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NURSING CARE PACKAGE REDUCES PAIN AND BRUISING FROM SUBCUTANEOUS ANTICOAGULANTS: A RANDOMIZED CONTROLLED TRIAL

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ABSTRACT

Background: Subcutaneous injectable anticoagulants, particularly low-molecular-weight heparins (LMWHs), constitute the cornerstone of venous thromboembolism (VTE) prophylaxis and treatment in hospitalized patients. Despite their established clinical efficacy, local adverse effects — notably pain and bruising at injection sites — are prevalent, undermining patient comfort, psychological well-being, and potentially compromising adherence to prescribed therapy. Variability in nursing injection technique represents a modifiable determinant of these adverse outcomes; however, standardized, evidence-based nursing care packages addressing the full spectrum of injection-related practices remain insufficiently studied, particularly in the Indian clinical context.

Objectives: (1) To determine the prevalence of local adverse effects among hospitalized patients receiving subcutaneous injectable anticoagulants; (2) to evaluate the effectiveness of a structured nursing care package on pain and bruising; (3) to compare adverse effect outcomes between the experimental and control groups; and (4) to examine the association between pain and selected co-morbid conditions.

Methods: A randomized controlled trial (RCT) with a parallel-group design was conducted among 180 hospitalized patients receiving subcutaneous anticoagulants (enoxaparin, dalteparin, or unfractionated heparin). Participants were randomly allocated (1:1) to an experimental group (n=90) receiving a structured nursing care package (comprising site rotation, pre-injection cold application, optimized needle gauge, slow-rate injection, air-bubble retention technique, and 60-second post-injection pressure) or a control group (n=90) receiving routine hospital care. The primary outcome was pain intensity, assessed using a standardized six-point categorical pain scale; the secondary outcome was bruising severity, measured by a five-point bruise scale. Assessments were performed at baseline (Day 0) and post-intervention (Day 7). Paired t-tests and chi-square analyses were employed; significance was set at $p<0.05$.

Results: Of 720 screened patients, 25% (n=180) developed clinically significant adverse effects. In the experimental group, mean pain score declined from 3.29±1.807 at baseline to 1.89±1.136 post-intervention (mean difference=1.40; t=6.89; df=89; $p<0.001$), representing a 43% reduction. In the control group, mean pain score decreased from 3.42±1.349 to 1.67±0.750 (mean difference=1.75; t=3.25; p=0.002). For bruising, the experimental group demonstrated a reduction from 2.46±0.889 to 1.77±0.720 (mean difference=0.69; t=7.23; $p<0.001$; 28% reduction), while the control group showed a modest reduction from 2.27±0.790 to 2.00±0.561 (mean difference=0.27; t=3.58; $p<0.001$). No significant association was found between pain and co-morbid conditions ($\chi^2=7.504$, df=9, p=0.585).

Conclusion: The structured nursing care package produced clinically and statistically significant reductions in both pain and bruising severity, with markedly superior bruising outcomes compared to routine care. This low-cost, easily trainable, evidence-based intervention warrants integration into standard nursing protocols for subcutaneous anticoagulant administration across Indian hospital settings.

KEYWORDS: Anticoagulants; subcutaneous injection; nursing care package; pain; bruising; randomized controlled trial; patient safety; venous thromboembolism prophylaxis

1. INTRODUCTION

Venous thromboembolism (VTE), encompassing deep vein thrombosis (DVT) and pulmonary embolism (PE), constitutes one of the leading preventable causes of in-hospital mortality and morbidity worldwide. Globally, the annual incidence of VTE is estimated at 1–2 per 1,000 persons, with hospitalized patients bearing a disproportionately elevated risk attributable to immobility, surgical trauma, and underlying prothrombotic states [1,2]. Low-molecular-weight heparins (LMWHs) — including enoxaparin, dalteparin, and tinzaparin — administered via the subcutaneous route, represent the pharmacological cornerstone of VTE prophylaxis and treatment in hospitalized patients, as endorsed by major international guidelines including those from the American College of Chest Physicians (ACCP) and the International Society on Thrombosis and Haemostasis (ISTH) [3,4].

Despite compelling evidence for their efficacy in reducing thromboembolic events, subcutaneous LMWH administration is associated with a significant burden of local adverse effects. Systematic analyses and meta-analyses have documented that hematoma formation occurs in 12–65% of injection episodes, ecchymosis or bruising in 24–78%, and clinically meaningful injection-site pain — with mean Visual Analogue Scale (VAS) scores of 3–5 on a 10-point scale — in a substantial proportion of patients [5,6]. A 2020 meta-analysis by Chan reported a pooled hematoma incidence of 34% (95% CI: 28–41%) and a pooled mean pain score of 3.8 across included trials [7]. These adverse effects extend beyond mere physical discomfort: they engender psychological distress, may precipitate therapy refusal or non-adherence, delay early mobilization, and have been associated with extended hospital stays and elevated healthcare costs [8].

The severity of injection-site reactions is not predetermined by pharmacology alone; it is substantially influenced by modifiable nursing technique variables. Evidence implicates injection velocity, needle caliber, site rotation practices, use of pre-injection cold application, post-injection pressure duration, and the decision to aspirate or to retain an air bubble in pre-filled syringes as key determinants of both pain and hematoma formation [9,10]. Individual nursing interventions have been evaluated in isolation across multiple studies. Cold application before injection has demonstrated efficacy in reducing pain through vasoconstriction and local analgesia [11]. Slow injection rate (10–15 seconds per 0.5 mL) has been associated with reduced subcutaneous tissue pressure and consequent pain reduction [12]. Adequate post-injection pressure (60 seconds) promotes hemostasis at the injection track, limiting ecchymosis [13]. Site rotation averts repeated trauma and cumulative tissue injury [14].

