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Comparing Pain of the First-generation Long-Acting Antipsychotic Injections among Three Different IM Techniques

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Abstract

Aim and objectives: To determine the optimal technique to prevent leakage and pain from LAIs, the study compared three types of intramuscular injection techniques: (a) Air-bubble technique, (b) Z-track method, and (c) a combination of the air-bubble technique and Z-track method.

Background: Long-acting antipsychotic injections (LAIs) are often injected through the muscle, allowing the medication to be slowly absorbed through it. Past literature yields inconclusive results in how to minimize the leakage and pain experienced at the injection site.

Design: This experimental study had a within-subjects design.

Methods: A total of 144 patients who received the first-generation LAIs were purposively sampled from a psychiatry hospital. All participants experienced the three types of injection methods over a 3-month period. They were all asked to rate their level of pain using the numerical rating scale, and after each injection, medical personnel rated the level of medication leakage at the injection site.

Results: No significant differences were found in the leakage level between the air-bubble technique, Z-track method, and the combination of the two ($F=0.53$, $p>0.05$). Pain level also showed no significant difference between the three types of injection methods during pre-injection ($F=0.68$ $p>.05$), 5 minutes post-injection ($F=0.87$, $p>0.05$), and 30 minutes post-injection ($F=0.97$, $p>0.05$).

Conclusion: During the injection of long-acting antipsychotic medication, we suggest consulting the guidance of a clinical injection expert. Choosing an injection method that is most familiar to the nursing staff would allow the minimization of medication leakage and pain at the injection site.

Relevance to clinical practice: Nurses should make sure the guidance of a clinical injection expert and verify knowledge of the IM injection skill. Choosing correct injection site and process that can effectively experience of pain and leakage at the injection site.

Keywords: Intramuscular injection; Long-acting antipsychotic medication; Pain; Leakage

What does this Paper Contribute to the Wider Global Clinical Community?

- Previous studies report that LAIs may cause occasional subcutaneous lumps and indurations, muscle granulomata, medication leakage, pain, redness, and fibrosis at the injection site.
- In attempting to minimize the problems resulting from LAIs, past studies have suggested that implementation of the air-bubble technique, the Z-track method, and a combination of the two methods are all more effective compared to standard IM injections.
- This study compared the level of leakage and pain after injection methods from air-bubble technique, the Z-track method, and the combination of the air-bubble technique and the Z-track method that was no difference.
- Nurses should make sure the guidance of a clinical injection expert and verify knowledge of the IM injection skill. Choosing correct injection site and process that can effectively reduce the experience of pain and leakage at the injection site.

Introduction

First- and second-generation long-acting antipsychotic injections (LAIs), made up of both oil-based and water-based depot injections, are used to improve the long-term treatment

of schizophrenia. Their development and introduction were part of the new age of antipsychotic medicine that began in the 1950s with the advent of the effective preparation fluphenazine enanthate [1]. LAIs can effectively lower the non-compliancy or frequency of patients with schizophrenia forgetting to take their medication, which in turn improves symptoms and decreases relapse. In addition, LAIs allow patients to maintain a better quality of life [2,3].

Intramuscular (IM) injection of LAIs allows the medication to be slowly absorbed through the muscle and is administered once every few weeks [1]. Due to its unique solvent, the first-generation long-acting antipsychotic medication is oil-based, while the second-generation is water-based. During the LAIs of the first-generation drug, leakage can occur that will cause different types of problems at the injection site. A number of studies report that LAIs may cause occasional subcutaneous lumps and indurations, muscle granulomata, medication leakage, pain, redness, and fibrosis at the injection site [4,5]. Local complications of the injection site may affect the quality of life of patients and negatively influence medication compliance.

A 1995 study recorded the acute and chronic responses from the injection of 224 psychiatry patients in the community. From the total of 5,072 injections, 42 patients (19.3%) experienced acute problems at the injection site, including the feeling of unusual pain (n=31), bleeding or hematoma (n=21), leakage (n=19), inflammation (n=11), and nodules (n=2). Additionally, injecting long-acting antipsychotic medication also resulted in chronic problems, including lump on injection site, and fibrosis, etc. Such problems may be related to the high dosage (injecting more than 1 ml), weekly injection, having at least a 5-year history of injection, and being older than 50 [6].

