Original Article

The Effects of Arnigol Cream on Pain Associated with Arteriovenous Fistula Puncture in Patients Receiving Hemodialysis: A Randomized Double-Blind Clinical Trial study

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Abstract

Background: In each hemodialysis session, hemodialysis patients undergo two vascular punctures with large-diameter needles, which are associated with great pain. The reduction of puncture pain helps these patients accept hemodialysis and enhances their quality of life. **Objective:** The present study was conducted to assess the effects of Arnigol cream on the pain associated with arteriovenous fistula puncture. **Methods:** As a double-blind single-group randomized clinical trial, the present study was made on 71 hemodialysis patients. Each patient received an arterial and a venous fistula puncture. One puncture site was randomly allocated to the experiment and the other one to the placebo. Before needle insertion, the experiment and the placebo sites were treated for 10 min with 5 ml of Arnigol cream or Vitamin A and D ointment, respectively. After needle insertion, pain intensity at puncture sites was assessed using a visual analog scale. The data were analyzed using the paired-sample *t*-test. **Results:** Participants were 71 hemodialysis patients, 49.3% were female. The mean of participants' age was 56.86 ± 15.10 years, with a range of 22–82. The length of receiving hemodialysis ranged from 4 to 96 months with a mean of 40.36 ± 22.79. Diabetes mellitus was the major cause of renal failure among participants (56.3%). The intensity of pain at the experiment site was significantly lower than the placebo site (2.83 ± 1.60 vs. 3.46 ± 1.57; $P = 0.006$). **Conclusions:** This study showed the effectiveness of Arnigol cream in reducing the pain associated with arteriovenous fistula puncture among patients receiving hemodialysis. Thus, nurses are recommended to use this simple, safe, and inexpensive modality to reduce fistula puncture pain.

Keywords: *Arnigol, Hemodialysis, Fistula, Pain management, Puncture pain*

Introduction

Chronic renal failure is a multifactorial physiopathologic problem which finally results in the reduction of the number and the function of nephrons.[1] Patients with chronic renal failure need treatments such as kidney transplantation, hemodialysis, or peritoneal dialysis.[2,3] The most common treatment for the disease is hemodialysis.[4] A prerequisite to regular long-term hemodialysis is permanent vascular access,[5] which can be established through central venous catheter, arteriovenous graft, or arteriovenous fistula.[6] The most preferred access route is arteriovenous fistula.[5]

Hemodialysis through arteriovenous fistula necessitates one arterial and one venous puncture using two large-diameter needles. Such punctures usually cause severe pain and discomfort for patients.[7] Patients who receive regular hemodialysis are frequently exposed to the pain associated with around 300 vascular punctures

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each year.[8] Such repetitive exposure to pain causes anxiety and depression, reduces the quality of life,[7,9] and interferes with effective role performance.[10]

Pain is an unpleasant emotional and sensory experience due to an actual or potential tissue injury. It is among the most important nursing diagnoses, and its management is among the most important nursing responsibilities.[11] Effective pain management improves patient satisfaction with nursing care,[12] encourages patients to actively engage in the process of treatment,[13] helps them readily accept hemodialysis, and enhances their quality of life.[7] Thus, effective plans are needed to manage vascular puncture pain among hemodialysis patients.

There are different pharmacological and nonpharmacological pain management strategies including topical heat or cold therapy,[3] rhythmic breathing,[14] music therapy, distraction,[15] transcutaneous electrical nerve stimulation,[16] aromatherapy,[17] acupressure, massage, touch,[15,18] awareness raising, active listening,[19] and topical treatments such as Arnica topical cream,[20] diclofenac sodium topical gel,[21] EMLA cream,[22] and lidocaine cream.[7]

Arnigol is an herbal cream (produced by Goldaru Co., Isfahan, Iran), each 100 mg of which contains 5 mg of *Arnica montana* extract. *A. montana* contains sesquiterpene lactones, polyynes, flavonoids, hydroxycumarines, and caffeic acid derivatives and has analgesic, anti-inflammatory, and antiseptic effects.[23] Thus, it is effective in managing skin wounds, particularly those with inflammation.[24] It has been reported to have no adverse effects. Clinical studies reported that Arnica-containing gels were effective in reducing muscular pain and improving venous tone.[25] However, it is unknown whether Arnigol cream is effective in reducing acute pain associated with arteriovenous fistula puncture.

Previous research studies introduced some pain-reducing methods. However, these methods are not routinely used by Iranian hemodialysis nurses due to their expensiveness, adverse effects, or difficulty of use. Despite the inexpensiveness and the safety of Arnigol cream, there are limited data about its effects on the pain associated with arteriovenous fistula puncture.

Objectives

The present study was conducted to assess the effects of Arnigol cream on the pain associated with arteriovenous fistula puncture.

Methods

Design and participants

This was a double-blind single-group randomized clinical trial. Each patient in the study was both the experimental and the placebo case. As pain is a subjective phenomenon, considering each patient as both the experimental and the placebo case could minimize the effects of intervening factors such as gender and age. Accordingly, one fistula puncture (either arterial or venous) was randomly regarded as the experiment and the other as the placebo.

