CASE REPORT

Using ultrasonography in evaluating the intramuscular injection techniques used for administering drug treatments to schizophrenic patients in Japan

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Abstract: This study was conducted with six patients with schizophrenia, four of whom received the atypical antipsychotic risperidone long-acting injectable (RLAI), and two patients receiving the typical depot injection (TDI). The purpose of this study was to determine the location (gluteus medius or maximus; deltoid muscles) and diffusion of typical and atypical antipsychotic medications administered intramuscularly using ultrasonography. When using the standardized depth of needle insertion, in some cases, the drug was injected into the gluteus maximus instead of the gluteus medius. Similarly, in some cases the TDI was not visible in the ultrasonographic images until sixteen days after the injection. This verifies how hard the injection site becomes when microspheres of RLAI is injected as compared to other muscle areas. These results confirmed that the gluteus muscle structure was the ideal muscle for depot injection as evidenced by the injection solution being dispersed and rendered not visible immediately after intramuscular injection (IM). With the use of ultrasonography, injection sites and drug dispersions were evaluated under a direct visual guidance, suggesting that ultrasonography is a useful method for establishing evidence for determining correct insertion of IM injection, diffusion of medications, and the effective administration of IM injections. J. Med. Invest. 59: 213-219, February, 2012

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The medication for patients with schizophrenic can be classified into two: oral drugs and long-acting intramuscular (IM) injections. Oral drugs are easy to take, however patients may easily forget to take them or may choose to discontinue them. In the course of drug treatment, even a short period of partial adherence could increase the risk of the occurrence of relapse.

On the other hand, a long-acting IM injection is accompanied by pain from injection, but the medicinal effects can last for about two weeks (risperidone long-acting injectable) or four weeks (fluphenazine decanoate and haloperidol decanoate). Since with a long-acting injection, definite adherence can be expected as long as an injection is given, it is reported to be more effective in preventing relapses than oral drugs (1, 2).

Typical depot agents are oil preparations and possess the property of being gradually hydrolyzed by esterase in vivo (3). The ester body is administered dissolved in oil. However, these are known to frequently cause injection site reactions. For this reason, a technique to encapsulate the IM drug solution using the Z track method was introduced as a means to prevent injection site reactions (4). However, little evidence for its efficacy has been demonstrated (5, 6). Moreover, there have been concerns about oil preparations that are not properly injected into the right muscles, causing stronger injection site reactions.

The long-acting injectable atypical antipsychotic, risperidone long-acting injectable (RLAI), on the other hand, does not have a hydroxyl group, hence, it could not be made slow-release using long-chain fatty acids. It became possible then to administer RLAI as a soluble suspension after making it slow-release through a technology utilizing microspheres (7, 8). Moreover, it is known to cause little injection site reactions (9). That is, with RLAI, pain or swelling after an injection may be milder than after an injection of a typical depot injection (TDI).

Both TDI, fluphenazine decanoate and haloperidol decanoate, have side effects. Some advantages atypical antipsychotics have over typical antipsychotics are that there are fewer anticholinergic side effects, less parkinsonian and dystonia side effects, and these also suppress negative symptoms including a lower propensity for causing extrapyramidal side effects. The medication in RLAI is enclosed in tiny beads called “microspheres”. After these are injected into the muscle, they slowly dissolve, releasing a constant amount of the risperidone medication. RLAI became available in 2009, possessing the advantage of being an atypical antipsychotics and depot agents using, “microspheres.”

IM injections need to be accurately administered. Factors such as the patient’s unique build and sebum thickness need to be carefully considered. Therefore, when an IM injection is given, the depth of needle insertion is left to the assessment of the nurse. Until now, there have been no studies to confirm whether the drug administered was actually injected into the right muscles. Furthermore, no studies have been found that illustrated how the injection solution is absorbed in the muscle and about the differences in absorption between different drugs. By ensuring that drugs are successfully administered through IM injection, the effect of medications can be achieved, and may lead to improvement of patients’ QOL. Moreover, investigating the differences in drug absorption of muscles can also guide in administering IM injection.

Accordingly, in this paper the following ultrasonographic results derived from six cases provided answers to: 1) whether the injection solution was actually infused into the muscle; 2) the pharmacokinetics of the solution after the injection; 3) differences in absorption images between RLAI (water-soluble suspension) and TDI; and 4) hardness of the muscular system using elastography.

METHODS

Participants

Six patients with schizophrenia from two hospitals (in western and east Japan) joined the study. Four of the six schizophrenic patients were treated with RLAI while two were treated with TDI. Five patients had their treatments injected into their gluteus muscle while one patient received the TDI into his deltoid muscle.

