

EVALUATION OF ANALGESIC EFFECT OF TAB TRAILOKYA VIJAYA VATI IN POST-OPERATIVE PAIN IN PATIENTS UNDERGOING KSHARKARMA: AN OBSERVATIONAL STUDY

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Abstract

Despite advances in technology and robotics, the fundamentals of surgical management have not changed drastically. Ayurveda, the science of life, has extensive knowledge of operations, including the complicated procedures mentioned in the classical texts. However, over time, the ability of anesthetics and analgesics was lost. This resulted in the backwardness of Ayurvedic surgical wisdom and the rise of modern analgesics and anesthetics in the market. These current products have potential side effects and therefore a safer and better alternative to these products can support Ayurvedic surgery worldwide. Trailokya Vijaya Vati (TVV) is one such Ayurvedic formulation which is explained by its potent analgesic activity. This study was conducted to evaluate the safety and efficacy of TVV in the treatment of postoperative pain in patients undergoing anorectal procedures. An observational study indicated a reduction in sleep time ($p < 0.05$), a lower incidence of insomnia and undisturbed sleep in the treatment group than in the control group. The formulation was also well tolerated with no or minimal requirements for rescue analgesics. The efficacy observed in the study suggests that the product can be further investigated in a larger population with a different activity profile.

Keywords: Trailokya Vijaya Vati, Bhanga, Ano-rectal disorders, Ksharakarma, Agnikarma.

INTRODUCTION

In today's world, Ayurveda is commonly considered only as treatment with herbal medicines and Panchakarma procedures. However, Ayurveda - the science of life is a complete life discipline for the prevention and treatment of physical, mental and spiritual disorders. It is described in classical texts as 'Ashtanga Ayurveda'¹ explaining the diverse paradigm of this ancient science. Her knowledge is spread in eight different fields like Kayachikitsa (General Medicine), Balaroga (Paediatrics), Graha Shastra (Property Treatment/Psychiatry), Urdhvanga (Treatment of Disorders Above Clavicle), Shalya (Foreign Body Removal Treatment/Surgery), Danshtra (toxicology), Jara (geriatrics or rejuvenation therapy) and Vrusha (aphrodisiology). Some of these areas of knowledge are still under-explored and under-promoted even today. One such area in this Ashtanga Ayurveda is Shalyashastra.

Shalyashastra was one of the most developed scientific branches of Ayurveda, proposed by Acharya Sushruta, who is known worldwide as the father of surgery. Many complicated surgical procedures, several surgical instruments and therapies are explained in detail in most Ayurvedic classical texts. It is believed that these procedures were successfully performed on many patients at the time. However, the traditional science of these procedures and devices has recently lagged behind for several reasons. A commonly considered reason is the lack of available literature on analgesics and anesthetics used before and after these procedures.

In earlier times Vijaya (Bhanga)² formulations were used as an analgesic, rejuvenating agent, sleep promoter and aphrodisiac in various patients. Due to the analgesic properties of Vijaya, it can be assumed that it may have been used in the treatment of post-operative pain at that time. The treatment of postoperative pain is one of the fundamental areas of research into safer and better alternatives to conventionally used NSAIDs and morphine-based drugs.

In our previous clinical experience using Trailokya Vijaya Vati (TVV) to manage perimenstrual pain, which is commonly caused by smooth muscle spasms, we observed a significant decrease in the need for conventional surgical NSAIDs to control patients' symptoms. Considering the probable relaxation potential of the smooth muscle of the TVV, we hypothesized that it could help prevent postoperative pain during minor surgical procedures.

Ksharakarma or Ksharsutra is one of the oldest surgical techniques mentioned in Ayurveda, mainly for the treatment of hemorrhoids and fistula-in-yes. It is done by applying Kshara and Ksharsutra (medicated alkaline paste and threads) on hemorrhoids and Fistula-in-ano for complete cure. Today, the procedure is performed under local anesthesia. However, patients may experience pain, discomfort and bleeding after the procedure, which must be controlled to prevent post-procedure complications and facilitate a speedy recovery.

