medical College, Jaipur, Rajasthan. This study is purely based on clinical examination and patient satisfaction response, after 4 weeks of therapy.

**Study Group:** 120 patients with inoperable progressive peripheral obliterative vascular disease admitted in the Department of Cardiothoracic & Vascular Surgery, S.M.S. Medical College, Jaipur, Rajasthan, whose condition had so far been resistant to treatment, were included in the study.

**Exclusion Criteria:** Patients with 1) acute hemorrhage, 2) acute myocardial infarction, 3) decompensated cardiac insufficiency, 4) severe hypertension and 5) pregnant and lactating mothers were excluded.<sup>4</sup> Special precaution was taken for patients suffering from peptic ulcer, hepatic impairment, pulmonary edema, and oliguria. Patients who opted out or were not tolerant to the drug were also excluded.<sup>4</sup>

**Data Collection:** Relevant data from a well-defined proforma was evaluated and analyzed to obtain the results of this study.

**Statistical Analysis:** Data is checked for completeness, consistency and analyzed using SPSS version 20.0. Descriptive statistics like mean proportions etc.; were used. Mc Nemar test is used as test of significance.

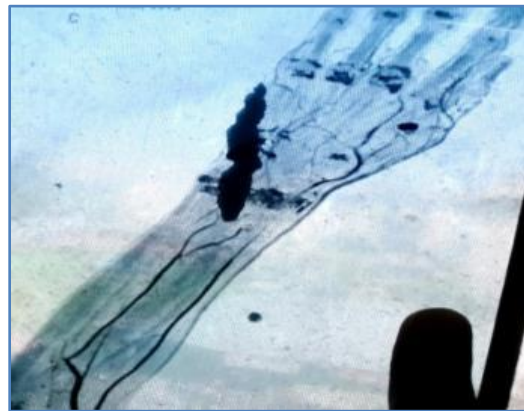
With comprehensive clinical examination and history taking, the signs and symptoms like pallor / colour changes / capillary filling, temperature (cold), distal pulses, claudication pain and rest pain were observed. For admission the patients had to have - a) intermittent claudication on walking less than 200 metres b) reduced or absent dorsalis pedis or posterior tibial pulses.

The above mentioned patients were diagnosed clinically and then screened by CT Angiography.

All the patients were screened with routine blood investigations, ECG and Chest X-Ray. Patients above 40 years of age were additionally examined with 2-D Echo and Coronary Angiography.



**Fig. 1: Digital gangrenous changes of finger tips**



**Fig. 2: Angiogram showing blockage of palmar arches**

## ORIGINAL ARTICLE

**Drug, Dosage and Route of Administration:** Xanthinolnicotinate belongs to category of theophylline drug.<sup>5</sup> It enhances blood flow to the peripheral and cerebral tissues.<sup>6</sup> It enhances microcirculation by decreasing platelet aggregation and increasing erythrocyte elasticity and thus improving the flow properties of blood.<sup>7</sup>

It also possesses vasodilatory effect by decreasing the peripheral resistance of the vessels.<sup>8</sup> Xanthinolnicotinate augments the glucose and oxygen utilization in the cells; and checks the rise in serum lipids and fibrinogen levels.<sup>9</sup> It is a combination of Xanthinol and Niacin.<sup>5</sup>

In our study the route of administration is by intravenous infusion. 6000 mg of Xanthinol Nicotinate was added to 500 ml of Dextran / NS and were infused at the rate of 30 microdrops per minute for an Indian adult patient with mean wt. 60 kg. The Xanthinolnicotinate infusion was given continuously for 4 weeks.

Patients under treatment were continuously observed clinically and through routine blood investigations. Special look out for hematuria, blood in stool and reduced Hb and low platelet count was done.

Under this study, patient is treated only with xanthinol nicotinate therapy in addition to conservative supportive therapy like abstinence from smoking, good balanced diet and adequate hydration and broad spectrum antibiotics coverage.

Care was taken not to prescribe the drug in combination with ganglion blocking and sympatholytic agents. Patients were advised to take orally Tab Xanthinolnicotinate 300mg thrice daily at the time of discharge for another 6 months.

