



Effectiveness of glycerine magnesium sulphate application on superficial thrombophlebitis among patients receiving intravenous infusion at selected hospitals of Belagavi District: A pre-experimental nursing research

¹ Shridhar Waghamore, ² Siddusing S Hajeri and ³ Shakeelahmed R Mujawar

¹ Final Year M.Sc., Nursing, Department of Medical and surgical nursing, Shri JG Co-operative Hospital Society's College of Nursing, Ghataprabha, Karnataka, India

² M.Sc. (Nursing), Ph.D. (N), H.O.D, Professor and PG Guide, Department of Medical and Surgical Nursing, Shri JG Co-operative Hospital Society's College of Nursing, Ghataprabha, Karnataka, India

³ M.sc (Nursing), Professor, Department of Medical Surgical Nursing, Shri JG Co-operative Hospital Society's College of Nursing, Ghataprabha, Karnataka, India

Corresponding Author: Shridhar Waghamore

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Abstract

Superficial thrombophlebitis is a prevalent complication among patients receiving intravenous (IV) infusion, resulting in significant discomfort. The aim of this research was to evaluate the effectiveness of Glycerine Magnesium application in alleviating superficial thrombophlebitis. A pre-experimental one group pre-test-post-test design was utilized, involving 50 patients receiving IV infusion at selected hospitals in Belagavi district. The Visual Infusion Phlebitis (VIP) Scale was employed to assess thrombophlebitis severity. Results indicated a statistically significant reduction in VIP scores post-intervention, confirming the effectiveness of the treatment. Further research is recommended to explore long-term outcomes and other demographic factors influencing thrombophlebitis management.

Keywords: Belagavi hospitals, glycerine magnesium sulphate, intravenous infusion, superficial thrombophlebitis, VIP Scale.

Introduction

Intravenous (IV) infusion is a common medical procedure in hospitals, often associated with the development of superficial thrombophlebitis, which manifests as inflammation and pain along the veins. Superficial thrombophlebitis results from the use of peripheral venous catheters (PVCs), typically leading to localized discomfort, redness, and cord-like veins at the insertion site. Research has suggested that Glycerine Magnesium Sulphate could be effective in reducing the severity of superficial thrombophlebitis. Previous studies have compared glycerine magnesium sulphate with other treatments, such as heparin ointment, in managing thrombophlebitis, demonstrating significant improvement in symptoms with glycerine magnesium sulphate application. This study was conducted to assess the effectiveness of glycerine magnesium sulphate application in reducing superficial thrombophlebitis in patients receiving IV infusions.

Methodology

Study Design

This study followed a pre-experimental one group pre-test-post-test design, focusing on newly cannulated patients with IV-induced superficial thrombophlebitis using VIP scale (Visual Infusion Phlebitis scale) to evaluate pre-test and

post-test levels of superficial thrombophlebitis Figure 1. A total of 50 subjects were selected through convenient sampling from Shri J.G. Co-operative Hospital Society Ltd. and Taluka General Hospital Hukkeri, Belagavi District. The study was conducted for a period of 1 month, from May 27, 2024, to June 27, 2024.

Visual Infusion Phlebitis Score	0	No signs of phlebitis OBSERVE CANNULA
IV site appears healthy		
One of the following is evident: • Slight pain at IV site • Redness near IV site	1	Possible first sign of phlebitis OBSERVE CANNULA
Two of the following are evident: • Pain • Erythema • Swelling	2	Early stage of phlebitis RESITE THE CANNULA
All of the following signs are evident: • Pain along the path of the cannula • Erythema • Induration	3	Medium stage of phlebitis RESITE THE CANNULA CONSIDER TREATMENT
All of the following signs evident and extensive: • Pain along the path of the cannula • Erythema • Induration • Palpable venous cord	4	Advanced stage of phlebitis or start of thrombophlebitis RESITE THE CANNULA CONSIDER TREATMENT
All of the following signs are evident and extensive: • Pain along the path of the cannula • Erythema • Induration • Palpable venous cord • Pyrexia	5	Advanced stage of thrombophlebitis INITIATE TREATMENT RESITE THE CANNULA

Fig 1: Modified visual infusion phlebitis scale

Data Collection

The Visual Infusion Phlebitis (VIP) Scale was employed to assess thrombophlebitis levels before and after glycerine magnesium sulphate application. A paired t-test was used to compare the pre-test and post-test VIP scores, while a chi-square test was employed to analyse associations between demographic variables and pre-test scores. The VIP scale is widely recognized for its accuracy in assessing phlebitis and has been validated in various clinical settings.

Ethical Considerations

The study was conducted following the ethical principles outlined by the Indian Council of Medical Research (ICMR), ensuring patient consent and confidentiality. Similar ethical frameworks have been applied in studies assessing interventions for IV-induced complications, ensuring compliance with regulatory standards.