Thus, this observational study is planned to evaluate the effect of TVV on postoperative pain in patients with Ksharakarma.

MATERIALS AND METHODS

Investigation Product: Herbal Bioactive and Mineral Formulation - Trailokya Vijaya Vati developed by HempStreet Medicare Private Limited, New Delhi, India.

Hypothesis: In classical literature, Vijaya (*Cannabis sativa*) leaves were a common remedy for many kapha, vata disorders and are known to reduce pain. It has also been shown to reduce neuropathic pain, diabetic neuropathy, and oxidative stress.³ Thus, we hypothesize that the traditional Ayurvedic formulation of TVV is equipotent to the standard of care for postoperative pain in patients undergoing the Ksharakarma procedure.

Objective: The aim of the study was to evaluate the analgesic effect of TVV in the management of postoperative pain in patients with Kshara karma using the pain scale, sleep parameters, bleeding, postoperative recovery, safety and need for conventional analgesics.

Study design: The study was an open (partially blinded), observational efficacy study in adult human subjects of both sexes (n=30 in each group). The control group received conventional treatment and the treatment group received TVV seven days after the procedure.

Inclusion criteria: Patients underwent a Ksharakarma and/or Agnikarma procedure for anorectal disorders at the clinical study site. Patients aged 18–60 years of both sexes and those willing to participate in the study were included.

Exclusion criteria: Patients with comorbid cardiac problems, liver disorders, renal impairment, uncontrolled plasma glucose levels, pregnant, lactating, with cancer of any site, and taking any psychoactive drugs. Patients who were not willing to participate in the study were excluded with complications during and after the procedure.

Ethical approval: The study design was submitted to an independent ethics committee for review and approval was required prior to evaluation. (IEC number: RPIEC0150121)

Drug Dosing: Patients who underwent Ksharakarma and/or Agnikarma procedure for anorectal disorders at the study site were detailed in the clinical trial. After receiving informed consent, they were screened for trial eligibility. Subjects were then randomly assigned to a treatment group (TVV tablets) and a control group (standard care). Subjects were administered the test formulation twice daily after both meals, which were consumed at home after the procedure. The subject kept a subject diary for dosing compliance. Doctor follow-up was done through phone calls and one weekly home visit. The total expected duration of the study was no longer than 60 days from the date of the first screening visit to the checkout after the last visit. Subjects were asked to report to the study site for each visit with a 10-hour overnight fast before sampling. Between visits to the study site, no body fluid samples were collected from subjects other than suggested blood tests, except in medical emergencies, as directed by the physician. Vital signs (sitting blood pressure, radial pulse rate, oral temperature, and respiratory rate) were measured at sampling. Each of the subjects was asked about well-being at the time of the clinical examination and during the recording of vital signs. Subject response was recorded in terms of pain scale scores, sleep parameters according to a standard scale, need for rescue analgesics, and changes in blood biochemistry assessed at baseline and at the end of the study. Subjects refrained from taking any other nutraceuticals, vitamin supplements, iron supplements, and medications other than conventional

postoperative antibiotics and other medications without informing the study site and/or study team or study coordinator.

Table 1: Schedule of events

Activities	Day 0	Day 5
Eligibility Criteria	Checked	X
Informed Consent	Checked	X
Demographic Data	Checked	X
Laboratory testing	Checked	X
Physical Examination	Checked	Checked
Vital Signs	Checked	Checked
Proctoscopy	Checked	As Required
IP dispensing and reconciliation	Checked	Checked
Verbal Pain Rating Score form4	Checked	Checked
Sleep Quality Scale5	Checked	Checked
Need of other analgesics	Checked	Checked
Adverse Events	X	Checked
Concomitant medications, if any	Checked	Checked

Investigations: For all the subjects participating in the study, the following blood investigations were conducted Haemogram with ESR, Urine Routine, BSL Fasting and Post Meal, Liver Function Test, Renal Function test. HIV, HBsAg, Pregnancy Test was conducted only before the study to confirm inclusion in the trial.