However, a critical gap persists in translating this evidence into structured, bundled nursing care protocols. While individual technique modifications have been tested, the synergistic impact of a comprehensive nursing care package combining multiple evidence-based components has received limited rigorous investigation. This gap is particularly pronounced in the Indian clinical context, where the use of injectable anticoagulants has risen substantially over the past decade in parallel with increasing rates of cardiovascular disease, cancer, and post-surgical care, yet nursing practice remains heterogeneous and largely unprotocolized [15]. No published randomized controlled trial from India has evaluated a comprehensive, multi-component nursing care package specifically targeting pain and bruising associated with subcutaneous anticoagulant therapy.

Furthermore, factors such as co-morbid conditions — particularly diabetes mellitus and hypertension, both prevalent in the Indian population — may theoretically modulate pain perception and vascular fragility; however, the association between these conditions and anticoagulant injection-site pain has not been rigorously examined.

The present study was therefore designed to fill these evidence gaps, with the following specific objectives:

- To determine the prevalence of clinically significant adverse effects (pain and bruising) among hospitalized patients receiving subcutaneous injectable anticoagulants.
- To evaluate the effectiveness of a structured nursing care package in reducing pain and bruising severity.
- To compare pain and bruising outcomes between patients receiving the nursing care package and those receiving routine care.
- To ascertain the association between pain levels and selected co-morbid conditions.

2. REVIEW OF LITERATURE

2.1 Prevalence and Burden of Local Adverse Effects

The clinical burden of subcutaneous anticoagulant-induced local adverse effects has been extensively documented over the past two decades. Pourghaznein et al. (2014) conducted a landmark prospective observational study among 150 patients receiving subcutaneous enoxaparin and reported ecchymosis in 64.7% of participants, with a mean hematoma diameter of 2.8 cm [16]. Avsar and Kasikci (2013) similarly observed bruising in 78% of their cohort, with mean pain scores of 3.5/10 [17]. More recently, a systematic review by Chan (2020) — encompassing 23 randomized controlled trials and 3,491 patients — reported a pooled hematoma incidence of 34% (95% CI: 28–41%) and highlighted injection technique as the most influential modifiable risk factor [7].

In the South Asian context, data on injection-site adverse effects are relatively sparse. Joseph et al. (2017) studied 60 patients receiving enoxaparin in Kerala, India, and documented mean pain scores of 3.9 and hematoma diameters of 2.8 cm under routine care conditions, underscoring the relevance of this problem in Indian hospitals [18]. National epidemiological data on anticoagulant-related injection complications in India remain limited, representing a significant knowledge gap.

2.2 Evidence-Based Nursing Interventions for Adverse Effect Mitigation

Cold application has emerged as a consistently effective pre-injection intervention. A randomized controlled trial by Celik and Khorshid (2018) among 100 patients demonstrated significantly lower pain scores following 5-minute pre-injection cold application (mean VAS 2.1 vs. 3.8; $p<0.001$) and reduced bruise diameter [19]. Kaya et al. (2021) confirmed these findings, reporting that ice application reduced both pain intensity and hematoma size compared to controls [20]. The proposed mechanism involves cold-induced vasoconstriction, reduction of cutaneous blood flow, and transient local analgesia through afferent nerve conduction slowing [11].

The significance of injection rate has been quantified in a meta-analysis by Parvez and Parvez (2019) incorporating eight RCTs (n=1,247), which found that slow injection (10–15 seconds per 0.5 mL) significantly reduced both pain (standardized mean difference [SMD]: -0.92; 95% CI: -1.21 to -0.63) and bruising (relative risk

[RR]: 0.64; 95% CI: 0.52–0.79) relative to rapid injection [12]. The physiological rationale lies in the reduction of acute tissue pressure at the injection site during drug deposition.
Post-injection pressure has received dedicated investigation. Zaybak and Khorshid (2019) demonstrated that 60 seconds of gentle pressure reduced bruise diameter from 2.4 cm to 1.1 cm ($p<0.01$), attributing this effect to facilitated hemostasis through compression of the needle track [13]. Ozdemir and Cakir (2022) further confirmed that 30 seconds of pressure was insufficient and 60 seconds constituted the minimum effective duration [21]. Aspiration prior to subcutaneous injection has been definitively discouraged based on a large RCT by Hadfield-Law (2018), which found no benefit and increased tissue trauma [22]. The air-bubble technique — retaining the factory air bubble in pre-filled syringes to seal the needle track — has been associated with reduced drug leakage and ecchymosis formation [23].
Site rotation represents a fundamental but frequently neglected practice. Yildirim et al. (2021) demonstrated that systematic rotation across four abdominal quadrants significantly reduced cumulative bruise area compared to unrotated injection ($p<0.01$), and Gupta et al. (2017) similarly found reduced pain and bruising with formalized rotation protocols [14,24].

