

Review Article

PAIN ATTENUATION IN VENOUS CATHETERISATION/VENIPUNCTURE: A NARRATIVE REVIEW OF TOPICAL ANAESTHESIA USE AMONG 448 RESPONDENTS IN AFRICA

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Abstract

Background: Pain associated with peripheral venous catheter (PVC) insertion and venipuncture can be a significant source of discomfort, particularly for children. The use of topical anaesthetic preparations before PVC insertion can reduce discomfort and enhance health-seeking behaviour.

Objective: This review aimed to assess the efficacy of topical anaesthesia in reducing pain during PVC insertion compared with placebo or no treatment, and to evaluate the associated adverse effects of topical anaesthetic preparations among the African population.

Methods: This review was conducted using a systematic literature search of the following databases and registers: PubMed, NDLTD, OATD, TROVE, LILACS, Scopus, The Cochrane Library, CINAHL & MEDLINE [via EBSCOhost], Africa Journal Online (AJOL), Google Scholar, and MedNar, conducted between November and December 2023. Prospective observational studies, randomised controlled trials, case-control studies, longitudinal studies, theses and dissertations were considered in these searches. A total of four studies and 448 respondents participated in the review.

Result: All studies investigated the efficacy of various topical agents, including 5% EMLA and 10% lidocaine cream, and demonstrated a significant reduction in pain with topical anaesthesia compared to placebo or no treatment. The adverse/side effect profile was generally favourable, with no major adverse reactions reported.

Conclusion: Topical anaesthesia is a valuable tool in reducing procedural pain during peripheral venous catheterisation and venipuncture in the African population. This review establishes its superiority over placebo or no treatment. Specifically, 10% lidocaine outperforms 5% EMLA in minimising procedural pain with minimal side effects.

Keywords: Peripheral venous catheterisation/cannulation; Venipuncture; Topical Anaesthesia; Pain attenuation; Africa.

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INTRODUCTION

William Harvey's identification of blood circulation in 1653 was a turning point in the practice of medicine and surgery; this milestone prompted several attempts at blood transfusion, much to the demise of patients and the chagrin of society at the time. The first working peripheral venous infusion device was created in 1658 by Christopher Wren from a quill and a pig's bladder following an unlikely peaceable encounter. This device's invention served as the template for subsequent evolutions, such as Crile's cannula, up to the modern peripheral venous cannula [1-2]. The peripheral venous cannula [or catheter] is a device inserted temporarily into a patient's peripheral vein, a process known as peripheral venous cannulation or catheterisation, to deliver fluids, blood products, and medications [3].

Venipuncture, as a medical procedure, on the other hand, developed from the practice of phlebotomy, a popular bloodletting operation during the Middle Ages, which initially stemmed from the Hippocratic belief in the four humours [4]. Venipuncture involves the piercing of a vein with a needle for either peripheral venous injection or the collection of blood for investigative purposes [5]. Venipuncture and the insertion of the peripheral venous catheter (PVC) device, though having a lot of long-term benefits for the patient, may also be a source of unwanted anxiety due to an expectation of associated pain. The International Association of the Study of Pain (2020) defines pain as an uncomfortable sensory and emotional experience linked to or resembling sensations related to real or potential harm to tissues [6].

The pain experienced during peripheral venous cannulation/venipuncture has the potential to heighten a patient's healthcare-related anxiety and contribute to poor health-seeking behaviour [7]. Additionally, anxiety associated with a procedure may induce an autonomic response, leading to vasoconstriction, which could subsequently result in reduced venous access, necessitating multiple cannulation attempts, thus not only increasing the risk of infection and other complications for the patient but also making the PVC insertion procedure an ordeal for the practitioner [7].