This study was done from February to May 2016, in the hemodialysis units of Ali Ibn-e- Abi Talib (PBUH) Hospital, Rafsanjan, Iran, and Shafa hospital, Kerman, Iran. Population of the study consisted of all hemodialysis patients who had an arteriovenous fistula in their hand and received hemodialysis in the study setting. Patients were included if they were receiving hemodialysis through arteriovenous fistula at least two times a week for 3 consecutive months, were fully conscious, aged 18 or more, did not suffer from neuropathies or peripheral vascular problems, had no sign of inflammation at fistula site, received no topical analgesic at fistula site before the study intervention, and had no known allergy to Arnigol cream. Exclusion criteria were unsuccessful puncture at the first attempt and participants' voluntary withdrawal from the study. Primarily, selected patients were tested for any allergy to Arnigol cream through applying 1 ml of the cream to a 5 cm surface area on their arms.

Sample size was calculated based on the results of an earlier study which reported two pain mean scores of 8.09 ± 1.92 and 10.11 ± 4.85.[3] Accordingly, with a type I error of 0.05 and a power of 0.90, the sample size calculation formula showed that 71 patients were needed for the study [Figure 1].

Instruments and measurements

Two instruments were used to collect data. The first instrument was a demographic and hemodialysis-related questionnaire which comprised of items such as age, gender, marital and educational status, cigarette smoking, drug abuse, underlying cause of renal failure, and history of receiving hemodialysis. The second instrument was a visual analog scale (VAS) for puncture pain assessment. VAS was a 10 cm ruler on which 0 and 10 represented "no pain" and "the severest experienced pain," respectively.

$$n = \frac{(s_1^2 + s_2^2)(z_{1-\frac{\alpha}{2}} + z_{1-\beta})^2}{(\bar{x}_1 - \bar{x}_2)^2}$$

$$= \frac{(1.96+1.28)^2\,(1.92^2 + 4.85^2)}{(2.02)^2} = 71$$

Figure 1: Sample size calculation

Procedure

Arterial and venous punctures were performed on one hand of each patient with a 5 min interval. One site was randomly allocated to the experiment and the other to the placebo. Accordingly, for the first patient, arterial puncture was allocated to the experiment, and venous puncture was allocated to the placebo. For the second patient, this allocation was reversed. At the experiment site, 5 ml of Arnigol cream was applied 10 min before the puncture. The placebo site was similarly treated with 5 ml of Vitamin A and D mixture ointment. After 10 min of ointment application, the puncture sites were cleaned using antiseptic agents and then punctures were made. All participants were blind to the interventions, i.e., to the type of the cream used for them. The distance between the site of applying Arnigol cream and Vitamin A and D ointment was about 10 cm to prevent the effects of Arnigol cream on the placebo site. Moreover, the time interval between arterial and venous punctures was 5 min to remove the effects of the first puncture on the outcomes of the second. All punctures were performed by an experienced hemodialysis nurse, and then needles were fixated using hypoallergenic adhesive tape. Immediately after each puncture, the level of patient's puncture pain was assessed and documented by another nurse using VAS. All punctures were performed similarly using 16-gauge needles and with a needle insertion degree of 30°–45°. Beside participants, the nurse who did pain assessments was also blind to the interventions.

Data analysis

The data were analyzed using the SPSS software version 13 (SPSS INC., Chicago, IL, USA). The distributions of the numerical variables were assessed through the Kolmogorov–Smirnov test, and all were normally distributed. Then, pain intensity comparisons were done using the paired sample *t*-test at a significance level of 0.05.

Ethical considerations

The ethical approval for this study was provided by the Ethics Committee of Rafsanjan University of Medical Sciences, Rafsanjan, Iran, with the code of IR.RUMS.REC.1394.166. In addition, the study was registered in the Iranian Registry of Clinical Trials with the code of IRCT2016112615965N8. The aim and the methods of the study were described to all participants, and their written informed consents were secured. They were ensured that participation in the study was voluntary. We also adhered to the ethical principles of medical research reported in the Declaration of Helsinki.

Results

Participants were 71 hemodialysis patients [Figure 2], 35 of them (49.3%) were female. The mean of participants' age was 56.86 ± 15.10, with a range of 22–82. The length of receiving hemodialysis ranged from 4 to 96 months, with a mean of 40.36 ± 22.79. Diabetes mellitus was the major cause of renal failure [56.3%; Table 1].

The results of the paired-sample *t*-test illustrated that pain intensity at the experiment site was significantly lower than the placebo site (2.83 ± 1.60 vs. 3.46 ± 1.57; $P = 0.006$). Comparison of pain intensity with respect to the history of diabetes mellitus indicated that Arnigol cream was more effective in reducing puncture pain among nondiabetic patients compared with diabetic ones (2.61 ± 1.35 vs. 3.48 ± 1.65; $P = 0.008$). Moreover, patients who had received hemodialysis for more than 48 months experienced slighter pain compared with those who had a shorter history of hemodialysis [$P = 0.005$; Table 2].