In attempting to minimize the problems resulting from LAIs, past studies have suggested that implementation of the air-bubble technique, the Z-track method, and a combination of the two methods are all more effective compared to standard IM injections [7,8].

The principles of the three types of IM injection techniques are the following: The first technique suggested by previous literature is the air-bubble technique. Medication is drawn into the syringe, leaving a 0.1 c.c. [9] or a 0.2 c.c. [10] air bubble in the barrel. Aspiration involves the standard injection technique, pulling back on the syringe plunger after the needle enters the skin. The air bubble helps to seal the injection site and prevents pain and leakage of medication from the muscle tissue. Drawing an additional air bubble into the empty syringe has two purposes: (a) to make sure the dosage is accurate, the air assists in pushing the remaining medication dosage out of the syringe; and (b) the air bubble helps to seal the injection site and prevents the medication from leaking out of the muscle tissue by Chaplin et al. Other researchers have believed that the air-bubble technique is outdated [11] or unsafe by Chaplin et al; however, the air-bubble technique is still currently widely applied in clinical injection [12].

The second technique suggested by previous literature is the Z-track method. The Z-track method is suitable on the IM injection among individuals aged 18-60 [13]. The Z-track method allows the nursing staff to stretch the skin of patients around the injection site. This technique pulls the skin in one direction prior to inserting the needle, allowing the skin and other tissue layers to be moved slightly, and to give better access to muscle tissues, while minimizing medication leakage and chronic reactions at the injection site [8,11]. The third type of technique suggested by previous literature combines the air-bubble technique with the Z-track method for IM injection [4,9].

When used in the injection of long-acting antipsychotic medication, the air-bubble technique, Z-track method, and the combined method have resulted in inconsistent findings in the minimization of pain and leakage. A comparison between the air-bubble technique and the Z-track method found no significant difference in patients' subjective pain level [7], while another study found that the air-bubble technique was effective in reducing pain, skin irritation, and injury at the injection site [14]. Regarding the medication leakage at the injection site, the air-bubble technique has been reported to effectively reduce the discomforts resulting from leakage [7,14]. Researchers have also published their experiences on the Z-track method injection, believing that this method could reduce the feelings of burn and pain, as well as fewer overall tissue reactions [13]. Combining the air-bubble technique and the Z-track method when injecting long-acting antipsychotic medication to reduce problems associated with medication leakage and pain has also been suggested [4,9].

IM injection is a frequent technique used by nurses in clinical settings; however, the injection process encompasses a complex association of judgment and skill. Past researchers did not describe whether the medication dosage for injection was different [15] or whether it was the same personnel who implemented the injection and set a standard protocol in the injection process, etc. [15,16], thus making it difficult to assess the effectiveness of various injection methods in reducing leakage and pain at the injection site. Although past literature has suggested different injection techniques for IM injection, findings remain inconclusive. Modern high-quality nursing provides empirical evidence as the basis for knowledge and skill. Intramuscular injection is a skill that nurses practice independently, but the skill often lacks effective empirical research to support its foundation. The present study was empirically designed to examine the first-generation LAI's pain and leakage effects of three types of IM injection techniques: the air-bubble technique, the Z-track method, and the combination of the air-bubble technique and the Z-track method.

Methods

Design, sampling, and setting

We employed a within-subjects design to compare the injection site reactions and pain among the three types of injection techniques. A purposively selected sample of participants was recruited from the outpatient department and rehabilitation ward of a psychiatric hospital in central Taiwan. This study was calculated the sample size for a repeated-measures ANOVA in G*Power version 3.1.9. The power of this

study was set at 80%, with a 95% confident interval and effect sixe was the effect size at 0.24 [14]. The calculated sample size was 150 patients. This study based on a previous study to calculate the dropout rate 30.6% [14]. Finally, 210 patients were needed.