Duration of treatment: The duration of medication each subject was 7 days.

RESULTS AND DISCUSSION

The study included pain response scale analysis, need for other non-steroidal or morphine-based analgesics for pain relief, sleep quality index scale, and comparative wound healing as methods to evaluate the efficacy of the tested formulation. The effectiveness of TVV was compared to the standard of care protocol. Subject compliance, tolerability, development of drug-related adverse events, and adverse changes in liver function tests and renal function tests were also evaluated to assess the safety profile of the formulation.

Sex-Wise Distribution

Males and females were similar in both groups. (Figure 1)

Distribution by age

The median age of subjects in both groups was similar (34 years in the control group and 35.5 years in the treatment group). (Figure 2)

Patients undergoing procedures for anorectal disorders

Out of a total of 60 patients enrolled, eight patients in the control group and seven patients in the treatment group underwent Agnikarma and Ksharakarma procedures for their anorectal disorders. A total of 27 patients in the control group and 29 in the treatment group underwent Ksharakarma procedures. (Figure 3)

Analysis of pain

One subject reported no pain on the third day after standard treatment in the control group. On the fourth day, approximately two and five subjects reported zero pain from the control and treatment groups, respectively. The number of subjects reporting zero pain increased until day 7. However, it was found that the rate of pain relief was maximal in the treatment group compared to the control group, especially after the 4th day of surgery. Box and plot of pain score (VAS) of control and treatment groups for seven days are shown in Figures 1 and 2, respectively. The middle line in each box represents the median value, the outer edges of the box represent the interquartile range (25th and 75th percentiles). (VAS – Visual Analog Scale) (Figure 4 and 5)

Sleep parameters

Patients in the treatment group showed a significant ($p=0.007$) reduction in sleep time compared to the control group. However, sleep time in both groups was comparable. (Table 2). In the treatment group, fewer subjects showed insomnia; more subjects fell asleep within 30 minutes, did not wake up in the middle of sleep, had no symptoms of coughing or snoring, had less nightmare disturbance, and less pain than the control group. However, more subjects showed nocturia in the treatment group than in the control group. Only one subject in the treatment group experienced dyspnoea and difficulty staying awake. (Figure 6)

Complete blood count (CBC) and hemogram

Participants had their blood biochemistry assessed before and after the study to assess the safety of the formulation. The evaluation showed comparable complete blood count and hemogram parameters, suggesting no safety issue for both TVV and standard care during the treatment period. (Table 3, Figure 7-10)

Lipid profile, liver function test and kidney function test analysis are shown in the following table. The treatment group showed a non-significant decrease in post-treatment serum glucose compared to the control group. The serum lipid profile was non-significantly increased in the treatment group compared to the control group. Serum liver and kidney enzymes were comparable in both groups before and after treatment. (Table 4)