The pain from PVC insertion/venipuncture could be minimised by using analgesic agents, which are topical anaesthetics in the case of the present discourse [8]. Topical anaesthetics are agents that produce topical anaesthesia, a reversible loss of sensation in a circumscribed area of the skin or mucous membranes, by reversibly blocking the conduction of nerve impulses at free nerve endings [9]. Some of the topical anaesthetic agents that have been employed to achieve topical anaesthesia before peripheral venous cannulation include the Eutectic Mixture of Local Anaesthetics (5% EMLA): a mixture of 2.5% Lidocaine and 2.5% Prilocaine in an emulsion base; 4% Amethocaine gel, 10% Lidocaine, coolants such as ethyl chloride, alkane mixtures, and fluorohydrocarbons [10–13]. Although reviews [7,14] evaluating reductions in PVC insertion/venipuncture pain with topical anaesthetic agents compared with placebo had been conducted globally, none had been conducted in Africa. The purpose of this review is to address the aforementioned gap and assess the available evidence on the African continent.

Aims

This review aims to answer the following inquiries:

1. Does the use of topical anaesthetic agents in children, adolescents and adults result in a reduction of PVC insertion/venipuncture pain when compared with placebo or no treatment?
2. What are the adverse effects associated with the use of topical anaesthetic agents?

REVIEW METHOD

Search Databases and Search Strategy

The following databases and registers: PubMed, Networked Digital Library of Theses and Dissertations (NDLTD), Open Access Theses and Dissertations (OATD), TROVE, Latin American and Caribbean Centre on Health Sciences Information (LILACS), Scopus, The Cochrane Library, Cumulative Index of Nursing and Allied Health Literature (CINAHL) & MEDLINE [via EBSCOhost], Africa Journal Online (AJOL), Google Scholar, and MedNar were electronically searched between November and December 2023 using the Population, Intervention, Comparison and Outcome

[PICO] framework [15] to collect clinical studies on reduction in PVC insertion/venipuncture pain with or without topical anaesthesia:

Patient/Population: Children, adolescents, and adults.

Intervention: Topical anaesthetic agents

Comparison: Placebo or no treatment

Outcome: Pain (Reduction in PVC insertion/venipuncture pain), adverse/side effects.

A thorough investigation of the citation lists within the selected studies was done, and a manual search was performed to ensure that all eligible studies were included. Exclusive consideration was given to research conducted in English and available online. The following keywords were used for the search: peripheral venous catheterisation, venous cannulation, venipuncture, pain reduction, topical anaesthesia, children, adults, elderly, Africa, and English. Furthermore, the following search strings were created using the aforementioned keywords and their synonyms in combination with Boolean operators [“AND” and “OR”] and wildcards [“*” “?” and “\$”]:

1. (“Children” OR “Child*” OR “Minor*” OR “Adolesc*” OR “Teen*” OR “Adult” OR “Elder*” OR “Middle?aged”)
2. (“Peripheral venous cannulation” OR “Venipuncture” OR “Venous cannulation” OR “Venous catheterisation” OR “IV cannulation” OR “Peripheral catheterisation” OR “PICC placement?”)
3. (“Pain reduc*” OR “Discomfort reducti*” OR “Soreness reduc*” AND “Local an?esthetic” OR “Local analgesia” OR “Local an?esthesia” OR “Topical an?esth*” OR “Topical analg*” OR “Topical an?esthesia” OR “Local pain relief”)
4. (“Topical” OR “Surface” OR “External” AND “Placebo” OR “Treatment”)
5. (“Africa”)
6. (“English language”), and
7. (S1 AND S2 AND S3 AND S4 AND S5 AND S6).

Inclusion and Exclusion Criteria

The inclusion criteria were as follows:

1. Prospective observational studies, cohort studies, case-control studies, non-randomised controlled trials, and randomised controlled trials

2. Research articles that evaluated the efficacy of a topical anaesthetic agent in reducing PVC insertion pain compared to placebo.
3. Research articles that evaluated the efficacy of a topical anaesthetic agent in reducing PVC insertion pain compared to another topical anaesthetic agent.
4. Theses and dissertations; and
5. Studies conducted in the African continent.

The exclusion criteria were as follows:

1. Review articles, viewpoints, books, letters, editorials, book chapters, perspectives, and news
2. Research articles, theses, and dissertations undertaken outside the African continent
3. Research articles, theses, and dissertations published in languages other than English; and
4. Research articles, theses, and dissertations without accessible full texts.