Results

The data was arranged, presented in a table and assessed in accordance with the study's objectives in the sections below: Section 1: Given below is the description of the demographic variables of the subjects with superficial thrombophlebitis who received intravenous infusion. The below Table 1 depicts the description:

With respect to *Age in years* from the total 50 subjects, 2 (4%) were between 16-25 yrs of age, 11 (22%) were between 26-35 yrs of age, 19 (38%) were between the age group of 36-45 yrs, 13 (26%) subjects were of 46-55 yrs of age, 05 (10%) were between the age of 56-65 yrs and above 65 yrs there were none.

With regards to *Gender*, Among 50 subjects, 31 (62%) were males, 19 (38%) were females and in others none.

While considering the *Habits*, 06 (12%) had habit of smoking cigarettes, 10 (20%) of were addicted to alcohol consumption, 02 (04%) were addicted to tobacco chewing and 32 (64%) subjects had no indulgence in any unhealthy habits.

With regard to *Ambulation of subjects*, 13 (26%) were partially mobilized, 34 (68%) were in complete mobilization and 03 (06%) were immobilized, sometimes because of their disease condition.

With visualization of the *Veins cannulated*, 10 (20%) subjects had their Basilic vein cannulated, 13 (26%) had their Cephalic vein cannulated, 04 (08%) of them had their Median vein forearm cannulated and the remaining 23 (46%) had Dorsal metacarpal vein inserted with the IV.

While considering the *Size of the cannula*, none of the 50 subjects had inserted 16 G & 24 G cannula, 07 (14%) had been inserted with 18 G cannula, 23 (46%) had inserted with 20 G cannula, 20 (40%) had inserted with 22 G cannula respectively.

With respect to the *Duration of the cannula In-situ*, 01 (02%) had it for < 2 days, 39 (78%) had the cannula In-situ for 2-3 days, 09 (18%) had it for 4-5 days and 01 (2%) subjects had In-situ for > 5 days.

By observing the *Site of the cannulation*, we can tell that, 11 (22%) were cannulated on the Right hand, 14 (28%) were cannulated on Left hand, 12 (24%) were cannulated on the Right forearm, 13 (26%) were cannulated on the Left forearm and no one was cannulated on both lower limbs.

By Looking at who did the IV *Cannulation*, we can say 42

(84%) were Registered Nurse, 02 (04%) were student nurse, 02 (04%) were Doctors and 04 (08%) were Interns who did IV *cannulation* on the admitted subjects *priorly*.

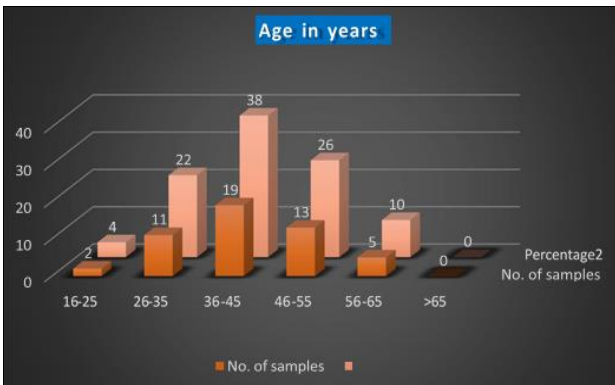
Lastly by noting the *H/o chronic vascular disease*, 05 (10%) of the subjects had some history of chronic vascular disease and the remaining 45 (90%) didn't provide any such significant histories.

Table 1: Demographic variables of the subjects with superficial thrombophlebitis who received intravenous infusion, N=50

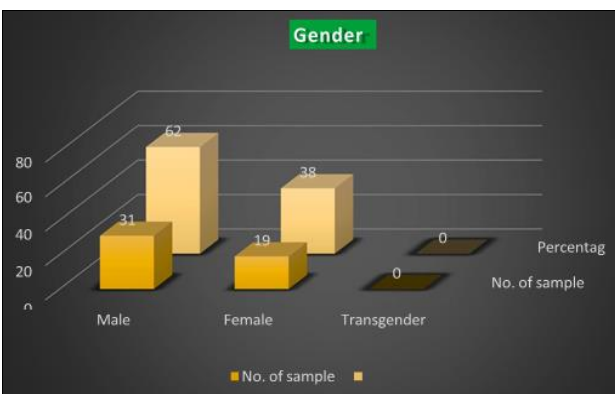
Demographic Variables	No of Samples	Percentage (%)
Age (in years)		
16-25	2	4%
26-35	11	22%
36-45	19	38%
46-55	13	26%
56-65	5	10%
>65	0	0%
Gender		
Male	31	62%
Female	19	38%
Transgender	0	0%
Habits		
Cigarette smoking	6	12%
Alcohol	10	20%
Tobacco chewing	2	4%
None	32	64%
Ambulation		
Partially mobilized	13	26%
Mobilized	34	68%
Immobilized	3	6%
Vein cannulated		
Basilic vein	10	20%
Cephalic vein	13	26%
Median vein forearm	4	8%
Dorsal Metacarpal vein	23	46%
Size of the cannula		
16 G	0	0%
18 G	7	14%
20 G	23	46%
22 G	20	40%
24 G	0	0%
Duration of the cannula in situ		
<2 days	1	2%
2-3 days	39	78%
4-5 days	9	18%
>5 days	1	2%
Site of the cannulation		
Right hand	11	22%
Left hand	14	28%
Right forearm	12	24%
Left forearm	13	26%
Right leg	0	0%
Left leg	0	0%
IV cannulation done by		
Registered nurse	42	84%
Student nurse	2	4%
Doctor	2	4%
Intern	4	8%
History of chronic vascular disease		
Yes	5	10%
No	45	90%