Patients who were 20 years old and above, had a diagnosis of schizophrenia or affective schizophrenia, and were receiving IM injections of the first-generation LAIs were recruited into the study. Patients were excluded if they could not maintain their appointments at the outpatient department or if they had a refectory syndrome of psychosis. Additionally, patients whose medications were changed by their doctor during the three different types of injection were also excluded from the study analysis. Data were collected from April 2014 to October 2014.

We compared the three types of IM injections in the effectiveness of medication leakage and pain from LAIs. During the first injection phase, a total of 207 patients participated in the process. Thirty patients dropped out of the study, including 15 (7.25%) who have refused, 14 (6.76%) who lost connection in this study, and 1 patient who was admitted to the acute ward (0.5%). Participating in the second injection were 177 patients. Sixteen patients dropped out, including 15 (8.47%) who refused and 17 (9.6%) who lost connection in this study. The third injection included 145 participants. One patient did not complete the questionnaire, bringing the final total to 144 participants who completed all three injections, the results of which were entered into statistical analysis (**Figure 1**). The study dropout rate was 30.4%.

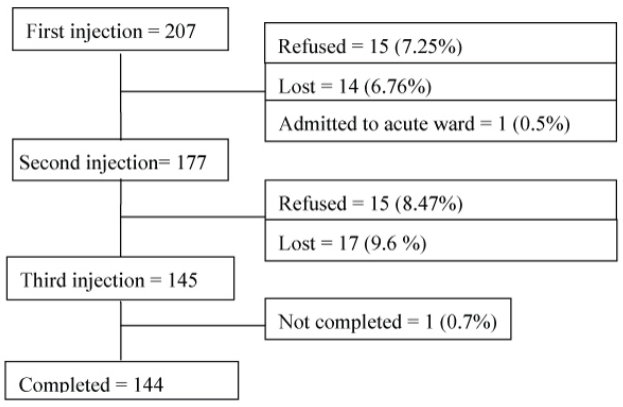

Figure 1: Sample flow chart of inclusion and dropout process.

Instruments

A structured questionnaire was developed by the researchers for data collection. The questionnaire contains three sections, which are addressed below:

1. Demographic information: Age, gender, onset of disorder, time duration receiving IM injections, number of hospitalizations, prior reactions at the injection site from IM injection, concerns about the injection reaction, type and dosage of medication injection, etc.

2. Hospital Anxiety and Depression Scale (HADS): The HADS, developed by Zigmond and Snaith [17], is a self-report questionnaire that assesses the anxiety and depression level of clinical patients. Answered on a 0-3 Likert-type scale, the HADS has a total of 14 items that include 7 on depression and 7 on anxiety. Questions on depression and anxiety are scored separately, with the subscales of each ranging from 0-21. Those who score 7 and below are not anxious or depressed; those who score 8-10 have a borderline level of anxiety or depression; and those who score an 11 or higher are considered to have anxiety or depression. Higher scores indicate a higher tendency for anxiety or depression. Anxiety (HADS-A) and depression (HADS-D) have correlations between the two subscales that vary from 0.40 to 0.74 (mean 0.56). Cronbach's alpha for HADS-A varies from 0.68 to 0.93 (mean 0.83) and for HADS-D from 0.67 to 0.90 (mean 0.82) [18]. In this study, Cronbach's alpha for HADS-A was 0.90 (mean 0.83) and for HADS-D was 0.87. The present study assessed the anxiety and depression level of the patients prior to each LAIs.

3. Pain and leakage assessment: For pain evaluation, the present study adopted the numerical rating scale (NRS), for which past studies have provided a good validity and reliability [19-21]. The patient's subjective pain level at the injection site was assessed and evaluated at three time points: pre-injection, 5 minutes post-injection, and 30 minutes post-injection. Actual feelings at the injection site were evaluated, and patients were asked to rate their level of pain from 0 (no pain) to 10 (great pain). The NRS was adopted to assess for subjective feelings of pain.