Discussion

The study was conducted on a single group of patients to remove the probable effects of intervening factors (such as age and gender). The findings indicated that the intensity of puncture pain at the Arnigol-treated puncture site was significantly lower than the site treated with Vitamin A and D ointment. Similarly, Jeffery and Belcher found that Arnica cream and tablet were more effective than a placebo in reducing pain after carpal tunnel release surgery.[20] The similarity between our findings and the findings reported by Jeffery and Belcher may be due to the similarity of the active ingredients of Arnica and Arnigol creams, i.e., sesquiterpenes

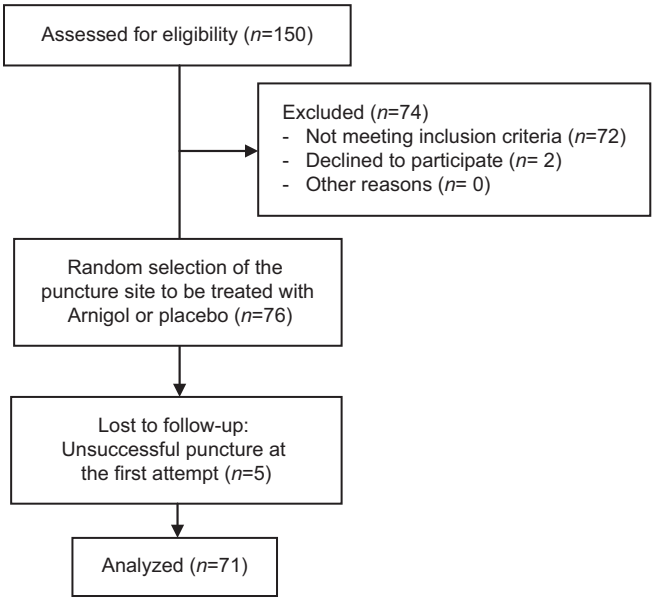

Figure 2: The flow of participants during the study

Table 1: Participant's demographic characteristics

Variable	Frequency (%)
Gender	
Female	35 (49.3)
Male	36 (50.7)
Age groups (years)	
≥40	11 (15.5)
41-60	27 (38.0)
>60	33 (46.5)
Marital status	
Single	6 (8.5)
Married	65 (91.5)
Drug abuse	
Yes	6 (8.5)
No	65 (91.5)
Cause of renal failure	
Diabetes mellitus	40 (56.3)
Other	31 (43.7)
Educational status	
Illiterate	24 (33.8)
Elementary school	24 (33.8)
High-school diploma and higher	23 (32.4)
Length of hemodialysis (months)	
≤12	9 (12.7)
13-48	38 (53.5)
>48	24 (33.8)

Table 2: Comparing pain intensity with respect to the cause of renal failure and the duration of receiving hemodialysis

Variable	Pain intensity[a]		*P*[b]
	Arnigol cream	Placebo	
Overall pain intensity	2.83 ± 1.60	3.46 ± 1.57	0.006
Cause of renal failure			
Diabetes mellitus	3.00 ± 1.77	3.45 ± 1.52	0.170
Other	2.61 ± 1.35	3.48 ± 1.65	0.008
Length of hemodialysis (months)			
≤12	3.11 ± 2.31	4.11 ± 2.08	0.382
13-48	2.95 ± 1.62	3.34 ± 1.47	0.183
>48	2.54 ± 1.25	3.42 ± 1.50	0.005

[a]Data are presented as mean±SD, [b]Paired-sample *t*-test.
SD: Standard deviation

lactones. Goedemans *et al*. also found that both Arnica and Hirudoid creams were effective in significantly reducing bruising and pain induced by infiltration at hemodialysis cannulation site.[21] Another study also reported that Arnica gel was as effective as ibuprofen gel in alleviating hand osteoarthritis.[26] In addition, Iannitti *et al*. found that Arnica significantly reduced posttrauma and postoperative pain, ecchymosis, and edema.[27]

Our findings also revealed that patients with a longer history of hemodialysis experienced slighter pain than those with a shorter history. In line with this finding, Verhallen *et al*. showed that pain perception at puncture site reduced 3 months after the initiation of hemodialysis.[28] This finding may be due to the reduction of pain perception over time. Moreover, we found that Arnigol cream had stronger analgesic effects on nondiabetic patients compared with diabetic ones. This finding can be attributed to reduced pain perception among diabetic patients due to the peripheral neurovascular complications of diabetes mellitus.

One study limitation was the probable effects of patients' psychological conditions on their pain perception. Pain is a subjective perception, and people differ from each other respecting pain perception. Such difference might have affected the study results. We assessed pain perception only through the self-report method and hence could not verify the accuracy of pain intensity reported by participants.

Conclusions

The findings of this study suggest that Arnigol cream is effective in reducing the intensity of the pain associated with arteriovenous fistula puncture and thereby improving comfort among patients receiving hemodialysis. Thus, nurses are recommended to use this simple, safe, and inexpensive modality to reduce fistula puncture pain. Still, we recommend the future investigators to use more objective pain assessment methods to produce more conclusive evidence regarding the effects of Arnigol cream.

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Conflicts of interest

There are no conflicts of interest.

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