Figure 1: Sex-wise Distribution of patients

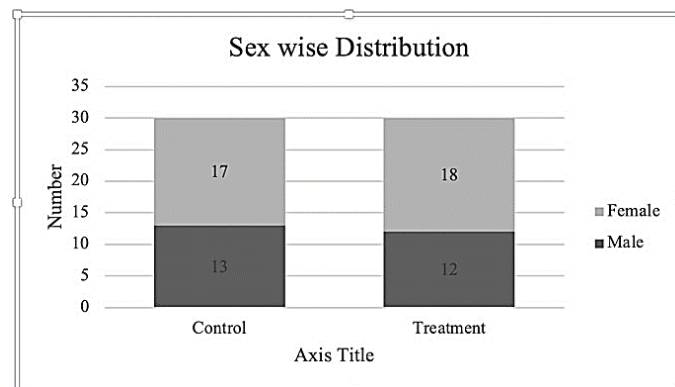


Figure 2: Age-wise distribution of patients

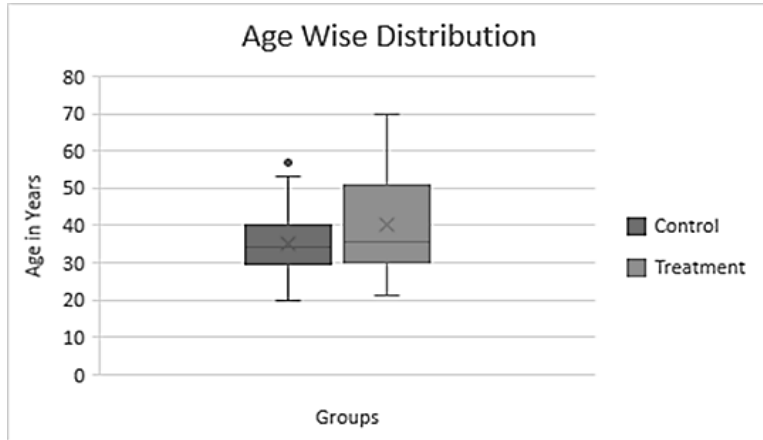


Figure 3: Patients undergoing procedures

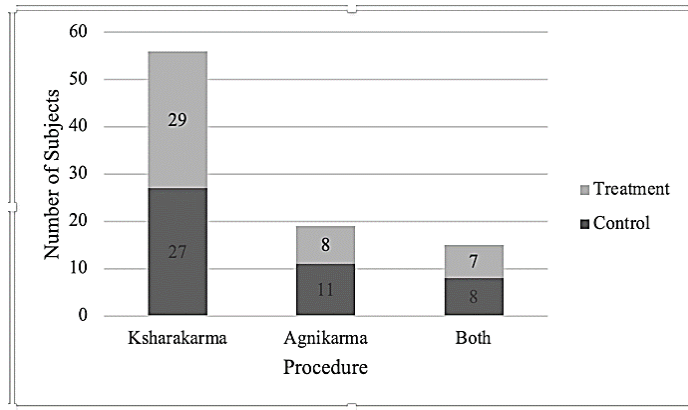


Figure 4: Box and plot graph of pain scores (VAS) of the control group

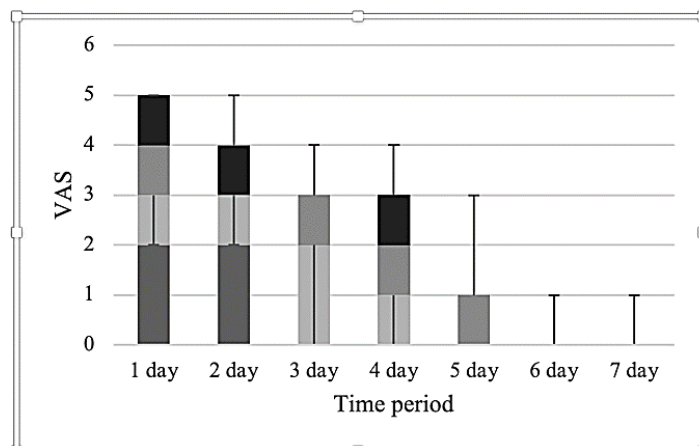


Figure 5: Box and plot graph of pain scores (VAS) of treatment group over seven days