Following are the multiple graphs illustrated to show various demographic variables in superficial thrombo-

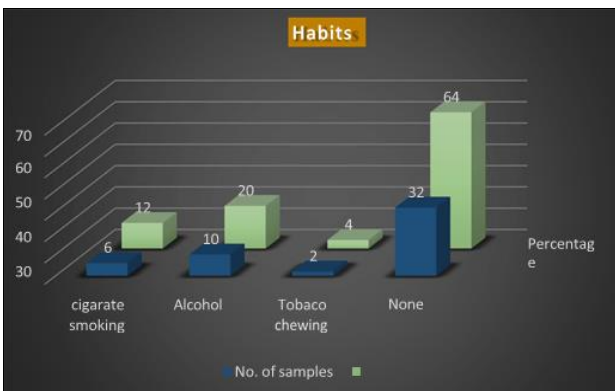
phlebitis according to the tables and descriptions mentioned above and graphs shown in Figures below respectively.



Graph 1: (Age in years)



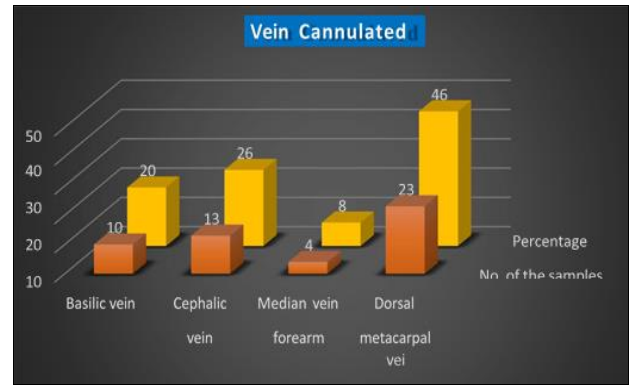
Graph 2: (Gender)



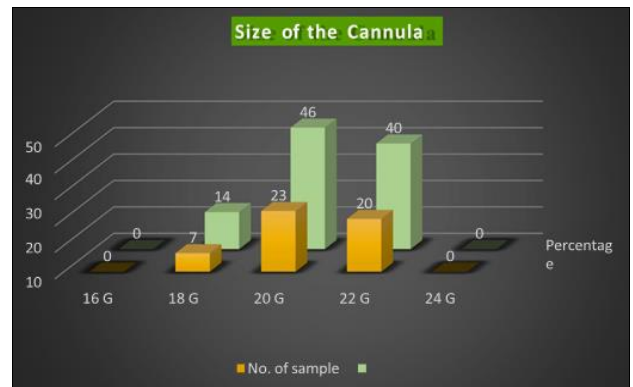
Graph 3: (Habits)



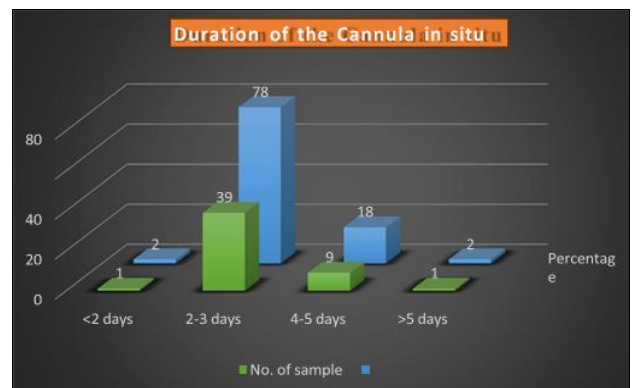
Graph 4: (Ambulation)