Date collection

The study was conducted for a period of eight months (June 2010 to January 2011). Body weight and height were measured and body mass index (BMI) was calculated for all patients. Just before RLAI injection, the distance from epidermis to underfascia (DEUF), distance from epidermis to ilium (DEI) at bilateral gluteal sites, and the most recent RLAI injections were assessed through ultrasonography. Two patients treated with TDI were immediately evaluated after their injection as well as 16 days
thereafter. Additional measurements were taken for
(a) the distance from epidermis to upper-arm bone
and (b) the distance from epidermis to fascia of del-
toid muscle. All ultrasonographic measurements
were performed by an experienced sonographer us-
ing a 7.5 MHz linear and convex array transducer.
Ultrasonographic images were based on the dor-
sogluteal injection site. DEUF and DEI measure-
ments were made above and outside a line drawn
from the posterior superior iliac spine to the greater
trochanter of the femur. Gluteus maximus, medius,
and minimus muscles were used as common IM
injection regions.
Elastography is a quantitative approach for im-
aging linear elastic properties of tissues in order to
detect suspicious tumors (10). In this study, elas-
tography was used to visualize the tension of mus-
cle tissues after injection (11). When it was difficult
to determine the boundaries between the fascia or
subcutaneous tissues and muscles, the sonographer
applied pressure on the epidermis to identify the
boundaries through ultrasonography. In addition,
the patients were requested to clench their buttocks
for the sonographer to identify measurement sites
while observing the movement of the muscles and
subcutaneous tissues.
One particular nurse who had 15 years of expe-
rience of administering IM injection reported that
they identified the measurement site on the gluteal
muscles by using the “four-and three-way split”
method (12, 13), a method they perceived to be
valid and reliable (Fig. 1). Moreover, the nurse
noted that the injection site should not be at an
uneven surface of the skin. Ultrasonographic eval-
uation and neurosurgical expertise were also done
by two experienced nurses (23 and 30 years, respec-
tively). The results of the measurements were based
on the recorded image and after due discussion
among all the data gatherers (nurses, physicians,
and sonographers).
Date analysis
The ultrasonographic images of the six cases
were evaluated for the following: 1) whether the
solution was administered into the gluteus medius
or the deltoïd muscle; 2) absorption of the injection
solution; 3) differences in absorption images be-
tween RLAI and the TDI; and 4) hardness of the
muscular system using elastography. In RLAI injec-
tion, inserted needle length was calculated through
the total needle length subtracted by the remaining
needle length visible on the surface of the buttocks.
Further evaluation was then made through ultra-
sonography.
Ethical considerations
We conducted this study with the approval of the
ethics committees of the Tokushima University
Hospital, Tokushima Prefectural Central Hospital,
and Fujishiro Kensei Hospital. Verbal and written
informed consents were given by the six study par-
ticipants.
RESULTS
Case 1: It was confirmed through ultrasonogra-
phy that RLAI was injected and diffused into the
gluteus medius (Fig. 2). Nurses inserted the needle
while checking the needle position through echo
images. From the epidermis to the fascia was 13

![Figure 1. IM injection region in the buttocks “upper, outer quadrant” and “four-and three-way split” method.](image1)

![Figure 2. The left gluteal region to which the injection was inserted (Case 1).](image2)

Patient Information: Gender; female. Age: 48. Height; 142 cm. Weight; 70 kg. BMI; 34.8 kg/m². RLAI dosage; 50 mg.
mm. When the needle passed through the epidermis and the fascia, RLAI was injected while still monitoring the position of the needle tip. The depth of needle insertion was 46 mm.

Case 2: This ultrasonographic image shows that immediately after RLAI had been injected into the gluteus maximus muscle instead of the gluteus medius (Fig. 3). The encircled part shows that RLAI was injected into the gluteus muscle. From the epidermis to the fascia of the gluteus muscle was 11.1 mm.

Case 3: RLAI was administered to the patient two weeks ago. The length of the RLAI needle inserted was 32 mm. The distance from the epidermis to the fascia was 18.19 mm. The penetration depth was 21.66 mm. The encircled part shows that RLAI was injected into the gluteus maximus muscle. The needle was considered to be obliquely-inserted at an angle against the skin surface. In this image, the injected RLAI seemed like an echogenic mass in the gluteus maximus muscle (Fig. 4).

Case 4: With the evaluation immediately after the RLAI injection using elastography, there were differences in the hardness between the areas around the injection site and the other muscle sites. The left part of the elastographic image below illustrates the muscle tissues. The blue portions show the hardening of muscle tissue (Fig. 5).

Case 5: The pharmacokinetic evaluation of the solution two weeks after the injection confirmed the actual infusion of the RLAI into the gluteus medius. (Fig. 6) It was able to confirm that the assessment
made on the depth of needle during insertion by the nurse who performed the IM injection was appropriate.