2.3 Structured Nursing Care Packages: Bundled Interventions

The comparative efficacy of individual versus bundled interventions represents a critical area of inquiry. Gul and Demir (2020) implemented a nursing care protocol combining site rotation, slow injection, and cold application in a quasi-experimental study among 200 Turkish patients receiving enoxaparin. Pain scores decreased from 4.2 to 2.1 ($p<0.001$) and bruising incidence from 72% to 34% ($p<0.001$) following protocol implementation [25]. The additive benefit of combining these techniques is consistent with the multifactorial pathophysiology of injection-site injury. A systematic review by Mohammady et al. (2020) supported the superiority of bundled approaches over single-technique modifications in reducing composite adverse effect burden [26].
In the Indian context, Joseph et al. (2017) evaluated a structured injection technique among 60 patients in Kerala and reported significant pain reductions (2.1 vs. 3.9, $p<0.001$) and smaller hematoma dimensions (1.2 cm vs. 2.8 cm, $p<0.001$) compared to controls [18]. However, this study was limited by its small sample size and its single-technique focus, falling short of a comprehensive bundled care package. Akgün Sahin and Dayapoglu (2020) reported the superiority of combined cold and warm application protocols over single thermal modalities in patients with cardiovascular disease [27]. To date, no Indian RCT has evaluated a multi-component nursing care package with an adequately powered randomized design.
The extant literature thus confirms the efficacy of individual nursing techniques but reveals a critical evidence gap regarding comprehensive, protocolized, bundled nursing care packages evaluated through rigorous RCT methodology in the Indian context. The present study was designed to address this gap directly.

3. MATERIALS AND METHODS

3.1 Research Design and Study Setting

This study employed a parallel-group, randomized controlled trial (RCT) design with a 1:1 allocation ratio and was reported in accordance with the Consolidated Standards of Reporting Trials (CONSORT) 2010 guidelines [28]. The study was conducted in the medical, surgical, and orthopedic wards of a tertiary care teaching hospital in Vadodara, Gujarat, India, during a defined data collection period spanning four months. These wards routinely administered subcutaneous anticoagulants as part of standard perioperative and medical care protocols.

3.2 Population, Sample, and Sampling

The target population comprised all hospitalized adult patients receiving subcutaneous injectable anticoagulants (enoxaparin, dalteparin, or unfractionated heparin). A total of 720 consecutive patients receiving these medications were prospectively screened over the study period using a consecutive sampling approach. From this screening population, 180 patients (25%) who developed one or more local adverse effects (pain and/or bruising) were enrolled and constituted the study sample.
Sample size was calculated based on a pilot study that established a clinically meaningful mean pain score difference of 1.5 (SD=1.2) between intervention and control groups. Using 80% statistical power, a two-tailed significance level of 5%, and accounting for 10% potential attrition, a minimum of 80 participants per group was required; 90 were enrolled per group (total N=180).

3.3 Randomization and Allocation Concealment

The 180 eligible participants were randomly allocated to the experimental (n=90) or control (n=90) group using a computer-generated random number sequence. Allocation concealment was achieved through sequentially numbered, opaque, sealed envelopes prepared by an independent biostatistician not involved in data collection. Envelopes were opened sequentially at the time of enrolment to prevent anticipation of allocation.

3.4 Inclusion and Exclusion Criteria

Patients were eligible if they were: (i) aged 30 years or above; (ii) currently hospitalized and receiving subcutaneous injectable anticoagulants for a minimum of three consecutive days; (iii) willing and capable of providing written informed consent; and (iv) able to communicate their pain experience using the study

assessment tool. Patients were excluded if they had: (i) documented bleeding disorders (e.g., haemophilia, thrombocytopenia with platelet count <50,000/μL); (ii) known hypersensitivity to the prescribed anticoagulant; (iii) concurrent oral anticoagulation therapy; (iv) cognitive impairment precluding valid self-report of pain; or (v) critical illness requiring intensive care unit admission.

3.5 Description of the Nursing Care Package (Experimental Intervention)

The nursing care package was developed through a systematic literature review and subjected to content validation by a panel of five subject-matter experts (three nursing professors with doctoral qualifications and two clinical nurse specialists in medical-surgical nursing). The panel achieved consensus on all components, with an overall Content Validity Index (CVI) of 0.92. The package comprised the following standardized, evidence-based components:

Component	Standardized Technique	Evidence Base
Anatomical site selection	Anterolateral abdominal wall; four-quadrant rotation; minimum 2 cm from umbilicus	Site rotation prevents cumulative tissue trauma [24]
Needle selection	25–26 gauge, 16 mm length needle	Smaller caliber reduces mechanical tissue injury [9]
Pre-injection cold application	Ice pack (wrapped) applied for 2–3 minutes over the designated injection site	Vasoconstriction and local analgesia [11,20]
Skin fold technique	Gentle pinch-fold maintained throughout injection duration in patients with low BMI	Ensures subcutaneous (not intramuscular) deposition [9]
Injection rate	Slow, controlled injection over 10–15 seconds per 0.5 mL	Reduces subcutaneous pressure and pain [12]
Air bubble retention	Do not expel the factory air bubble in pre-filled syringes prior to injection	Air bubble occludes needle track, limiting drug leakage and bruising [23]
Needle withdrawal angle	Withdraw needle at same angle as insertion; no lateral movement	Minimizes tissue laceration during withdrawal [9]
Post-injection pressure	Gentle, sustained pressure with dry sterile cotton for 60 seconds; no rubbing or massage	Facilitates hemostasis; rubbing disrupts platelet plug [13,21]

Six staff nurses deployed in the study wards were trained on all components of the nursing care package over two structured training days (total: four hours), incorporating didactic instruction, live demonstration, return demonstration, and assessment against a standardized procedural checklist. Inter-rater reliability among trained nurses was established at kappa=0.85, indicating near-perfect agreement.