Data Extraction

Two authors [Osadolor AJ and Okpalaugo PN] searched the databases and made a first selection based on the title and abstract, using the established criteria. Subsequently, two independent researchers [Ugwoke GE and Oladepo OO] reviewed the full texts of each selected study and compiled articles that integrated the results of this review. A total of 2326 articles were identified during literature searches from the identified databases, and 2226 were excluded because their titles and abstracts and/or related controlled trials of the review were not relevant to the screening; an additional 95 were excluded based on study location. Meanwhile, from the five articles retrieved, one was excluded due to the language of publication [French]. Every study considered in the current review was undertaken within Africa and published between August 1989 and February 2019 [Figure 1].

RESULTS

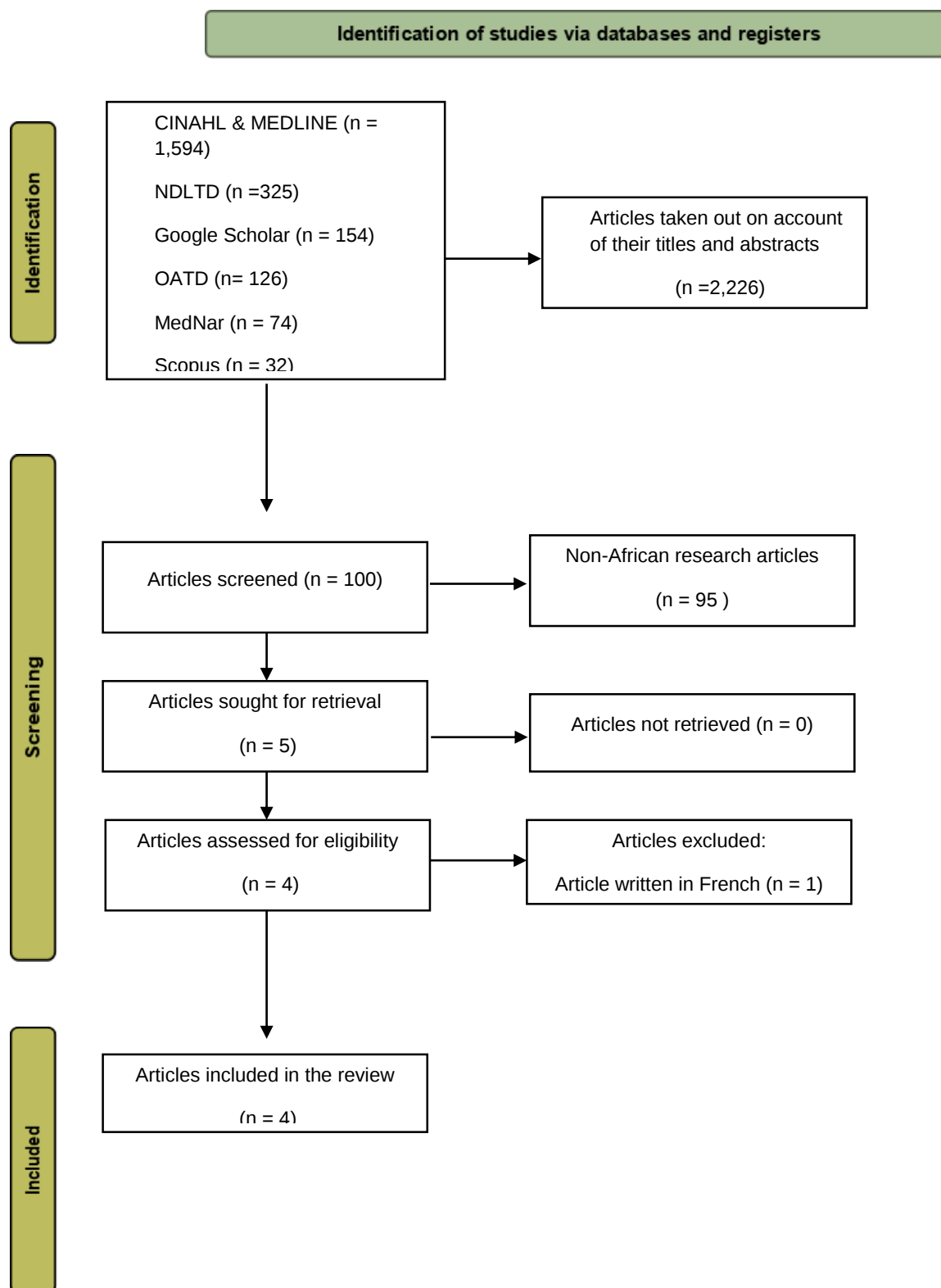


Figure 1: PRISMA flow diagram of study identification and selection process.