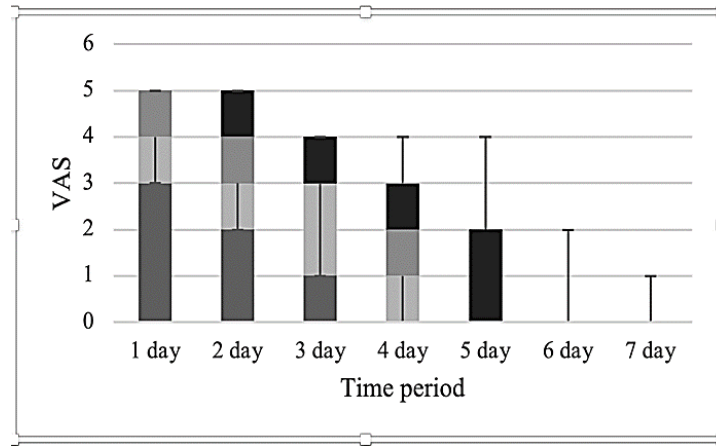


Table 2: Time to sleep and analysis of the hours in enrolled groups

	Control	Treatment	P-value
Time to sleep	24.83±1.88	18.16±1.36**	0.007
Sleeping hours	7.93±0.13	7.8±0.13	0.726