### OBSERVATIONS AND RESULTS:

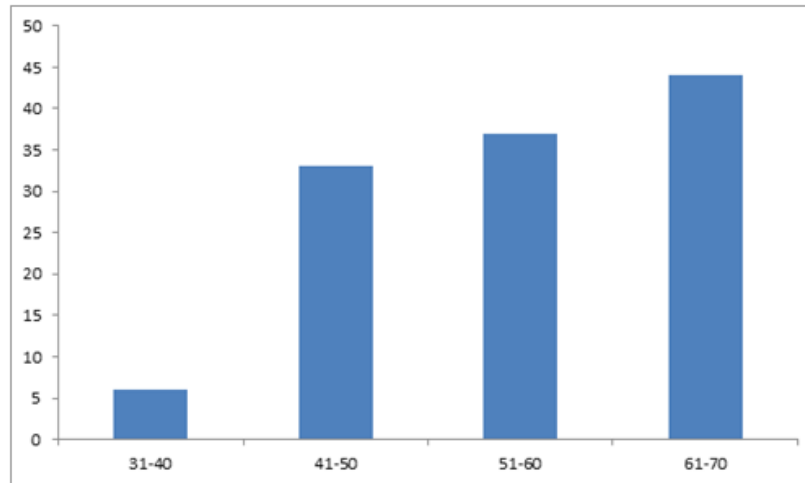
	N	%
Age	60.7+ 5.3	
Male	98	78%
Female	26	22%
Weight	59.5+ 3.5	
BMI	23.4+ 2.1	
Chronic smoking habit	79	64.8%
Obesity with malignancy	6	4.9%
Generalized arteritis	16	13.1%
Coronary artery disease	19	15.6%
Lower limb vessel involvement	96	80%
Upper limb vessel involvement	24	20%

**Table 1: Baseline demographic characters**

Continuous data/ variable are expressed as mean +SD. Categorical data are expressed in numbers.

## ORIGINAL ARTICLE

Chart 1: Bar diagram showing age distribution of the 120 patients of inoperable peripheral vascular disease.



**Chart 1**

Signs & symptoms	No. of patients before treatment n (%)	No. of patients after 4 weeks treatment with Xanthinolnicotinate n (%)	Asymp. Sig. (2-tailed) P value
1. Claudication pain	117 (97.5%)	11 (9.2%)	.000 <sup>a</sup>
2. Rest pain	74 (61.7%)	14 (11.7%)	.000 <sup>a</sup>
3. Cold Clammy extremity	38 (31.1%)	11 (9.1%)	.000 <sup>a</sup>
4. Pregangrenous cyanotic changes	18 (14.8%)	3 (2.5%)	.000 <sup>a</sup>

**Table 2: Signs & symptoms in inoperable cases of Peripheral Vascular Disease before & after 4 weeks of treatment with Xanthinolnicotinate**

P value <0.05 signifies statistically significant Mc Nemer Test is used as test of significance.

Variable	n (%)
1. Reduction in claudication	106(87.9%)
2. Relief of rest pain	60(49.8%)
3. Rise in limb temperature	27(22.4%)
4. Reversion of cyanotic change	15(12.5%)

**Table 3: Patients showing improvement in signs and symptoms after 4 weeks treatment with Xanthinolnicotinate**

**RESULTS:** The mean age of patients (n=120) in this study is 60.7 years with SD of 5.3. Out of total 120 patients, 98(78%) cases were male and 26(22%) were female (p < 0.001). In the history, chronic smoking habit (64.8%), obesity with malignancy (4.9%), generalized arteritis (13.1%) and coronary artery disease (15.6%) were elicited. 96 cases (80%) of the cases presented with involvement of vessels of lower limb affecting the anterior tibial artery, posterior tibial artery and arches of foot.

## ORIGINAL ARTICLE

---

24 cases (20%) of the cases showed upper limb involvement affecting the palmar arches and distal radial and ulnar arches. The number of patients with inoperable peripheral vascular disease was found to be higher with increasing age with maximum patients, 44 cases in 61-70 year age group followed by 37 cases in 51-60 year age group (Figure 2). This finding collaborated with the finding of Davis E.<sup>2</sup>

After 4 weeks treatment with Xanthinolnicotinate, 11(9.2%) cases had claudication pain compared to 117(97.5%) cases before treatment (p value =.000 which is <0.005 signifies statistically significant). 14(11.7%) cases had rest pain after therapy compared to 74(61.7%) cases before start of the trial (p value =.000).

Patients having cold clammy extremity was reduced from 38(31.1%) cases to 11(9.1%) cases after treatment (p value=.000). Initially pregangrenous cyanotic changes was present in 18 (14.8%) cases compared to 3(2.5%) cases after therapy (p value =.000).

106(87.9%) patients had relief of claudication pain/pain while using limb with increase in time. Claudication distance increased to 400 metres compared to less than 200 m before treatment. The relief was not marked but patients' response was satisfactory.