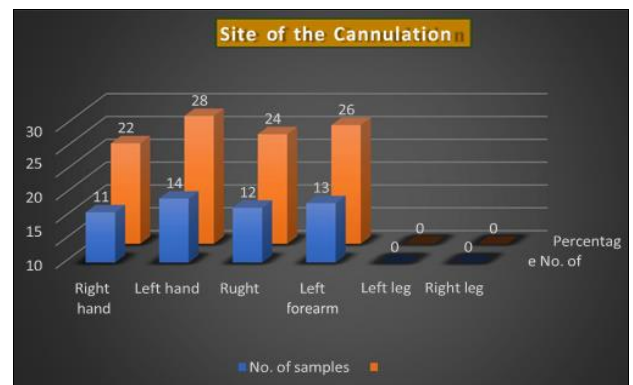
Graph 5: (Vein cannulated)



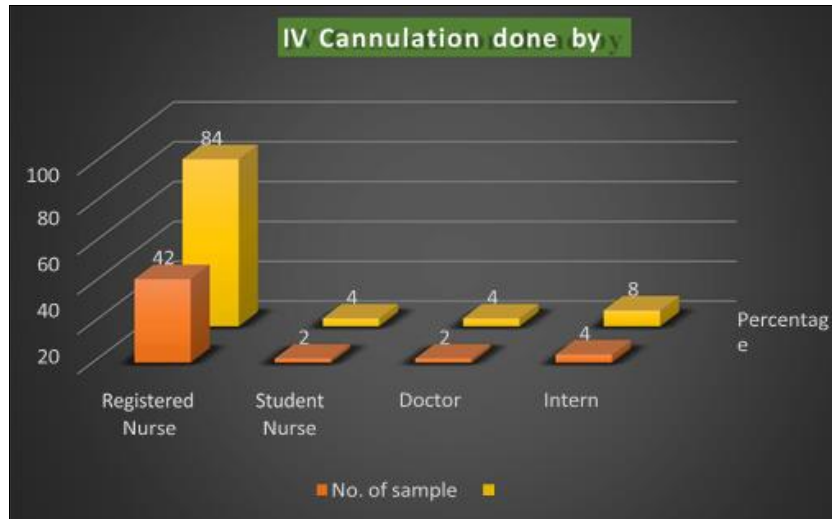
Graph 6: (Size of the cannula)



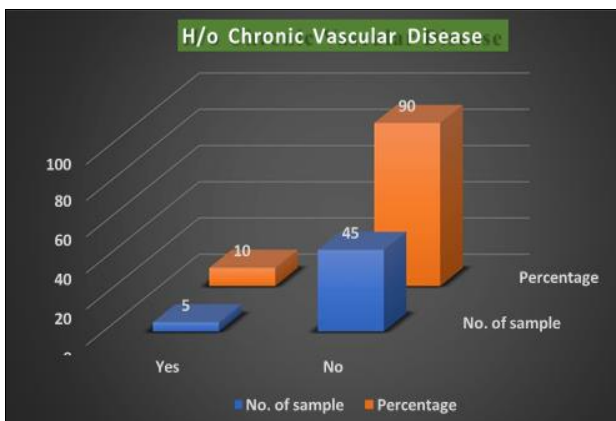
Graph 7: (Duration of cannula In-situ)



Graph 8: (Size of the cannulation)



Graph 9: (IV cannulation done by)



Graph 10: (H/o chronic vascular disease)

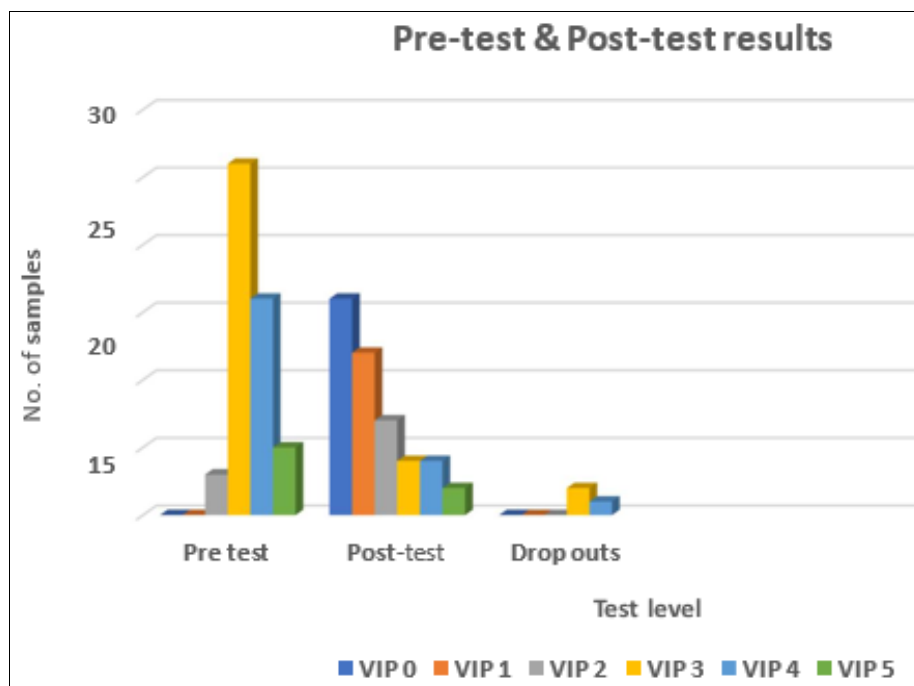
Section 2: Next is to assess the Pre-test and post-test level

of superficial thrombophlebitis of subjects who received intravenous infusion.

