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Original Research Article

EVALUATING THE THERAPEUTIC EFFICACY OF XANTHINOL NICOTINATE IN INOPERABLE PERIPHERAL VASCULAR DISEASE: A COMPREHENSIVE CLINICAL OBSERVATIONAL STUDY

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Abstract

Background: This prospective study aimed to investigate the therapeutic potential of Xanthinol Nicotinate in 350 patients with inoperable peripheral vascular disease, who underwent a 4-week regimen of intravenous continuous infusion. **Material and Methods:** The study involved 350 patients diagnosed with inoperable progressive peripheral obliterative vascular disease, admitted during July 2020 to July 2023 the Department of Cardiothoracic & Vascular Surgery, Sawai Man Singh Medical College, Jaipur, Rajasthan. Clinical responses, including limb temperature, peripheral pulses, skin color, capillary filling time, relief of rest pain, and claudication pain, were systematically recorded. **Results:** The observed responses were monitored during and immediately after follow-up, with the long-term efficacy still under scrutiny. Out of the 350 patients, 341 cases (97.5%) experienced claudication pain, and following treatment, 307 cases (87.9%) reported some relief and an improved sense of well-being. Among the 216 cases (61.7%) presenting with rest pain, 174 cases (49.8%) achieved relief with reduced analgesic usage. Notably, 78 cases (22.4%) exhibited an increase in limb temperature, regained pulses, and enhanced capillary filling. Pulsation reappeared in an acute case with post intra-arterial annulation blockage. Reversion of pre-gangrenous cyanotic changes occurred in 44 cases (12.5%), although three cases ultimately progressed to amputation during follow-up. **Conclusion:** Xanthinol Nicotinate demonstrates utility as a beneficial drug for patients with peripheral vascular disease, particularly when vascular surgery is either not indicated or contraindicated. The findings highlight its potential in managing symptoms and improving the overall well-being of individuals with inoperable cases of peripheral vascular disease.

INTRODUCTION

Peripheral Vascular Disease (PVD) presents a formidable challenge in terms of treatment efficacy, especially when surgical interventions are either contraindicated or impractical in inoperable cases. While surgical procedures are crucial in acute conditions for preserving life and limb, the effectiveness of drug therapy, specifically those targeting peripheral circulation, in alleviating symptoms in inoperable PVD cases alongside conservative measures has been disheartening.

Prophylactic strategies employing drugs that inhibit platelet aggregation and induce vasodilation are theorized to mitigate thromboembolic events and delay atherosclerosis progression, presenting a potential avenue for managing PVD symptoms.[1] The capacity of drugs to influence existing arteriosclerotic plaques is doubtful, but there is speculation regarding their ability to prevent or

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decelerate plaque formation and enhance overall circulation.[2] However, the quest for an ideal therapeutic drug remains elusive, with skepticism surrounding the likelihood of such a discovery.

MATERIALS AND METHODS

A prospective study spanning three year (July 2020 to July 2023) was conducted on 350 patients in the Cardio-Thoracic and Vascular Surgery Department of SMS Medical College, Jaipur, Rajasthan. The study relied on clinical examination and patient satisfaction responses after a 4-week therapy period. The study group comprised individuals with inoperable progressive peripheral obliterative vascular disease resistant to previous treatments, excluding those with specific medical conditions such as acute hemorrhage, acute myocardial infarction, decompensated cardiac insufficiency, severe hypertension, and pregnant or lactating mothers. Special precautions were taken for patients with peptic ulcer, hepatic impairment, pulmonary edema, and oliguria. Data collection involved a well-defined proforma, and statistical analysis was performed using SPSS version 20.0.

Comprehensive clinical examinations, history taking, and diagnostic procedures, including CT Angiography, were conducted. Signs and symptoms such as pallor/color changes, capillary filling, temperature, distal pulses, claudication pain, and rest pain were observed for diagnosis.