For medication leakage evaluation, previous studies often used visual estimations, which can result in error or bias. In the present study, the injection site was first pressed for 30 seconds. Next, oil-absorbing sheets were placed at the injection site, and the oil absorbed onto the sheet was measured and calculated for the greatest diameter.

Data Collection Process

Three IM techniques were compared to assess for the leakage and pain in the injection site from long-acting antipsychotic medication. The study was double-blinded (subjects and rater), and only the injection nurse knew the injection technique. Based on evidence-based research, the ventrogluteal site was chosen for injection [22-25]. The ventrogluteal site is considered safe because it is distant from the sciatic nerve and is an easy mark for nurses [23]. The Latin square design was used. It contained the three IM techniques and both ventrogluteal sites so that injections could be rotated [26]. Why change injection sites for depot antipsychotic medication? The injection nurse filled out an injection card for each participant to record the injection site and injection technique according to the Latin square.

The injections were administered with standard-size needles (3 ml syringe) and standard procedure (**Table 1**). Each injection was implemented by the same nurse, who had been trained by an injection expert, to make sure the three techniques were

carried out properly. All medication dosages and durations were made according to the doctor's orders.

Table 1: The steps of injection techniques used in this study.

	Air-bubble technique	Z-track method	Combination of air-bubble technique and Z-track method
Volume	As prescribed by doctor		
Air lock	0.1 ml air lock inserted	nil	0.1 ml air lock inserted
Syringe	3 ml		
Needle	23 G		
Injection site	Right or left ventrogluteal site (as the Latin square)		
Patient's position	Side-lying position, with the knee and hip joint of the uppermost leg flexed and placed anterior to the lower ley.		
Sterilization of injection site	Using 75% alcohol swab, cleanse the site in a circular motion for 30 s and allow to dry for 30 s prior to administration.		
Skin preparation	Hold the muscle firmly.	Nurse uses non-dominant hand to pull the skin and subcutaneous tissue 1–1.5 inches to one side of the injection site prior to injecting.	
Injection angle	90 degrees		
Aspiration for blood	If blood is aspirated, withdraw needle, and place dry gauze or sponge over site, and change to a new sterile equipment.		
Injection rate	10 s/ml		
After injection	Wait at least 10 s before removing the needle to prevent leakage of the medication at the site. Nurse removes the needle and uses gauze or sponge to cover the injection site. Don't massage the injection site.		

In order to prevent subjective bias, the present study was double-blinded (subjects and rater), and only the injection nurse knew the injection technique. The pre- and post-evaluations of leakage and pain at the injection site were made by a different nurse.

Ethical Considerations

This study was approved by the institutional review board of a psychiatric center located in central Taiwan (TTPC-102020). Written informed consent was obtained from all participants, who understood the purpose, procedure, and rights of the study. Their right to medical treatment was not affected if patients dropped out of the study.

Data Analysis

Data from the completed questionnaires were entered into a computerized database and analyzed using SPSS version 15.0 for Windows (SPSS Inc., Chicago, IL, USA). Data were analyzed by frequency, percentage means, standard deviations, one-way ANOVA, and Scheffé's post hoc test. The significance level was set at $p<0.05$.

Results

1. Demographic Information of the Participants: The majority of participants were male (n=82, 56.9%), with a mean age that ranged between 50 and 59 (n=56, 38.9). Over half of the participants had carried a diagnosis of schizophrenia for more than 21 years (n=81, 56.3); a majority had received LAIs for 5 years or less (n=49, 29.2); a majority have been hospitalized 2 to 5 times (n=63, 43.8). Almost half of the patients with schizophrenia received Haldol/Haldol Decanoate as their LAIs (n=71, 49.3%); the second most frequent was Flanxol depot (n=67, 46.5). Most medication dosages were 1 ml (n=107, 74.3; **Table 2**).

Table 2: Demographic Data of the Participants (n=144).