In the below given Table 2 & Graph 11, It shows that, 0 (0%) subjects had VIP score-0 and 1, 3 (6%) subjects were showing VIP score-2, 26 (42%) were showing VIP score-3, 16 (32%) were showing VIP score-4 and only 5 (10%) of them showed VIP score-5 level respectively.

Later, in the Pre-test VIP scores level, the data showed a drastic change in the post-test levels in the subjects like 16 (32%) subject's VIP score reduced to score-0, 12 (24%) subject's VIP score reduced to score-1, 7 (14%) subject's VIP score reduced to score-2, 4 (12%) of them had remained on VIP score-3, 4 (10%) VIP scores remained at score-4 and 2 (4%) subject's VIP score were at score-5.

Unfortunately we saw an attrition in the study showing 2 (4%) at the VIP score level of 3 and 1 (2%) at the level of VIP score-4 showing drop outs from the study.



Graph 11: Pre-post-test results

Table 2: Pre-test and post-test level of superficial thrombophlebitis of subjects who received intravenous infusion

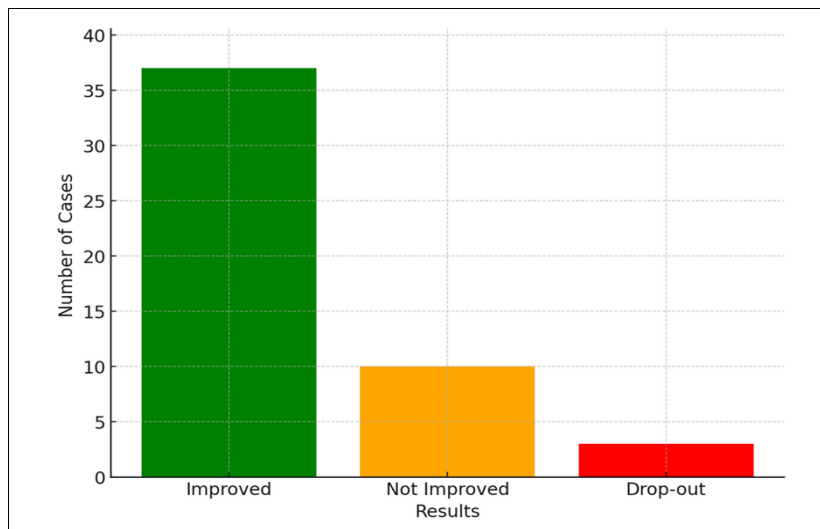
Level of Superficial thrombophlebitis	Pre-test		Post-test			
	No of samples	%	No. of samples	%	No of samples drop-out	%
Score-0	0	0%	16	32%	0	0%
Score-1	0	0%	12	24%	0	0%
Score-2	3	6%	7	14%	0	0%
Score-3	26	42%	4	12%	2	4%
Score-4	16	32%	4	10%	1	2%
Score-5	5	10%	2	4%	0	0%

Section 3: To assess the effectiveness of the Glycerine Magnesium Sulphate application for the reduction of superficial thrombophlebitis among the subjects who received intravenous infusion which is shown in Table 3 below.

Table 3: The effectiveness of the Glycerine Magnesium Sulphate application for the reduction of superficial thrombophlebitis among the subjects who received intravenous infusion

Results	No. of cases	Percentage (%)
Improved	37	74%
Not improved	10	20%
Drop-out	03	06%
Total	50	100%

With the given observations and results above in the Table: 3, It shows that 37 (74%) of subjects were showing “Improved” results after the study, while 10 (20%) did “Not Improved” and 3 (6%) of the subjects were shown as “Drop outs” from the study showing an attrition.



Graph 12: (Results)

Descriptive Statistics

To assess the effectiveness of the Glycerine Magnesium Sulphate application for reducing superficial thrombophlebitis among patients receiving intravenous infusion, we compare the pre-test and post-test VIP scores using the descriptive statistics. This involves calculating and plotting on box plots to understand the distribution and central tendency of the data.

Now by calculating the basic descriptive statistics for both pre-test and post-test VIP scores and further calculations and analyzing the results to draw conclusions.