Figure 6: Sleeping parameters analysis in enrolled groups

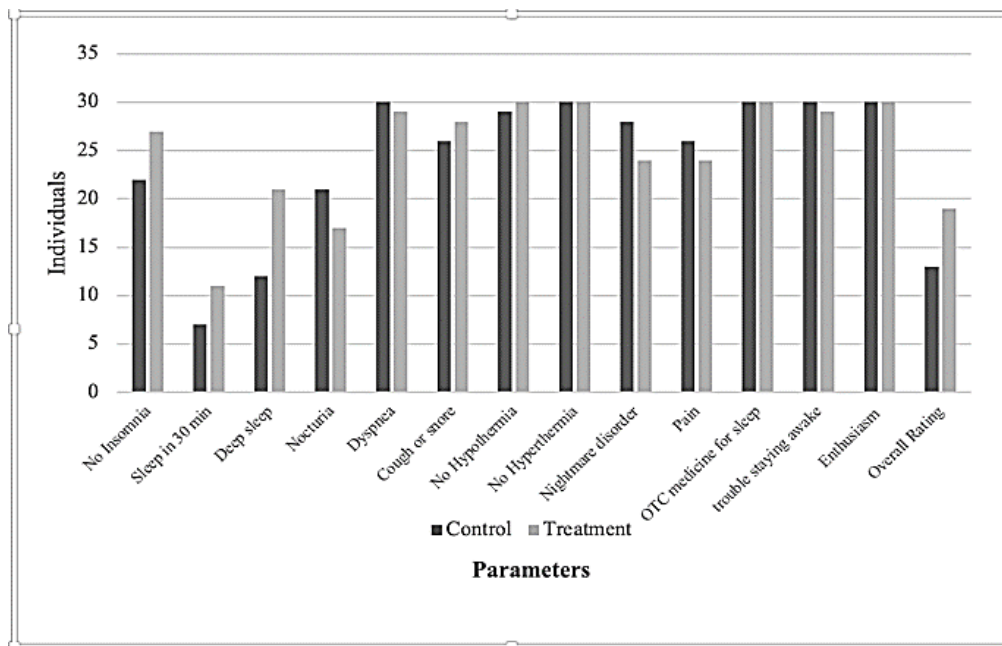


Figure 7: Haemogram Before the treatment

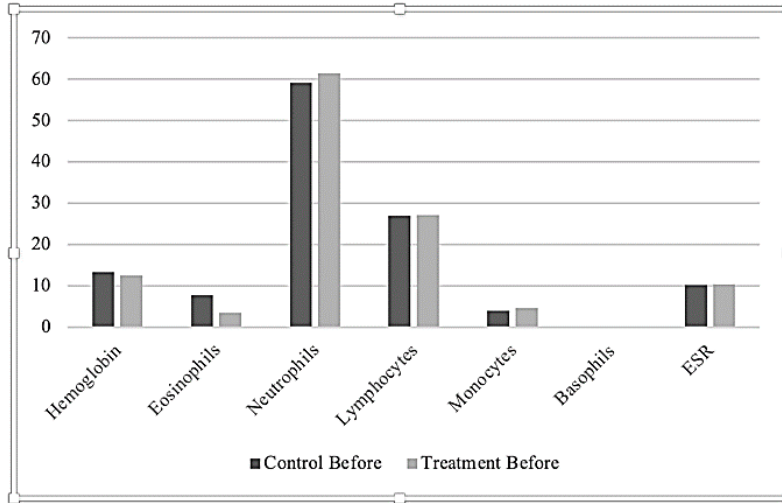


Figure 8: Haemogram after the treatment

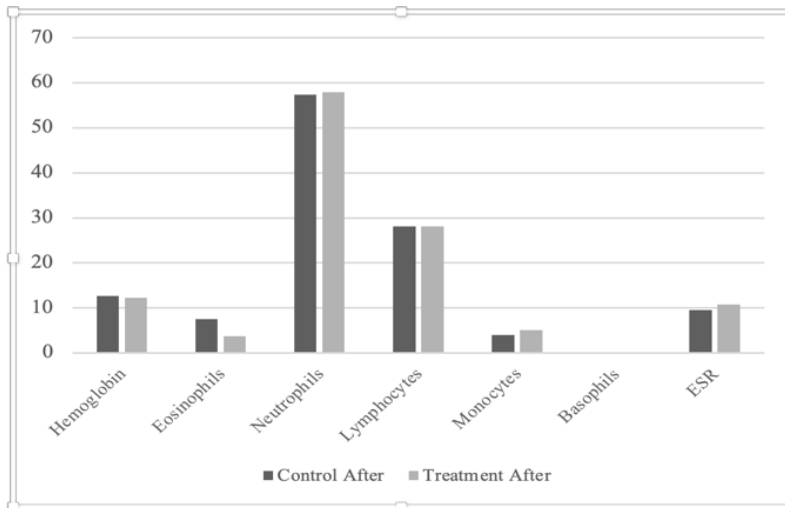


Figure 9: Total Leukocyte Count

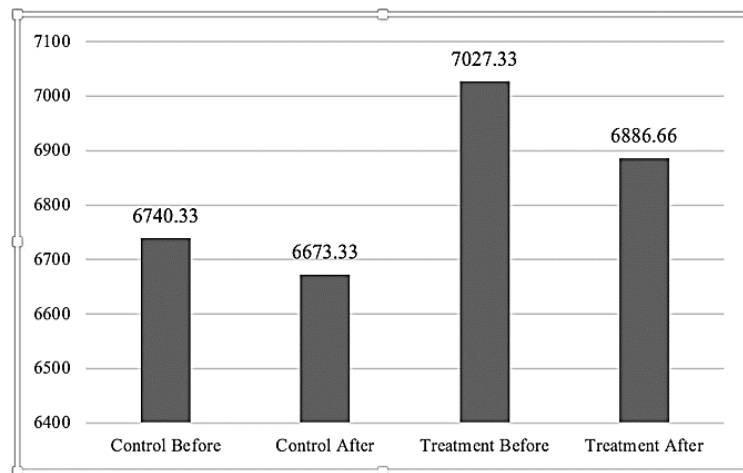


Figure 10: Platelets

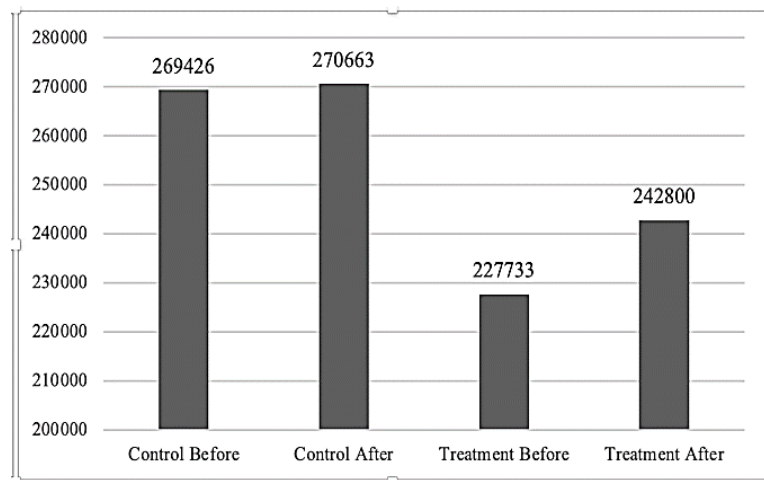


Table 3: Blood parameters comparison in both the groups

	Control group		Treatment group	
	Before	After	Before	After
Hemoglobin	13.40±0.78	12.66±0.26	12.49±0.20	12.2±0.17
Eosinophils	7.73±2.97	7.53±2.81	3.43±0.28	3.7±0.30
Neutrophils	59.13±1.90	57.4±1.87	61.5±1.47	57.86±2.30
Lymphocytes	26.96±1.56	28.13±1.84	27.16±1.19	28.1±1.08
Monocytes	4.06±0.26	3.93±0.31	4.7±0.49	5.1±0.65
Basophils	0.03±0.03	0.06±0.06	0.23±0.11	0.2±0.13
Platelets	269426±15283	270663±11563	227733±8573	242800±14337
ESR	10.23±0.38	9.53±0.28	10.43±0.55	10.81±0.34
TLC	6740.33±294.33	6673.33±224.01	7027.33±246.06	6886.66±202.44

ESR: Erythrocyte Sedimentation Rate; TLC: Total Leucocyte Count

Table 4: Blood Biochemistry

	Control group		Treatment group	
	Before	After	Before	After
Glucose	105.72±4.11	105.2±3.53	106.73±2.52	102.66±1.91
Lipid profile				
Total Cholesterol	199.63±3.02	194.4±2.92	170.16±6.40	171.25±4.71

Triglycerides	103.16±2.64	103.46±2.72	102.35±3.39	108.16±3.3
LDL	125.6±2.99	125.66±2.84	109.43±1.96	112.68±2.62
VLDL	9.96±0.27	9.53±0.20	18.24±4.02	17.19±3.66
HDL	42.36±1.82	41.86±1.86	44.50±1.59	43.88±1.54