Variable	n (%)
Gender	
Male	82 (56.9)
Female	62 (43.1)
Age	
20–39 years	24 (16.7)
40–49 years	45 (31.3)
50–59 years	56 (38.8)
≥ 60 years	19 (13.2)
Duration of sickness	
≤ 10 years	18 (12.5)
11–20 years	45 (31.2)
≥ 21 years	81 (56.3)
Duration of LAIs	
≤ 5 years	42 (29.2)
6–10 years	23 (16.0)

11–15 years	19 (13.2)
16–20 years	29 (20.1)
≥ 21years	31 (21.5)
Hospital admissions	
Never	13 (9.0)
Once	31 (21.5)
2–5 times	63 (43.8)
≥ 6 times	38 (26.4)
Types of LAIs	
Haldol/Haldol Decanoate	71 (49.3)
Flanxol depot	67 (46.5)
Clopixol depot	6 (4.2)
Medication dosage/injection	
0.5 ml	2 (1.4)
1 ml	107 (74.3)
2 ml	35 (24.3)

2. Experience and Concerns about Reactions at the Injection Site: Participants recalled their experiences of LAIs and reported reactions at the injection site, including pain, the most frequent (n=55, 38.2%), followed by bleeding (n=32, 22.2%), itching (n=16, 11.1%), nodules (n=8, 5.6%), swelling (n=6, 4.2%), edema (n=2, 1.4%). Only one of the 144 patients experienced abscess at the injection site (0.7%).

Participants were the most concerned with two types of reactions at the injection site, which were pain and bleeding, with an average score of 0.08 (SD ± 0.37) and 0.08 (SD ± 0.28), respectively. In addition, other reactions of concern at the injection site included itching and nodules, with an average score of 0.06 (SD ± 0.34) and 0.06 (SD ± 0.26), respectively; followed by swelling, edema, and abscess, with an average score of 0.04 (SD ± 0.29), 0.02 (SD ± 0.14), and 0.01 (SD ± 0.12; **Table 3**).

3. Injection site reaction among the three types of intramuscular injections: Prior to injection, the anxiety and depression of each participant were assessed using the HADS. No significant difference was found between the three types of injections prior to injection (F = 1.20, p>0.05). In addition, the level of pain was also measured before each of the three types of injections, showing no significant difference (F=0.68, p>0.05).

The pain level assessed 5 minutes after injection showed no statistical significance (F=0.87, p>0.05) between the air-bubble technique, Z-track method, and the combined method. Comparisons of pain level between the three types of injection methods were again assessed 30 minutes after injection, also indicting no statistical significance (F=0.97, p>0.05). Leakage at the injection site showed no significant difference between the three types of injection methods (F=0.53, p>0.05; **Table 4**).

Table 3: Past Experience of Injection Site Reactions and Degree of Concern (n=144).

	Reactions Experienced		Ranking	Degree of Concern	Ranking
	No n (%)	Yes n (%)		Mean(SD)	
Pain	89 (61.8%)	55 (38.2%)	1	0.08 (0.37)	1
Swelling	138 (95.8%)	6 (4.2%)	5	0.04 (0.29)	3
Abscess	143 (99.3%)	1 (0.7%)	7	0.01 (0.12)	5
Edema	142 (98.6%)	2 (1.4%)	6	0.02 (0.14)	4
Nodules	136 (94.4%)	8 (5.6%)	4	0.06 (0.34)	2
Itching	128 (88.9%)	16 (11.1%)	3	0.06 (0.26)	2
Bleeding	112 (77.8%)	32 (22.2%)	2	0.08 (0.28)	1

Table 4: Injection Site Reactions among the Three Types of Injections (n=144).