Table 1: Summary of the identified research articles.

Author (Year)	Study sample	Study design	Study region
Hellgren, Kihamia, and Premji <i>et al.</i> [16]	Forty-two [42] school-age children	A prospective study.	Tanzania
Gwetu and Chhagan [17]	Two hundred and four [204] school-age children.	A longitudinal study.	South Africa
van Straten, Murray, and Levin [18]	One hundred [100] adult surgical patients (including pregnant women).	A randomised controlled trial.	South Africa
Oluwadun, Adekola, and Dada <i>et al.</i> [19]	One hundred and two [102] adult surgical patients.	A randomised controlled trial.	Nigeria

A total of 448 respondents participated in the reviewed studies: 202 adults were included in two of the four studies, and 246 children were included in the other two.

Regarding the focus of the studies, two studies [16-17] evaluated the efficacy of 5% EMLA in reducing pain in children before venipuncture. Meanwhile, one study [18] assessed the efficacy of 10% lidocaine in reducing pain in adult patients compared to saline; the other study [19] compared the efficacy of 5% EMLA to 10% lidocaine in

reducing peripheral venous cannulation pain among a group of adult patients. One study was a prospective study [16], another a longitudinal study [17], and the other two [18-19] were randomised controlled trials. The study regions were Tanzania [16], South Africa [17-18], and Nigeria [19]. [

Table 1].

Table 2: The objectives and outcomes of the identified research articles.

Author (Year)	Study objective	Primary outcome	Secondary outcome
Hellgren, Kihamia, and Premji <i>et al.</i> 1989 [16]	To evaluate the usefulness of 5% EMLA cream in Tanzanian school children undergoing venepuncture.	No pain was observed in 39 participants (93%), slight pain in 2 participants (4.7%), and moderate pain in 1 participant (2.3%).	No skin reaction [general or local] was observed
Gwetu and Chhagan 2015 [17]	To evaluate the efficacy of 5% EMLA cream in reducing pain in school-aged children in a field setting.	Pain reduction in 168 (91.3%) participants who received 5% EMLA compared to 5 (25%) in the control group [no treatment] Furthermore, 3 (1.6%) and 13 (7.6%) participants in the 5% EMLA group complained of moderate pain and mild discomfort, respectively.	No systemic, dermatological, itching or local reactions were observed.

Lower VAS score in participants who received 5% EMLA compared to control ($p < 0.001$)

*5% EMLA: Eutectic mixture of local anaesthetics (contains 2.5% Lidocaine and 2.5% Prilocaine in an oil-water emulsion); VAS: Visual analogue scale; NRS: Numerical rating scale; VRS: Verbal rating scale; CI: Confidence interval.

Table 2: The objectives and outcomes of the identified research articles [continued].

Author (Year)	Study objective	Primary outcome	Secondary outcome
van Straten, Murray, and Levin 2018 [18]	To evaluate whether pre-treatment with Xylocaine® 10% Pump Spray could facilitate analgesia for venipuncture.	Lower NRS scores in participants who received the Xylocaine® 10% Pump Spray [median 2; 95% CI 2-3] compared to the score for those who received saline [median 4; 95% CI 3-5] ($p < 0.001$) Nil pain in 10 (20%) participants who received Xylocaine® compared with 2 (4%) in those who received saline.	No adverse reactions or skin changes were observed.
Oluwadun, Adekola, and Dada <i>et al.</i> 2019 [19]	To compare the efficacy of 5% EMLA to 10% lidocaine cream and placebo in the reduction of PVC insertion pain.	Lower mean VAS scores in the 5% EMLA group (2.62 ± 1.76 cm) and 10% Lidocaine group (1.85 ± 1.58 cm) compared with placebo [KY gel] treatment (4.78 ± 1.88 cm), $p < 0.001$. Thirteen (38.2%) and 18 (52.9%) patients who received 5% EMLA and 10% Lidocaine, respectively, were expressionless during cannulation compared to 6 (17.6%) patients who received placebo.	Burning skin sensations were observed in one participant (2.9%) who received 5% EMLA and two participants (5.9%) who received 10% lidocaine. A tingling sensation was observed in 1 participant (2.9%) who received 10% lidocaine. Blanching of the skin was observed in one participant (2.9%) in all three groups after cessation of treatment creams.