Statistic	Pre-test VIP Scores	Post-test VIP Scores
Sample size (N)	50	50
Mean	3.46	1.52
Standard Deviation	0.76	1.50
Minimum	2.00	0.00
25th Percentile	3.00	0.00

Analysis of the data

Descriptive statistics indicated that mean scores for VIP decreased significantly from pretest to post test. The pre-test mean was 3.46 and the post-test mean was 1.52. In addition, the standard deviation increased from 0.76 in the pre-test to 1.50 in the post-test, indicating a greater difference in the test scores.

Visualization graphical representation of data

To further illustrate the data, a box plot comparing the before and after VIP scores is shown below:

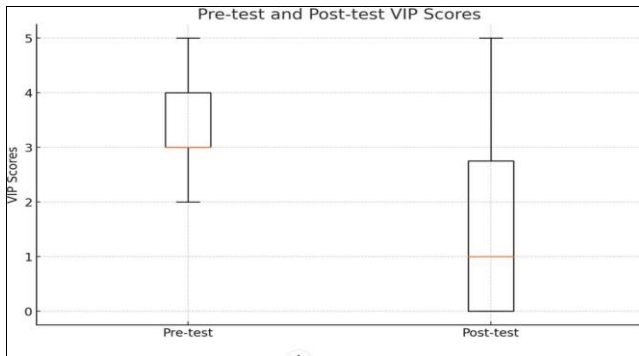
Interpretation

Here are the key observations:

- **Pre-test Scores:** The distribution is centered on a median of 3, with the interquartile range (IQR) between 3 and 4. The scores range from 2 to 5, indicating a

relatively tight distribution.

- **Post-test Scores:** The distribution is centered on a median of 1, with the IQR between 0 and 2.75. The scores range from 0 to 5, showing a wider distribution compared to the pre test scores.



Graph 13: (Pre-test post-test box plot)

Conclusion

The descriptive statistics and box plot indicate a significant decrease in the VIP scores from before to after test results. The mean VIP score decreased from 3.46 to 1.52, and the variability in scores increased, as evidenced by the larger standard deviation in the post-test scores. This suggests that the Glycerine Magnesium Sulphate application can be effective in reducing superficial thrombophlebitis in subjects.

For detailed analysis, other statistical tests, such as a paired t-test, are performed to determine the statistical significance of the observed differences.

Paired T-Test

Steps are as follows

1) Stating the Hypothesis

- Null Hypothesis (H0): There is no significant difference between pre-test and post-test VIP scores.
- Alternative Hypothesis (H1): There is a significant difference between pre-test and post-test VIP scores.

Calculate the Differences

- To calculate the difference (*di*) between each pair of pre-test (*xi*) and post-test (*yi*) scores.

Calculating the Mean and SD of the Differences:

- Mean difference ($d^- = 1.94$)
- Standard deviation of the differences ($Sd = 1.41$)

Calculating the t-Statistic

$$t = \frac{d}{Sd / \sqrt{n}} = \frac{1.94}{1.41 / \sqrt{50}} = 9.76$$

Calculating the Degrees of Freedom (df):

1. $df = n - 1 = 50 - 1 = 49$

Determine the Critical Value and p-Value:

- For a 95% level of confidence, the critical value (two-tailed) for $df = 49$ is approximately 2.0096.

- The *p*-value calculated is 4.50×10^{-13}

Section 4: Comparison of pre-test and post-test mean score of thrombophlebitis among patients received intravenous infusion.

In the below given Table: 4, on the basis of descriptive statistics it shows that Pre-test mean is 3.46, Standard deviation is 0.76 and post-test mean is 1.52, standard deviation is 1.50 and their mean difference is -1.940 with paired t-test value of -8.158.

Table 4: Statistical Interpretation

Group	Max VIP Score	Mean	S.D	Mean Difference	Paired T-Test Value
Pre-Test	05	3.46	0.76	-1.940	-8.158
Post-Test	00	1.52	1.50		

Interpretation

- **T-Statistic:** 9.76, is bigger than the critical value of 2.0096.
- **P-Value:** 4.50×10^{-13} , is lesser than the level of significance of 0.05.

Since the t-statistic exceeds the critical value and the *p*-value is much smaller than 0.05, we reject the null hypothesis. This indicates that the observed difference between pre-test and post-test VIP scores is statistically significant.

Conclusion

The paired t-test results show a major reduction in VIP scores from pre to post test. This suggests that the Glycerine Magnesium Sulphate application is effective in alleviating superficial thrombophlebitis among patients receiving intravenous infusion. The descriptive statistics support this conclusion, showing a clear reduction in the mean and median VIP scores, despite the increased variability in post-test scores.

Section 5: To show the association between the pre-test level VIP scores of superficial thrombophlebitis subjects who received intravenous infusion with their selected demographic variables in the study group.

Here chi-square test of independence is performed to determine the association between the pre-test levels of superficial thrombophlebitis subjects with various demographic variables.