3.6 Control Group Intervention

Patients allocated to the control group received routine nursing care as conventionally practiced in the study wards. This encompassed standard subcutaneous injection technique without protocol-defined cold application, standardized injection duration, prescribed post-injection pressure duration, or formalized site rotation. Routine practice varied across individual nursing staff members, reflecting real-world heterogeneity.

3.7 Outcome Measures

Primary outcome — Pain Intensity: Pain was assessed using a six-point categorical pain scale adapted from the Wong-Baker FACES scale, scored 0 (no pain) to 5 (worst imaginable pain). Each numerical score corresponded to a descriptor: 0=very happy, no hurt; 1=hurts just a little bit; 2=hurts a little more; 3=hurts even more; 4=hurts a whole lot; 5=hurts as much as you can imagine. Test-retest reliability of this scale in the study population was r=0.85.

Secondary outcome — Bruising Severity: Bruising was assessed using a five-point ordinal scale: 1=light (no discoloration, no palpable mass); 2=mild (discoloration <1 cm diameter); 3=moderate (discoloration 1–3 cm, no palpable mass); 4=severe (discoloration >3 cm, palpable mass); 5=extreme severe (discoloration >5 cm, palpable mass). Inter-rater reliability between two trained assessors was kappa=0.88, indicating excellent agreement.

Both outcomes were assessed at two time points: pre-test (Day 0 — within 24 hours of study enrolment) and post-test (Day 7 — after seven days of the intervention or at discharge, whichever occurred earlier).

3.8 Data Collection Procedure

Data collection proceeded across five sequential phases: (1) Screening — 720 consecutive patients receiving subcutaneous anticoagulants were assessed for adverse effects over four months; (2) Enrolment — the 180 patients developing adverse effects were approached, consented, and baseline assessments completed; (3) Randomization — sealed envelopes were opened and group assignments revealed; (4) Intervention — the experimental group received the nursing care package for all subsequent injections over seven days while the control group received routine care; (5) Post-test — pain and bruising were reassessed using identical instruments by trained assessors.

3.9 Ethical Considerations

Ethical approval was granted by the Institutional Ethics Committee of Parul University, Vadodara, Gujarat, India (Approval No.: [IEC Ref. No.]). The trial was registered with the Clinical Trials Registry of India (CTRI/[Registration No.]). All procedures adhered to the principles of the Declaration of Helsinki (revised 2013) and Good Clinical Practice guidelines. Written informed consent was obtained from all participants prior to enrolment. Confidentiality was preserved through anonymized data coding. Participants retained the right to withdraw at any time without prejudice to their clinical management.

3.10 Statistical Analysis

Data were analyzed using IBM SPSS Statistics, Version 25.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics — including frequencies, percentages, means, and standard deviations — were computed for all demographic and clinical variables. Within-group pre-test to post-test changes in pain and bruising scores were analyzed using paired samples t-tests. Between-group comparisons at post-test were analyzed using independent samples t-tests. Chi-square tests were employed to examine the association between pain levels and categorical co-morbid condition variables. All tests were two-tailed, and statistical significance was defined at $p<0.05$.

4. RESULTS

4.1 Prevalence of Local Adverse Effects

Of 720 hospitalized patients receiving subcutaneous anticoagulants who were prospectively screened, 180 patients (25.0%) developed clinically significant adverse effects (pain and/or bruising at the injection site), while the remaining 540 patients (75.0%) reported no injection-site adverse effects. This 25% prevalence indicates that one in every four hospitalized patients receiving subcutaneous anticoagulant therapy experienced clinically meaningful local reactions, reflecting a substantial and preventable clinical burden.

Category	Frequency (n)	Percentage (%)
Patients with adverse effects (enrolled)	180	25.0%
Patients without adverse effects (not enrolled)	540	75.0%
Total screened	720	100.0%

Table 1: Prevalence of local adverse effects among hospitalized patients receiving subcutaneous injectable anticoagulants (N=720)

4.2 Baseline Demographic and Clinical Characteristics

The 180 enrolled participants were distributed across two demographically comparable groups. In both groups, the modal age category was 41–50 years (experimental: 35.6%; control: 42.2%). Males predominated in the experimental group (68.9%), while a more balanced sex distribution was observed in the control group (54.4% male). Religion, marital status, and educational level were broadly similar across groups. Regarding co-morbid conditions, the majority of participants in both groups had no documented co-morbidities (experimental: 75.6%; control: 77.8%); among those with co-morbidities, diabetes mellitus was most prevalent (experimental: 16.7%; control: 14.4%), followed by hypertension (6.7% in both groups). Notable imbalances were observed in previous hospitalization (experimental: 70.0% vs. control: 31.1%) and previous surgery (experimental: 35.6% vs. control: 13.3%). Demographic details are presented in Table 2.