Case 6: On the other hand, when the TDI was taken immediately after the injection, the echogenic image did not appear in the ultrasonographic image (Fig. 7). The distance from epidermis to fascia of muscle was 9.1 mm, and distance from epidermis to the ilium measured 59.9 mm.

**Figure 7.** The right gluteal region where an injection was given immediately after the injection (Case 6).
*Patient Information : Gender ; male. Age ; 51. Height ; 177 cm. Weight ; 67 kg. BMI ; 21.39 Kg/m². Haloperidol decanoate dosage ; 100 mg.*

Case 7: The ultrasonographic images also showed cyst-like (peanut-shaped) images for the TDI (fluphenazine decanoate) sixteen days after the injection, and little diffusion was observed (Fig. 8).

**Figure 8.** The light region where an injection was given 16 days ago. The distance from epidermis to upper-arm bone was 21.6 mm, and from epidermis to fascia of deltoid muscle was 3.5 mm (Case 7).
(a) Distance from epidermis to upper-arm bone.
(b) Distance from epidermis to under-fascia of deltoid muscle.
*Patient Information : Gender ; male. Age ; 58. Height ; 160 cm. Weight ; 51 kg. BMI ; 19.99 Kg/m². Fluphenazine decanoate dosage ; 25 mg.*

**DISCUSSION**

It has been commonly believed that an injection site located using the upper outer quadrant method should have the gluteus medius below the subcutaneous tissues; however in some cases in this study, the gluteus maximus overlaid that area. It is said that in about 30% of autopsied bodies, the gluteus maximus overlies the gluteus medius as observed in the cases in the present study (14). From the viewpoint of IM injection, the same efficacy can be expected from the injection into the gluteus maximus, however the gluteus medius is believed to be thicker than the gluteus maximus, allowing safer and more accurate absorption of the drug solution. For this reason, when giving an injection in such cases, we need to insert the needle into the gluteus medius while taking into account the thickness of the gluteus maximus.

In this study, the examiners confirmed the depth of the needle insertion by putting a mark on the needle with a pen. In some cases the needle still did not reach the gluteus medius, even though it was inserted over 10 mm deeper than the depth to the fascia. These cases are believed to have been caused by the position of the nurse upon administering the injection. The needle might have been inserted at an angle other than 90 degrees and did not reach the gluteus medius. Furthermore, in some cases, the injection solution was seen flowing between the gluteus medius and gluteus maximus, and there might have been many such IM injection cases in the past.

We gave injections while checking the ultrasonographic images. It was considered that there would be limitations to the assessment of the three-dimensional IM structure through the two-dimensional images, so recognizing these limitations may be important for giving IM injections safely.

The elastographic examination indicated differences in the hardness between the areas around the injection site and other muscle sites and the injected muscle was considered harder compared to the rest of the area. This verifies how hard the injection site becomes when microspheres of RLAI are injected into muscle areas. Since we only focused on this particular aspect, further investigation needs to be done regarding the effect of other IM injections to muscle hardness.

Also, two weeks after the injection, it was confirmed that the RLAI remained inside the buttok muscles with its microspheres intact and was
diffused across a wide area. From these results it became clear that with RLAI it is easy to check the actual IM injection and diffusion using ultrasonography.

On the other hand, when the image was taken immediately after the TDI the absorption did not appear in the ultrasonographic images, perhaps due to the composition of the drug a difference between water-soluble and oil-based solutions. However, cyst-like (peanut-shaped) ultrasonographic absorption images can be seen 16 days after. The peanut-sized cyst-like image seen was believed to be due to the hardness of the muscles as a resulting effect of the ability of oily TDI medication absorption. This muscle hardening was also confirmed by the patient.

**CONCLUSION**

This study compared two cohorts of patients with schizophrenia treated with different types of RLAI and TDI injected into the gluteus and deltoid muscles through ultrasonography. When the standardized depth of needle was inserted following the standard procedure, the drug was injected into the gluteus maximus instead of the gluteus medius in some cases. However, the TDI did not appear in the ultrasonographic images immediately after injections, rather sixteen days after. From these results, it was affirmed that the buttock muscle structures are the ideal areas for RLAI injection as evident in the ultrasonographic images indicating appropriate dispersion of medication within this sites.

With the use of ultrasonography, injection sites and drug diffusion can be checked under direct visual guidance. Therefore, it was suggested that ultrasonography could be a very useful tool in establishing evidence for safe administration of IM injections.

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**CONFLICT OF INTEREST**

None of the authors have any conflicts of interest to declare.

**REFERENCES**