After performing the Chi-square test on *MS-Excel data analysis* for each categorical variables like Gender, etc & continuous variable i.e. Age (years) against the Pre-test VIP score, we get the following analysis and results. The following steps are:

1) State the Hypothesis

- Null Hypothesis (H0): There is no significant association between the demographic variables and pre-test VIP scores.
- Alternate Hypothesis (H1): There is a significant association between the demographic variables and pre-test VIP scores.

After calculating the Chi-square statistic with the formula

Degrees of Freedom $df = (r-1) \times (c-1)$

We compare it to the critical value from the Chi-square distribution table with ($df = 25$) at a 0.05 significance level. We reject the null hypothesis, if the Chi-square statistic exceeds the critical value, indicating a significant association between age groups and pre-test VIP scores. If it

does not exceed the critical value, we fail to reject the null hypothesis.

The chi-square test results for the association of pre-test levels of superficial thrombophlebitis with selected demographic and clinical variables are summarized below:

$N = 50$ p -value > 0.05 Confidence level-95%

Table 5: Chi-square test results for the association of pre-test levels of superficial thrombophlebitis with selected demographic and clinical variables

S. No	Demographic variables	Chi-square statistic (x2)	P-Value	Degrees of freedom (df)	Significance
1	Age group	21.51	0.368	20	0.05
2	Gender	5.19	0.393	5	0.05
3	Habits	14.11	0.517	15	0.05
4	Ambulation	9.30	0.504	10	0.05
5	Vein cannulated	14.49	0.489	15	0.05
6	Size of cannula	7.40	0.687	10	0.05
7	Duration of cannula In-situ	28.99	0.264	25	0.05
8	Site of cannulation	19.75	0.182	15	0.05
9	Cannulation done by	10.40	0.794	15	0.05
10	H/o chronic vascular disease	5.82	0.324	5	0.05

4.8 Interpretation

According to the analysis and data shown in Table 5, None of the population characteristics studied had a great significance relationship with the pre-test level of superficial thrombophlebitis (all p -values > 0.05). This means that, based on this dataset, there is no evidence to suggest that these factors are associated with the pre-test level of superficial thrombophlebitis significantly. Since (all p -values > 0.05), we fail to reject the null hypothesis (means we accept the Null hypothesis), indicating that there is no significant association between the demographic variables and pre-test VIP scores in our research study “To assess the effectiveness of Glycerine Magnesium Sulphate application on superficial thrombophlebitis among patients receiving intravenous infusion at selected hospitals of Belagavi district”.

Discussion

The demographic analysis revealed that the majority of participants were between 36-45 years old (38%), with a significant portion being male (62%). Habits such as smoking and alcohol consumption were present in a minority of participants, with 12% and 20% respectively. Most patients (68%) were completely mobilized, and the dorsal metacarpal vein was the most commonly cannulated site (46%). The most frequently used cannula size was 20G (46%), and the typical duration of cannulation was 2-3 days (78%) in the study.

A study conducted by Alwin T, Varghese and Moly KT provided support for the current investigation. Of the patients in Group A, 13 (43.4%) are between the ages of 33 and 46, and of Group B, 14 (46.7%) are between the ages of 47 and 60. In both groups, the other demographic factors were roughly equal. Two punctures were used to introduce the IV cannula in Group A, (18%) and Group B (83.4%). The cannula size that was utilized was 22G for the most part, with 20 (66.7%) in Group A and 22 (73.3%) in Group B. In Group B (175.6%) and Group A, (12.5%), the metacarpal vein was the most often used vein for cannula

insertion, respectively.

Priyanka and Navreet Kaur Saini’s study provided support for this main study. Demographic variable sample frequency and experimental group percentage distribution are shown above. 10 (33.3%) experimental samples were 42-51. 8 (26.7%) were 32-41. 7 (23.3%) were 21-31. 15 (50%) experimental samples were gender-balanced. 43.3% of experimental group 13 samples are tobacco-free. Alcoholics: 8. 15 (50.0%) had normal BMIs. 6 (20%) were obese. 4 (13.3%). The experimental group had 10 COPD patients (33.3%). 7 (23.3%) samples had renal failure. 14 (46.7%) were chronic, 16 (53.3%) acute. The experimental group had 15 mobile (50.0%) and 14 partially mobile (46.7%) samples. The experimental group had 22 (73.3%) cephalic vein and 6 (20.0%) median vein cannulated samples. 17 (56.7%) Post-Basic (N) nurses and 7 (23.3%) GNM nurses cannulated experimental samples. 12 samples (40.0%) were cannulated with 22 G needles, 11 (36.7%) with 18 G. 83.33% of experimental group 25 samples had cannulas for over 3 days. 5 (16.7%) had cannula 1-3 days. 12 (40.0%) experimental group samples received anticoagulants. Nine had inotropes (30%). 24 (80.0%) of the experimental group were vascular disease-free. 18 (60.0%) experimental group infusion samples received saline and 6 (20%) heparin.