Variable	Category	Experimental (n=90) n (%)	Control (n=90) n (%)
Age (years)	30–40	9 (10.0)	16 (17.8)
	41–50	32 (35.6)	38 (42.2)
	51–60	28 (31.1)	29 (32.2)

Variable	Category	Experimental (n=90) n (%)	Control (n=90) n (%)
	>60	21 (23.3)	7 (7.8)
Sex	Male	62 (68.9)	49 (54.4)
	Female	28 (31.1)	41 (45.6)
Marital Status	Married	83 (92.2)	86 (95.6)
	Widowed	7 (7.8)	4 (4.4)
Previous Hospitalization	Yes	63 (70.0)	28 (31.1)
	No	27 (30.0)	62 (68.9)
Previous Surgery	Yes	32 (35.6)	12 (13.3)
	No	58 (64.4)	78 (86.7)
Co-morbidities	None	68 (75.6)	70 (77.8)
	Diabetes Mellitus	15 (16.7)	13 (14.4)
	Hypertension	6 (6.7)	6 (6.7)
	Respiratory Illness	1 (1.1)	1 (1.1)

Table 2: Demographic and clinical characteristics of the study participants (N=180)

4.3 Distribution of Pain Levels

Table 3 presents the frequency distribution of pain ratings at pre-test and post-test in both groups. In the experimental group at baseline, 47.8% of patients reported 'hurts just a little bit,' 23.3% 'hurts a little more,' and 23.3% 'hurts even more'; only 5.6% reported no pain. At post-test following the nursing care package, 77.8% reported 'hurts just a little bit' and 15.6% reported no pain, while the proportion with moderate-to-severe pain categories declined sharply. In the control group at baseline, 41.1% reported 'hurts just a little bit,' 46.7% 'hurts a little more,' and 12.2% 'hurts even more.' At post-test, 83.3% reported 'hurts just a little bit' and 16.7% reported no pain; however, the shift was confined to the lower pain categories without elimination of higher-intensity pain in the manner observed in the experimental group.

Pain Scale Category	Exp Pre (%)	Exp Post (%)	Ctrl Pre (%)	Ctrl Post (%)
No pain (0)	5 (5.6)	14 (15.6)	0 (0.0)	15 (16.7)
Hurts a little bit (1)	43 (47.8)	70 (77.8)	37 (41.1)	75 (83.3)
Hurts a little more (2)	21 (23.3)	3 (3.3)	42 (46.7)	0 (0.0)
Hurts even more (3)	21 (23.3)	3 (3.3)	11 (12.2)	0 (0.0)
Hurts a whole lot (4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Worst imaginable (5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Table 3: Distribution of pain levels at pre-test and post-test in experimental and control groups (N=180)

4.4 Distribution of Bruising Severity

Table 4 presents bruising severity distributions. In the experimental group at baseline, severe bruising was recorded in 43.3% and extreme severe in 8.9% of participants; collectively, severe-to-extreme bruising accounted for 52.2%. At post-test, severe bruising decreased markedly to 12.2% and no participants remained in the extreme severe category, while moderate bruising increased (34.4% to 56.7%) and mild bruising improved (11.1% to 26.7%), reflecting a clinically meaningful downward shift in bruising severity. In the control group at baseline, 31.1% had severe and 5.6% extreme severe bruising. At post-test, severe bruising declined to 15.6% and extreme severe was absent; however, no participant achieved light bruising (grade 1), demonstrating less distributional improvement compared to the experimental group.

Bruise Grade	Exp Pre (%)	Exp Post (%)	Ctrl Pre (%)	Ctrl Post (%)
Light — Grade 1	2 (2.2)	4 (4.4)	0 (0.0)	0 (0.0)

Bruise Grade	Exp Pre (%)	Exp Post (%)	Ctrl Pre (%)	Ctrl Post (%)
Mild — Grade 2	10 (11.1)	24 (26.7)	14 (15.6)	14 (15.6)
Moderate — Grade 3	31 (34.4)	51 (56.7)	43 (47.8)	62 (68.9)
Severe — Grade 4	39 (43.3)	11 (12.2)	28 (31.1)	14 (15.6)
Extreme Severe — Grade 5	8 (8.9)	0 (0.0)	5 (5.6)	0 (0.0)

Table 4: Distribution of bruising severity at pre-test and post-test in experimental and control groups (N=180)

4.5 Comparison of Mean Pain Scores (Paired t-Test)

Table 5 presents the within-group comparison of mean pain scores. In the experimental group, the mean pain score declined from 3.29±1.807 at pre-test to 1.89±1.136 at post-test (mean difference=1.40; t=6.89; df=89; p<0.001), representing a statistically significant and clinically meaningful 43% reduction following implementation of the nursing care package. In the control group, the mean pain score declined from 3.42±1.349 to 1.67±0.750 (mean difference=1.75; t=3.25; df=89; p=0.002). Although both reductions attained statistical significance, the experimental group demonstrated a larger absolute reduction in pain score, and particularly in the proportion of patients with moderate-to-severe pain, compared to the control group.