*5% EMLA: Eutectic mixture of local anaesthetics (contains 2.5% Lidocaine and 2.5% Prilocaine in an oil-water emulsion); VAS: Visual analogue scale; NRS: Numerical rating scale; VRS: Verbal rating scale; CI: Confidence interval.

Concerning the outcome variable, pain was measured using the VRS by two studies [16,19], the NRS by one study [18] and the VAS by two other studies [17,19]. One of the reviewed studies [19] used two pain scales to measure pain; Oluwadun *et al.* [19] employed the VRS and the VAS for all their participants; van Straten *et al.* [18], on the other hand, created ordinal categories of patients' pain from their NRS scores. Among the three studies [17-19] that compared topical anaesthesia with placebo or no treatment, all reported statistically significant differences in favour of the experimental group ($p < 0.001$). Moreover, one study [16] reported that 93% of participants who received topical anaesthesia experienced no pain during venipuncture. Oluwadun *et al.* [19] observed that the VAS scores were significantly lower among participants who received 10% lidocaine compared to those who received 5% EMLA ($p < 0.001$); more so, a greater proportion of participants who received 10% lidocaine experienced pain-free cannulation compared to those who received 5% EMLA, or placebo.

Regarding adverse effects, all four studies evaluated this outcome, and three observed no adverse reactions [16-18] with the various topical interventions. One study [19], on the other hand, discovered more adverse reactions with the 10% lidocaine treatment compared to the 5% EMLA treatment; blanching of the skin was noticed in both the treatment groups and the control group [

Table 2].

DISCUSSION

The results of this review demonstrate that administering topical anaesthetics effectively reduces pain during peripheral venous catheterisation and venipuncture. In all reviewed studies, topical anaesthesia was effective in preventing pain during peripheral venous catheterisation/venipuncture. In all but one [16] of the studies, the efficacy of the local anaesthetic agent/s was evaluated against a placebo or control, with the observation of similar results for each. All the reviewed studies investigated the efficacy of one or both of the following topical anaesthetic preparations: 5% EMLA and 10% lidocaine. This finding may be ascribed to the availability of these preparations in the studied locations.

In the Hellgren *et al.* [16] study, the median topical anaesthetic contact time with the skin was 135 minutes. In contrast, Gwetu and Chhagan [17] observed a shorter contact time of 72 minutes. Van Murray and Levin [18] reported an even briefer contact period of 20 minutes, while Oluwadun *et al.* [19] documented a contact time of 60 minutes. The variations in applied topical anaesthetic contact durations observed across the studies may be attributed to differences in the pharmacodynamic profiles of the topical anaesthetic preparations used, coupled with the need to achieve varying depths of anaesthesia [20-22]. The onset of action of 5% EMLA ranges between 60 and 90 minutes [23-24]. Meanwhile, its anaesthetic effect has been reported to reach a skin depth of 3mm with a 60-minute contact time, increasing by an additional 2mm after another 60 minutes [25]. The 10% lidocaine preparation has been noted to possess a faster onset of action (about 1 to 3 minutes) but a short duration of action (10 to 15 minutes) [24, 26].

With respect to the active principle concentration, all four studies consistently demonstrated that concentrations ranging from 5% to 10% effectively reduced procedural pain during peripheral venous cannulation and venipuncture. These concentrations were observed in two anaesthetic formulations: cream and spray. Other topical anaesthetic formulations include ointments, solutions, eye drops, gels, and sprays [27].