The pre-test levels of superficial thrombophlebitis, assessed using the VIP scale, showed that the majority of subjects had moderate to severe superficial thrombophlebitis (VIP scores of 3 and 4). After the application of Glycerine Magnesium Sulphate, an evident curtail in VIP scores was observed in the post-test. Specifically, 32% of subjects had a VIP score of 0 post-intervention, and 24% had a VIP score of 1. This reduction indicates marked improvement and the effectiveness of the Glycerine $MgSO_4$ application in mitigating the symptoms of superficial thrombophlebitis. The reduction in VIP scores from pre-test to post-test suggests that the intervention was effective in alleviating the condition. The mean VIP score decreased from 3.46 in the pre-test to 1.52 in the post-test, and the standard deviation

increased from 0.76 to 1.50, indicating greater variability in the post-test scores. These results are consistent with the hypothesis that Glycerine Magnesium Sulphate application can significantly reduce the severity of superficial thrombophlebitis.

The current study was supported by Kamlesh Sharma and Kuldeep Patidar's in their studies conducted, most of the participants in the first study had a mild form of thrombophlebitis, 5 people (25%) were in the early stages, 3 people (15%) in the first period none of them had symptoms of phlebitis, first possible sign of thrombophlebitis. High level or high level of thrombophlebitis. Similarly, in the post-test of superficial thrombophlebitis, 10 (50%) had early stages, 8 (40%) had possible signs of phlebitis, 2 (10%) had intermediate stages and others had no signs of phlebitis. It can be the first symptom of phlebitis, the early stage of phlebitis, or the advanced stage of thrombophlebitis respectively.

Descriptive statistics showed a major decrease in the VIP scores post-application of Glycerine Magnesium Sulphate. The pre-test mean VIP score was 3.46, and the post-test mean was 1.52, with a mean difference of -1.94. The paired t-test value of -8.158 and a p-value of 4.50×10^{-13} indicated a statistically significant reduction in superficial thrombophlebitis severity post-intervention.

These findings are supported by the descriptive and inferential statistical analyses, which both show a much better quality of life of patients. The reduction in mean VIP scores and the significant t-test results provide strong evidence that Glycerine Magnesium Sulphate is an effective treatment for superficial thrombophlebitis in the studied population.

Tamilselvi, Dr. Arthi A, provided evidence to support the study's conclusions by due to a substantial difference in the effects of applying cold packs and magnesium sulphate with glycerine on days two and three. By the conclusion of the fourth day, both groups had significantly reduced their phlebitis levels, and there was little difference in their visual infusion phlebitis scores. The experimental group I's mean and standard deviation are 6.42 ± 2.54 , which is lower than the experimental group II's mean and standard deviation of 8.08 ± 2.94 . This demonstrated that the experimental group I's application of magnesium sulphate and glycerine reduced the degree of phlebitis more quickly than the experimental group II's application of cold packs at the level of $p < 0.05$.

This study found no significant correlations between pre-test VIP scores and the selected variables, including age, gender, habits, ambulation, site of cannulation, cannula size, duration of cannulation, and history of chronic vascular disease. All p-values were greater than 0.05, suggesting that these variables did not significantly influence the treatment outcome.

This lack of association implies that the effectiveness of Glycerine Magnesium Sulphate is consistent across different demographic groups. It suggests that the intervention can be broadly applied without significant concern for variability in demographic factors affecting the treatment outcome.

This section of the study was supported by research conducted by Mayavati B Tupere, Amol C Temker, and colleagues provided support for this section of the study. The chi-square test was utilized to establish the connection between phlebitis prevention and particular baseline

performance measures. The findings indicate a strong correlation between phlebitis prevention and family type (7.13), income (4.67), cancer type (4.28), and systemic illness (6.62). However, there is no correlation found between specific preventive measures for phlebitis and gender, marital status, employment, food, religion, cancer history, personal habits, length of cancer, type of cancer, stages of cancer, intent of treatment, chemotherapy cycle, chemotherapy medication, diagnosis date, cannula site, and cannula size.

Conclusion

This study demonstrates that Glycerine Magnesium Sulphate is a valuable intervention for reducing superficial thrombophlebitis severity among patients receiving IV infusions. The consistent reduction in VIP scores supports the use of glycerine magnesium sulphate in clinical practice. Further research is needed to explore the broader applicability of this treatment and its long-term effects.

Limitations

The study was limited by its sample size and short duration. Future research could expand on these findings by incorporating a larger, more diverse patient population and examining long-term outcomes. Previous studies have also recommended exploring the combined use of glycerine magnesium sulphate with other treatments like heparinoid ointments to enhance therapeutic effects.

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