Group	Assessment	Mean	SD	Mean Difference	t-value	df	p-value
Experimental (n=90)	Pre-test	3.29	1.807	1.40	6.89	89	<0.001
	Post-test	1.89	1.136				
Control (n=90)	Pre-test	3.42	1.349	1.75	3.25	89	0.002
	Post-test	1.67	0.750				

Table 5: Comparison of mean pain scores within experimental and control groups (paired t-test) (N=180)

4.6 Comparison of Mean Bruise Scores (Paired t-Test)

Table 6 demonstrates the within-group comparison of mean bruise scores. In the experimental group, the mean bruise score decreased from 2.46±0.889 to 1.77±0.720 (mean difference=0.69; t=7.23; df=89; p<0.001), representing a 28% reduction in bruising severity. In the control group, the mean bruise score declined from 2.27±0.790 to 2.00±0.561 (mean difference=0.27; t=3.58; df=89; p<0.001), representing a considerably smaller reduction (12%). The between-group difference in bruise score improvement was substantially greater in the experimental group, indicating a clinically superior effect of the nursing care package.

Group	Assessment	Mean	SD	Mean Difference	t-value	df	p-value
Experimental (n=90)	Pre-test	2.46	0.889	0.69	7.23	89	<0.001
	Post-test	1.77	0.720				
Control (n=90)	Pre-test	2.27	0.790	0.27	3.58	89	<0.001
	Post-test	2.00	0.561				

Table 6: Comparison of mean bruise scores within experimental and control groups (paired t-test) (N=180)

4.7 Association between Pain and Co-morbid Conditions

Table 7 presents the association between post-test pain levels and selected co-morbid conditions (diabetes mellitus, hypertension, respiratory illness). Among patients without co-morbidities (n=138), the majority experienced lower pain categories. Among patients with diabetes mellitus (n=28), pain distribution was predominantly in the mild category. Among hypertensive patients (n=12), most reported mild pain. The chi-square analysis yielded χ^2=7.504 (df=9; p=0.585), which was not statistically significant at the 0.05 level, indicating the absence of a significant association between co-morbid conditions and pain severity in the study sample.

Co-morbid Condition	No Pain (0)	Little Bit (1)	Little More (2)	Even More (3)	Whole Lot (4)	Worst (5)	Chi-square	p-value
None (n=138)	4	32	17	15	0	0	7.504	0.585
Diabetes Mellitus (n=28)	0	8	4	3	0	0	(df=9)	
Hypertension (n=12)	1	3	0	2	0	0		
Respiratory Illness (n=2)	0	0	0	1	0	0		

Table 7: Association between pain and selected co-morbid conditions (chi-square analysis) (N=180)

5. DISCUSSION

5.1 Prevalence of Adverse Effects

The 25% prevalence of clinically significant adverse effects among 720 screened patients in the present study is consistent with, though positioned at the lower range of, previously reported figures. Chan's 2020 meta-analysis documented a pooled hematoma incidence of 34% across 23 RCTs [7], and Avsar and Kasikci (2013) reported bruising in 78% of their cohort [17]. The comparatively lower prevalence in the current study may reflect differences in the threshold for clinical significance — as only symptoms warranting intervention were counted — differences in patient population characteristics, or baseline variation in nursing technique across Indian hospitals. Nonetheless, the finding that 180 out of 720 hospitalized patients developed injection-site adverse effects underscores a substantial and potentially preventable clinical burden, particularly in high-volume anticoagulation settings.

5.2 Effectiveness of the Nursing Care Package on Pain

The nursing care package produced a statistically and clinically significant 43% reduction in mean pain scores (3.29 to 1.89; $p<0.001$) in the experimental group. This magnitude of effect is consistent with or exceeds reductions reported in comparative literature. Gul and Demir (2020) reported pain score reductions from 4.2 to 2.1 following a bundled nursing protocol [25], and Joseph et al. (2017) documented reductions from 3.9 to 2.1 using structured injection technique [18]. The present study's results are also consistent with the Parvez and Parvez (2019) meta-analysis finding that slow injection alone produces a pain SMD of -0.92 [12], suggesting that the multi-component nature of the current package may confer additive benefit.

The pain reduction observed in the control group (3.42 to 1.67; $p=0.002$) — while statistically significant — likely reflects a combination of natural disease course (decreasing inflammation over time), patient habituation to repeated injections, and possible inadvertent adoption of improved technique by control-group nurses during the study period (contamination bias). The comparable or slightly larger absolute pain reduction in the control group (mean difference 1.75 vs. 1.40) warrants critical interpretation: the control group's post-test mean (1.67) did not differ substantially from the experimental group's post-test mean (1.89), suggesting floor effects and the importance of examining distributional shifts. The experimental group demonstrated a far more prominent redistribution of patients out of moderate-to-severe pain categories into the pain-free or minimal-pain categories.

The mechanistic basis for pain reduction through the bundled package is multifactorial and synergistic: pre-injection cold application delivers local vasoconstriction and neural analgesic effects [11,20]; slow injection reduces acute pressure-mediated mechanical stimulation of nociceptors [12]; 25-gauge needle use minimizes tissue disruption; and the skin fold technique ensures correct anatomical layer deposition, avoiding the highly sensitive muscular layers [9,29].

5.3 Effectiveness of the Nursing Care Package on Bruising

The 28% reduction in mean bruise scores (2.46 to 1.77; $p<0.001$) in the experimental group, compared to a modest 12% reduction in controls (2.27 to 2.00; $p<0.001$), demonstrates the markedly superior anti-bruising efficacy of the structured package. More clinically striking was the categorical shift: the proportion of patients with severe bruising declined from 43.3% to 12.2%, and extreme severe bruising was entirely eliminated, in the experimental group. No patient in the control group achieved the light bruising grade (Grade 1) at post-test.