The formulation of an anaesthetic agent, such as a cream or spray, involves the combination of the active ingredient with other ingredients, such as physical and chemical permeation enhancers, lipid delivery vesicles and preservatives, and has been noted to contribute to the effectiveness of the anaesthetic preparation [25, 28]

Other methods to enhance the effectiveness of a topical anaesthetic preparation include covering the application area with a dressing or patch of nonporous material such as micropore and Tegaderm [was employed in all of the reviewed studies], degreasing using alcohol [was undertaken in all of the reviewed studies], exfoliation of the skin, iontophoresis, electroporation, sonophoresis/phonophoresis, magnetophoresis, use of thermal energy, Erbium: Yttrium Aluminum Garnet laser pre-treatment, and skin pre-treatment with a hand-applied, plastic microneedle array [25].

No side effects were reported in three [16-18] out of the four reviewed studies. In the study [19], side effects were observed; however, both the treatment and control groups were affected. This finding suggests that any observed side effects may not be solely attributed to the topical anaesthetic but might be influenced by other factors such as patient characteristics like age and ethnicity, and the topical anaesthetic application technique. Some of the side effects documented with the use of 5% EMLA include regional pallor, flare, oedema, an early burning sensation, and, rarely, itching [22,29-30]. Additionally, induction of allergic and anaphylactic reactions, such as hives, vascular oedema, bronchospasms, as well as methemoglobinemia in children, has been noted [29-30]. On the other hand, erythema has been reported as a side effect of 10% lidocaine use [31-33]

In all studies included in this review that compared the efficacy of topical anaesthetics with a placebo or control, there was unanimous agreement that topical anaesthesia was superior for both peripheral venous catheterisation and venipuncture. This consensus across the reviewed studies indicates that topical anaesthetics are effective in the African population. Notably, all selected studies demonstrated a significant difference in effectiveness compared to a placebo or no treatment.

CONCLUSION

Topical anaesthesia serves as a valuable adjunct in alleviating procedural pain associated with peripheral venous catheterisation and venipuncture within the African population. This review discovered that topical anaesthesia was more effective than placebo or no treatment in the reduction of pain associated with PVC insertion and venipuncture. In addition, 10% lidocaine was more effective than 5% EMLA in the reduction of the associated procedural pain. The side effects observed in this review were minimal and consistent with findings in the medical literature. There is a need for more studies to explore the efficacy and adverse-effect profiles of other topical anaesthetic/analgesic preparations and formulations that can serve as alternatives in cases of adverse reactions or failure to achieve topical anaesthesia.

ABBREVIATIONS

CI: Confidence Interval

CINAHL: Cumulative Index of Nursing and Allied Health Literature

EMLA: Eutectic Mixture of Local Anaesthetics

LILACS: Latin American and Caribbean Centre on Health Sciences Information

NDLTD: Networked Digital Library of Theses and Dissertations

NRS: Numerical Rating Scale

OATD: Open Access Theses and Dissertations

PVC: Peripheral Venous Catheter

VAS: Visual Analogue Scale

VRS: Verbal Rating Scale

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Author Contributions

Osadolor AJ, Obazee OC, Ugwoke GE, and Okpalaugo PN conceived the study, developed the research concept, and designed the study. Osadolor AJ, Osadolor OO, Okpalaugo PN, and Ngban PM drafted the manuscript. Data were collected by Osadolor AJ, Omoruan DO, Obazee OC, Ugorji CV, Ubogu AN, and Okpara A. Data extraction was undertaken by Osadolor AJ, Ekpeta AP, Obazee OC, Onaghinor EM, Osadolor OO, Omorogbe KI, Ngban PM, and Okolie KN. Omorogbe KI, Sunday OG, Ugorji CV, Okpalaugo PN, Onaghinor EM, Okpara A, Osadolor AJ, and Okolie KN carried out project management. Osadolor AJ, Ugwoke GE, Obazee OC, Oladepo OO, Osadolor OO, Ekpeta AP, Ugorji CV, Omorogbe KI, Ubogu AN, Okpalaugo PN, Ngban PM, Sunday OG, Omoruan DO, Onaghinor EM, Okpara A, and Okolie KN provided consultation, including critical review of the manuscript before submission. All authors read and approved the final version of the manuscript.

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Competing interests

None

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