	Air-bubble	Z-track	Air-bubble + Z-track	F	p
	M (SD)	M (SD)	M (SD)		
HADS	7.61 (5.32)	7.82 (5.51)	8.31 (5.75)	1.20	>0.05
Pain before injection	0.06 (0.37)	0.03 (0.17)	0.07 (0.50)	0.68	>0.05
After 5 minutes	0.19 (0.63)	0.22 (0.58)	0.30 (0.93)	0.87	>0.05
After 30 minutes	0.02 (0.25)	0.01 (0.08)	0.04 (0.31)	0.97	>0.05
Leakage	0.08 (0.19)	0.10 (0.25)	0.08 (0.23)	0.53	>0.05

Discussion

IM injection is a skill that nurses practice independently. The present study compared three types of IM injection techniques, including the air-bubble technique, the Z-track method, and the combination of the air-bubble technique and the Z-track method. Our study was designed to examine and compare the leakage and pain effects resulting from LAIs.

Various reactions are often experienced at the injection site after an injection, the most frequent of which is pain. Since it is necessary for the needle to be inserted through the skin and into the muscle tissue, the feeling of pain is thus inevitable. Patients also consistently report being most concerned about the feeling of pain after an injection. However, using the 10-point NRS for pain evaluation, the 5-minute post-injection did not show significance in pain level. In contrast, past researchers used the visual analog scale rating from 0 to 10, and found that the 5-minute post-injection pain level was between 2 and 4.5 [16]. However, pain levels did not show a significant difference in our study. Reasons for the difference in findings could be that

patients in our study were asked to lie down in a muscle-relaxed position, possibly reducing their feelings of pain.

Consistent with the findings of MacGabhann [7], our study found that the three types of IM injections showed no difference in the experience of pain level during LAIs. Previous studies have reported reducing pain level at the injection site by the air-bubble technique [14], the Z-track method [11,13], and the combined method to reduce pain and leakage [4,9]. However, findings in the present study showed no difference in the experience of pain between the three types of IM injections.

Previous reports have found that the air-bubble technique was able to reduce medication leakage at the injection site compared to the Z-track method [7,14]. However, findings in the present study showed no difference in the amount of leakage between the air-bubble technique, the Z-track method, and the combined method. No statistical difference was found when comparing the leakage level among the three types of injections.

We compared three types of IM injection techniques, including the air-bubble technique, the Z-track method, and the combination of the air-bubble technique and the Z-track method, which have been stated in past literature to be more effective than standard injection methods in decreasing the pain level and other injection reactions. Thus, we did not compare the pain experience and injection reaction of standard injection methods. Our study comparisons of pain and leakage between the three types of IM injection methods suggest the need for a proper implementation of the injection. When done correctly, no differences were observed in the leakage and pain from LAIs among all three types of IM injection techniques, including the air-bubble technique, the Z-track method, and the combination of the air-bubble technique and the Z-track method.

Limitations

This study had two advantages: First, the study used a within-subjects design to conducted a methodology examination. This study can stand on an individual level to compare the pain and leakage condition of three injection techniques. But these injection techniques are not generally needed for water based depots. Second, because this study was double-blinded (subjects and rater), and only the injection nurse knew the injection technique, it avoided bias in rater and patients. However, the investigators encountered several methodological challenges that were inherent to both the design and implementation of the study. The most problematic issue concerned the pain level measurement of 30 minutes after each injection. This study had 62 participants who dropped out, a 30.4% dropout rate. A total of 31 participants did not return to the outpatient department because they changed to another hospital or moved to another city. And 30 participants needed to catch the shuttle bus after their injection and could not wait to evaluate their pain level. This may have affected the study results.

Conclusion/Implications for Practice

The present study results showed no difference in the experience of pain level and leakage at the injection site when implementing the first-generation LAIs by the air-bubble technique, the Z-track method, and the combined method.

Participants were asked to position themselves lying down in a muscle-relaxed posture, and medication was injected at the ventrogluteal site. Additionally, the injection nurse had been trained by an injection expert to be familiarized with each of the three types of IM injection techniques. When administering LAIs in the future, we suggest that nurses first seek the guidance of a clinical injection expert and verify their knowledge of the IM injection skill. Choosing an injection technique with which the nurse feels most familiar and apt, whether the air-bubble technique, the Z-track method, or the combined method, can effectively reduce the experience of pain and leakage at the injection site.

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