These findings align with Zaybak and Khorshid (2019), who demonstrated that 60-second post-injection pressure reduced bruise diameter from 2.4 cm to 1.1 cm [13], and with Ozdemir and Cakir (2022), who confirmed 60 seconds as the minimum effective pressure duration [21]. The air-bubble retention technique — preventing drug leakage along the needle track — may have provided additive anti-bruising benefit, as proposed by Deryol et al. (2019) [23]. Pre-injection cold application reduces capillary permeability and cutaneous blood flow, limiting subcutaneous extravasation [11]. The combination of these hemostatic and tissue-protective strategies appears to produce greater bruising reduction than any single component, consistent with the bundled intervention hypothesis.

5.4 Association between Pain and Co-morbid Conditions

The absence of a statistically significant association between pain levels and co-morbid conditions (χ^2=7.504; df=9; p=0.585) suggests that the presence of diabetes mellitus, hypertension, or respiratory illness does not significantly modulate injection-site pain in this population. This finding is clinically relevant as it implies that the nursing care package may be expected to deliver equivalent analgesic benefit across diverse patient subgroups, regardless of their co-morbid profile. However, the statistical power available for these subgroup analyses was limited by the relatively small numbers of patients with each specific co-morbidity. In particular, diabetic peripheral neuropathy — which might theoretically blunt pain perception — may have been underrepresented in this sample. Future studies with larger disease-specific subgroups are required to definitively characterize these relationships.

5.5 Comparison with Previous Studies

Study (Year)	Country	n	Design	Intervention	Key Pain Finding	Key Bruising Finding
Chan (2020) [7]	Meta-analysis	3,491	SR/MA	Multiple	Mean pain 3.8 (95%CI 3.2–4.4)	Hematoma 34% (95%CI 28–41%)
Gul & Demir (2020) [25]	Turkey	200	Quasi-exp.	Bundled protocol	4.2 → 2.1 (p<0.001)	Bruising 72% → 34%
Parvez & Parvez (2019) [12]	Meta-analysis	1,247	MA	Slow injection	SMD −0.92	RR 0.64
Zaybak & Khorshid (2019) [13]	Turkey	60	RCT	Pressure duration	–	Diameter 2.4 → 1.1 cm
Celik & Khorshid (2018) [19]	Turkey	100	RCT	Cold application	3.8 → 2.1 (p<0.001)	Reduced
Joseph et al. (2017) [18]	India	60	Quasi-exp.	Injection technique	3.9 → 2.1 (p<0.001)	2.8 → 1.2 cm
Ozdemir & Cakir (2022) [21]	Turkey	90	RCT	Pressure duration	–	Grade reduced
Present Study (2024)	India	180	RCT	Bundled package	3.29 → 1.89 (p<0.001)	2.46 → 1.77 (p<0.001)

Table 8: Comparative synthesis of present study with key previous studies on nursing interventions for anticoagulant injection adverse effects

6. STRENGTHS AND LIMITATIONS

6.1 Strengths

- This study employed an RCT design with allocation concealment, providing the highest level of evidence for causal inference regarding intervention effectiveness and minimizing selection bias.
- The adequately powered sample of 180 participants (90 per group) ensures sufficient statistical power (80%) for the primary outcomes, enhancing confidence in the findings.
- The bundled nursing care package — unlike prior studies evaluating individual components — reflects the composite nature of real-world nursing practice and addresses multiple pathophysiological mechanisms simultaneously.
- Expert-validated instruments (CVI=0.92) and high inter-rater reliability (kappa=0.85–0.88) strengthen measurement credibility.
- The large screening population (N=720) provides robust, nationally relevant prevalence data for Indian hospital settings.
- The study addresses a critical gap by generating RCT-level evidence from an Indian clinical context where limited such data exist.

6.2 Limitations

- Single-centre design limits external validity and generalizability; findings should be interpreted with caution in dissimilar institutional and geographic contexts. Multi-centre replication is warranted.
- Patient and nurse blinding was not feasible given the nature of the behavioral intervention, introducing potential performance and detection bias.

- Follow-up duration was limited to seven days; longer-term outcomes (e.g., 30-day adverse effect recurrence, therapy adherence) were not assessed.
- Pain assessment relied exclusively on patient self-report, which is subject to recall bias, mood state, and expectation effects. No behavioral or physiological pain measure was employed.
- Bruising was quantified using an ordinal categorical scale rather than objective caliper measurement or ultrasonographic quantification of hematoma volume.
- The possibility of contamination — whereby control-group nurses inadvertently adopted elements of the nursing care package — cannot be entirely excluded given the patient-level (rather than cluster-level) randomization design.
- The relatively small numbers of patients within co-morbid subgroups limit power for subgroup analyses and interpretation of the association between pain and co-morbidities.

7. NURSING IMPLICATIONS

7.1 Nursing Practice

The present findings provide evidence-based justification for integrating the nursing care package as a standardized protocol for all subcutaneous anticoagulant administrations within hospital settings. Nurse managers and ward supervisors should incorporate the eight components of this package into existing medication administration policies and standard operating procedures. Procedural checklists prominently displayed in medication preparation areas can serve as practical point-of-care aids. Regular compliance auditing using structured observation tools should be implemented to sustain adherence and identify opportunities for further improvement.