Rest pain was relieved in 60(49.8%) patients. 27(22.4%) patients had marked rise in skin temperature and clinically skin colour was improved with decreased capillary filling time. Reversion of cyanotic pregangrenous changes was present in 15(12.5%) of the patients. But 3 patients deteriorated resulting gangrene and amputation on follow up.

**DISCUSSION:** This is a simple prospective study of 120 patients, who completed full 4 week regimen. Here we use a fixed dose of the drug for a fixed period. But in some patients we reduced the dosage in between and again restored to the same dose due to drug intolerance and side effects.

There was also complication of thrombophlebitis and fever complicating the treatment which resolved by proper care. Regular blood and urine culture was repeated every 7<sup>th</sup> day and proper care was taken to prevent septicemia. Review CT Angiography after the treatment regime does not give any change in the primary blockage site. It is believed to improve the remaining collaterals and microcirculation which leads to the improvement in the ischemic symptoms.

It is also surprising that 3 patients progressed to gangrenous changes and ultimately were treated by amputation after 3 - 4 months. However, rest pain was relieved in 60(49.8%) which was appreciated by most patients as they can go back to sleep with mild analgesics. The long term effect has still not been known but the patients had a sense of wellbeing during the infusion period.

Side effects were common. 52(43.1%) patients presented with vomiting relieved by antiemetics; treatment was continued subsequently. 65(53.9%) patients presented with flushing and 83(68.9%) patients with headache - all relieved by medications.

These results are those present during treatment regime and immediate follow up in 7 days. Patients have been discharged with 300 mg tablet Xanthinolnicotinate thrice daily.

Overall Xanthinolnicotinate has been found a useful drug for significant number of patients in whom vascular surgery is not indicated or contraindicated.

**REFERENCES:**

1. Mc Nicol G P, Mitchell J R A, Van D L J, Born G R V. Platelets in thrombosis: Their clinical significance and the evaluation of potential drugs. *Thrombos Diathes Haemorrh* 1974; 31: 379-394.
2. Davis E, Rozov H. Xanthinol Nicotinate in peripheral vascular disease. *The Practitioner* 1975; 215: 793-798.
3. Musil HE. Treatment of chronic arterial vascular disorders with Complamin and Complamin retard. *Med Welt*. 1973 Jan 19; 24(3):103-13. German. No abstract available. PMID: 4617835 [PubMed - indexed for MEDLINE]
4. Afifi AM, Adnan M, Taha M, Amasha M E. Xanthinol Nicotinate in the management of leg ulcers associated with haemoglobinopathies. *Curr Med Res Opin* 1979; 6: 309.
5. K.D. Tripathi. *Essentials of Medical Pharmacology*, 5<sup>th</sup> edition: 2004; 500.
6. Loriaux S M, Deijen J B, Orlebeke J F, De Swart J H. The effects of nicotinic acid and xanthinolnicotinate on human memory in different categories of age: A double blind study. *Psychopharmacology* 1985; 87: 390-395.
7. Seidel G, Endell W. Effect of Xanthinolnicotinate treatment on platelet aggregation. *Int J Clin Pharmacol* 1977; 15: 139-143.
8. Sharma P L. Comparative effects of placebo and plain and slow-release tablets of Xanthinolnicotinate on exercise tolerance in normal human subject. *Int J Clin Pharmacol* 1978; 16: 19-21.
9. Beiron K, Swies J, Kostka-Trabka E, Gryglewski R J. Thrombolytic and anti-platelet action of xanthinolnicotinate: possible mechanisms. *Journal of Physiology and Pharmacology: an official journal of the polish physiological Society* 1998; 49: 241-249.

**AUTHORS:**

1. Lukram Sidartha
2. Mohit Sharma
3. Ramchandra Sherawat
4. Amit Sharan
5. Sunil Dixit
6. Anil Sharma

**PARTICULARS OF CONTRIBUTORS:**

1. Resident Surgeon, Department of CTVS, SMS Medical College.
2. Resident surgeon, Department of CTVS, SMS Medical College.
3. Resident, Surgeon, Department of CTVS, SMS Medical College.
4. Resident, Surgeon, Department of CTVS, SMS Medical College.
5. Assistant Professor, Department of CTVS, SMS Medical College.

6. Professor, Department of CTVS, SMS Medical College.

**NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:**

Dr. Lukram Sidartha,  
Resident Doctor's Hostel,  
Room No. 25,  
SMS Medical College,  
Jaipur-302004, Rajasthan.  
Email: victoriasidarth@gmail.com

Date of Submission: 06/07/2014.  
Date of Peer Review: 07/07/2014.  
Date of Acceptance: 15/07/2014.  
Date of Publishing: 21/07/2014.