Xanthinol nicotinate, categorized as a theophylline drug, was administered intravenously at a dose of 30,000 mg in 500 ml (150 mg/ml, 2ml vial, 10 vials used per infusion) of Dextran/NS at a rate of 20 micro drops per minute for four weeks. The drug enhances blood flow, micro circulation, and possesses vasodilatory effects, improving blood flow properties. Routine blood investigations were conducted during treatment, with a focus on potential side effects.

Patients received xanthinol nicotinate therapy along with conservative measures, including abstinence from smoking, a balanced diet, adequate hydration, and broad-spectrum antibiotic coverage. The drug was not prescribed in combination with ganglion-blocking and sympatholytic agents. Patients were advised to continue oral administration of Tab Xanthinol nicotinate 500mg twice daily for six months post-discharge.

Statistical Analysis

Data collection involved a well-defined proforma, and statistical analysis was performed using SPSS version 20.0. Quantitative data were expressed as mean and standard deviation. Quantitative data were expressed as proportion and were analysed using Mc Nemar Test. P value <0.05 was considered as statistically significant.

RESULTS

The study included a total of 350 patients with inoperable progressive peripheral obliterative vascular disease. The demographic profile revealed an average age of 58.49±4.66 years. The majority of participants were male (273 individuals, 78%) compared to females (77 individuals, 22%). The average weight was 59.45±4.93 kg, resulting in an average Body Mass Index (BMI) of 22.25±2.97. [Table-1]

Among 350 study participants, Chronic smoking habit was prevalent in 220 (62.86%) patients, obesity with malignancy was observed in 18 (5.14%) patients, generalized arteritis in 52 (14.85%) cases, and coronary artery disease in 49 (14%) cases. Lower limb vessel involvement was predominant in 287 (82%) cases, specifically the anterior tibial artery, posterior tibial artery, and arches of the foot. Upper limb involvement was noted in 63 (18%) cases, affecting the palmar arches, distal radial, and ulnar arches. [Table-2]

The study evaluated various signs and symptoms in inoperable cases of Peripheral Vascular Disease (PVD) before and after 4 weeks of treatment with Xanthinol nicotinate. Study revealed that after 4 weeks of treatment with Xanthinol nicotinate, Claudication pain was decreased significantly from 336 cases (96%) to 35 cases (10%) (p value < 0.001), Rest pain was decreased significantly from 203 cases (58%) to 36 cases (10.29%) (p value < 0.001). Cases with cold clammy extremities were reduced significantly from 104 (29.71%) to 32 (9.14%) (p value = 0.000) and Pregangrenous cyanotic changes were reduced significantly from 55 (15.71%) to 10 (2.86%) (p value = 0.000) after 4 weeks of treatment with Xanthinol nicotinate. [Table-3]

After treatment of 4 weeks, 301 cases (89.58%) showed reduction in claudication, 167 cases (82.27%) got relief of rest pain while 72 cases (69.23%) showed with rise in limb temperature. Reversion of cyanotic changes was observed in 45 cases (81.81%) after treatment of 4 weeks. [Table-4].

Table 1: Baseline Demographic Characteristics of study participants

Baseline variable (N=350)	Mean	SD
Age (years)	58.49	4.66
Weight (Kg)	59.45	4.93
BMI	22.25	2.97
Gender		
Male (n, %)	273	78%
Female (n, %)	77	22%

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Table 2: Associated morbidity among study participants

Associated morbidity	n	%
Chronic smoking habit	220	62.86%
Obesity with malignancy	18	5.14%
Generalized arteritis	52	14.85%
Coronary artery disease	49	14%
Lower limb vessel involvement	287	82%
Upper limb vessel involvement	63	18%