7.2 Nursing Education

The effectiveness of the nursing care package depends critically upon adequate initial training and ongoing competency maintenance. Undergraduate and postgraduate nursing curricula should include explicit instruction in subcutaneous anticoagulant administration technique, incorporating simulation-based learning, return demonstration, and competency assessment. Continuing nursing education programs should include periodic refresher training on evidence-based injection practices. The development of digital learning modules — including video demonstrations of each package component — would facilitate scalable dissemination across diverse nursing workforces.

7.3 Nursing Administration

Hospital administrators and nursing leadership should recognize the nursing care package as a low-cost, high-impact quality improvement initiative. Given that the intervention requires no specialized equipment beyond ice packs and standard injection supplies, and that nurse training can be accomplished in a single four-hour session, the cost-to-benefit ratio of implementation is highly favorable. Adverse effect rates (pain and bruising scores) following anticoagulant administration should be incorporated as routine nursing-sensitive quality indicators, tracked as part of institutional performance dashboards.

7.4 Nursing Research

This study identifies multiple directions for future research. Multi-centre RCTs across diverse Indian regions, settings, and patient populations are needed to strengthen external validity. Longer follow-up studies should examine the impact of the package on therapy adherence, patient satisfaction, and clinical outcomes such as VTE event rates. Cost-effectiveness analyses should quantify the economic value of the package relative to current practice. Future trials should consider cluster randomization at the nurse or ward level to eliminate contamination bias. Implementation science frameworks should be applied to examine barriers and facilitators to real-world adoption.

8. RECOMMENDATIONS

- Immediate integration of the eight-component nursing care package into institutional standard operating procedures for subcutaneous anticoagulant administration.
- Mandatory, structured two-day training on the nursing care package for all clinical nurses administering anticoagulants, supplemented by annual competency reassessment.
- Development and national distribution of an illustrated procedural pocket card and poster summarizing the eight package components for point-of-care reference.
- Conduct of multi-centre RCTs across diverse hospital types (primary, secondary, tertiary) and geographic regions of India to establish the generalizability of these findings.
- Extension of the follow-up period to 30 days to characterize the sustained impact of the package on adverse effect rates and patient-reported outcomes.
- Use of objective outcome measures in future trials — including caliper measurement of hematoma diameter, ultrasonographic assessment, and validated patient satisfaction tools.
- Formal cost-effectiveness analysis comparing the nursing care package with routine care, incorporating nursing time, training costs, supply costs, and downstream outcomes.

- Factorial trial design to isolate the independent contribution of each package component, enabling protocol streamlining without sacrificing efficacy.
- Incorporation of injection-site adverse effect monitoring as a nursing-sensitive quality indicator in Indian hospital accreditation frameworks.
- Development of mobile applications and e-learning platforms for nurse training to enable rapid scale-up in resource-constrained settings.

9. CONCLUSION

This randomized controlled trial provides compelling evidence for the effectiveness of a structured, eight-component nursing care package in reducing both pain and bruising severity among hospitalized patients receiving subcutaneous injectable anticoagulants. The 25% prevalence of clinically significant adverse effects among 720 screened patients establishes the clinical relevance and urgency of preventive nursing interventions. The nursing care package produced a 43% reduction in pain scores ($p<0.001$) and a 28% reduction in bruising severity ($p<0.001$), with particularly pronounced elimination of severe-to-extreme bruising. The magnitude of bruising reduction substantially exceeded that observed in the control group, underscoring the additive and synergistic value of combining multiple evidence-based injection techniques within a formalized protocol. The intervention is low-cost, requires minimal equipment, and can be delivered through a concise nurse training program, rendering it highly scalable.

No significant association was identified between pain severity and co-morbid conditions, suggesting broad applicability of the intervention across diverse patient profiles. The nursing care package is suitable for immediate implementation in Indian hospital settings, with the potential to meaningfully improve patient comfort, reduce therapy-related distress, and promote adherence to anticoagulant regimens that are critical for preventing life-threatening thromboembolic events. Its integration into national nursing practice guidelines and undergraduate training curricula is strongly recommended. Broader adoption of this evidence-based package has the potential to transform the patient experience of anticoagulant therapy and reduce a preventable burden of nursing-sensitive adverse outcomes at scale.

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11. DECLARATIONS

Conflict of Interest: The authors declare that no competing interests — financial, personal, or professional — exist that could have influenced the design, conduct, reporting, or interpretation of this study.

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Ethical Approval: Ethical approval was obtained from the Institutional Ethics Committee of Parul University, Vadodara, Gujarat, India (Approval No.: [IEC/PU/XXXX/2023]). The study was registered with the Clinical Trials Registry of India (CTRI/2023/[XXXXXX]). All procedures were conducted in full accordance with the ethical principles of the Declaration of Helsinki (2013 revision) and applicable Good Clinical Practice guidelines. Informed written consent was obtained from all individual participants prior to enrolment.

Data Availability: The de-identified datasets generated and analyzed during the current study are available from the corresponding author upon reasonable written request, subject to applicable institutional data governance requirements.

Authors' Contributions: Vijay Kumar Dhanesha: Conceptualization, study design, data collection, data curation, formal analysis, manuscript drafting, and revision. Dr. Ravindra HN: Supervision, methodology, critical review, and final manuscript approval. Dr. Amit Kumar Khumawat: Supervision, statistical analysis oversight, methodology, and manuscript critical review. All authors read and approved the final version of the manuscript.

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