Liver function test				
SGOT	32.45±0.82	32.17±0.85	27.28±0.75	27.69±0.66
SGPT	35.42±1.91	34.69±1.84	27.16±1.25	28.46±1.29
Direct Bilirubin	0.14±0.01	0.16±0.01	0.17±0.01	0.17±0.01
Total Bilirubin	0.38±0.04	0.4±0.03	0.37±0.05	0.34±0.04
Alkaline phosphate	139.06±2.35	139.11±2.3	125.11±4.55	124.23±4.27
Kidney function test				
Serum Urea	16.76±0.58	0.92±0.04	12.59±0.38	12.21±0.41
Serum Creatinine	0.92±0.04	0.92±0.03	0.85±0.03	0.97±0.04

CONCLUSION

This study was conducted to evaluate the safety and efficacy of Trailokya Vijaya Vati as an analgesic compared to standard care in patients undergoing surgery for anorectal disorders. The study revealed that all patients tolerated the drug well, as evidenced by no patient loss and similar blood biochemistry. None of the patients experienced any adverse side effects during the study, indicating excellent safety. When the efficacy of the formulation was compared to the standard of care for the management of postoperative pain and sleep disturbances, the TVV formulation showed comparable results, as evidenced by the lack of rescue medication, NSAIDs, favorable sleep patterns, and superior pain relief. This study suggests a potential safer and better alternative for postoperative management. Considering the efficacy observed in the study and the limitations of this study, the formulation can be further investigated in a larger population with a different activity profile.

CONFIRMATION

Hemp Street Medicare Pvt Ltd sponsored this observational study.