Table 3: Sign and symptoms of study participants before and after treatment

Sign and symptoms (Out of N =350)	Before treatment	After treatment	P value
	n(%)	n (%)	
Claudication pain	336(96%)	35(10%)	<0.001
Rest pain	203 (58%)	36 (10.29%)	<0.001
Cold Clammy extremity	104 (29.71%)	32 (9.14%)	<0.001
Pre gangrenous cyanotic changes	55 (15.71%)	10 (2.86%)	<0.001

Table 4: Patients showing improvement in signs and symptoms after 4 weeks treatment with Xanthinol nicotinate

Variable	n	%
Reduction in claudication	301	89.58%
Relief of rest pain	167	82.27%
Rise in limb temperature	72	69.23%
Reversion of cyanotic change	45	81.81%

DISCUSSION

This prospective study, encompassing 350 patients who completed a full 4-week regimen of Xanthinol nicotinate, aimed to explore the therapeutic efficacy of the drug in inoperable cases of peripheral vascular disease (PVD). The fixed dosage and treatment duration were employed, with occasional adjustments in dosage due to drug intolerance and side effects observed in some patients.

Complications such as thrombophlebitis and fever arose during treatment, necessitating proper care and vigilant monitoring. Regular blood and urine cultures, repeated every 7th day, were conducted to prevent septicemia. Although the post-treatment CT Angiography did not reveal alterations in the primary blockage site, it is postulated that the treatment may enhance remaining collaterals and microcirculation, contributing to the improvement in ischemic symptoms.

Surprisingly, three patients progressed to gangrenous changes, requiring amputation after 3–4 months. Despite this, 60 patients (49.8%) experienced relief from rest pain, a significant improvement appreciated by most patients who reported enhanced sleep quality with mild analgesics. The long-term effects remain unknown, but patients exhibited a sense of well-being during the infusion period.

Common side effects included vomiting in 43.1% of patients, alleviated with antiemetics, while flushing was observed in 53.9% and headache in 68.9% of patients, both managed effectively with medications. These results are reflective of the treatment regime and immediate follow-up within 7 days. Patients were discharged with a maintenance dose of 300 mg Xanthinol nicotinate tablets thrice daily. The findings suggest that Xanthinol nicotinate demonstrates utility as a useful drug for a significant number of patients in whom vascular surgery is either not indicated or contraindicated.

In a preliminary trial, Xanthinol nicotinate emerged as a promising candidate, demonstrating effectiveness in a substantial number of patients resistant to prior treatments for peripheral obliterative vascular disease.[3] Encouraging results with this preparation were also reported by more recent studies,[4,5] suggesting its potential as a valuable therapeutic agent in addressing the challenges posed by inoperable cases of PVD.

While the study provides valuable insights into the immediate effects and side effects of Xanthinol nicotinate, further research with extended follow-up is warranted to elucidate the long-term outcomes, potential complications, and sustained benefits associated with this treatment. Recent literature emphasizes the importance of considering individual patient profiles and tailoring treatment strategies to optimize therapeutic outcomes in the management of peripheral vascular disease.[5,6,7]

While the research on Xanthinol nicotinate in inoperable cases of Peripheral Vascular Disease (PVD) has provided valuable insights, it is essential to acknowledge certain limitations that may impact the interpretation and generalizability of the findings:

Limitations of our study: Small Sample Size, Single-Center Study, Limited Follow-up Duration Lack of Placebo Control Group, No Randomization. Addressing these limitations in future research endeavors can contribute to a more comprehensive understanding of the role of Xanthinol nicotinate in the management of inoperable cases of Peripheral Vascular Disease.

CONCLUSION

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Xanthinol nicotinate demonstrated significant effectiveness in alleviating the symptoms of inoperable cases of Peripheral Vascular Disease, as evidenced by the notable reduction in claudication pain, relief of rest pain, improved limb temperature, and reversion of cyanotic changes. The statistical significance of these improvements underscores the therapeutic potential of Xanthinol nicotinate in this patient population. However, continued monitoring and further investigation are essential for a comprehensive understanding of the long-term outcomes and potential side effects associated with this treatment.

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