

Quantification of Injection-Induced Pain in Rats Using Electromyography



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Introduction

Protein-based therapeutics, such as various vaccines and antibody drugs, are commonly injected through subcutaneous or intramuscular routes, and the injection-induced pain is a frequent adverse effect. Therefore, when multiple drugs exhibit similar efficacy, it is important to select ones with less injection-induced pain. However, predicting and evaluating the pain during preclinical studies remains challenging. In this study, we quantified injection-induced pain using electromyograms (EMGs) recorded during injection.

Materials and Methods

Animals

Male Wistar rats (7–10 weeks old) and male Sprague-Dawley (SD) rats (both from Japan SLC, Inc.) were used for the subcutaneous and Intravascular administration studies, respectively. The animals were housed in a room maintained at 20–26° C with a relative humidity of 35–75%, under a 12-hour light/dark cycle (lights on from 07:00 to19:00)

Experimental groups

Subcutaneous injection

Treatment	N
0.9% NaCl, 50 μL	5
10% NaCl, 50 μL	5
Dilute HCl (pH3) , 50 μL	4
0.9%NaCl, 200μL	2

Femoral circumflex artery injection (500μL/animal)

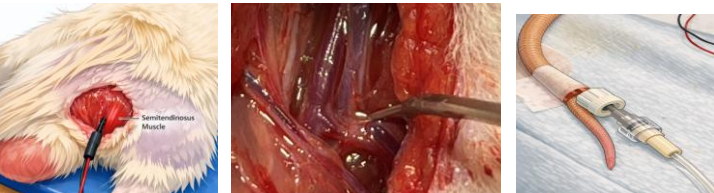
Treatment	N	Pre treatment
Saline	10	-
20%Glucose	4	-
0.05%Gemcitabine	3	-
Fentanyl/Gemcitabine	3	Fentanyl 5 μg/kg, i.v.

Tail vein injection (300 μL/animal)

Treatment	N
0.9% NaCl	7
Citrate buffer (pH4.5)	7

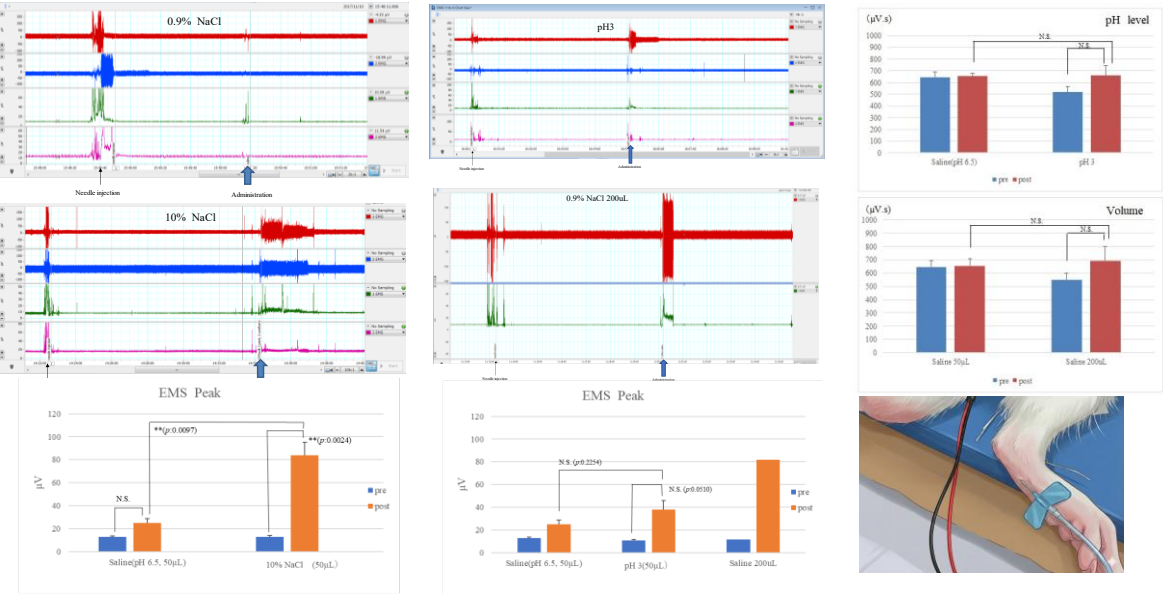
Measurement

Rats were anesthetized and bipolar stainless electrode was inserted into the semitendinosus muscle. And GND was placed subcutis of head region of rat. The EMG signals were recorded using Powerlab 8/35 and LabChart (AD Instruments) . After insertion of the bipolar electrode, the digits of the hind paws were firmly pinched to confirm an increase in electromyographic (EMG) activity. Administration was initiated once the baseline EMG activity had stabilized.

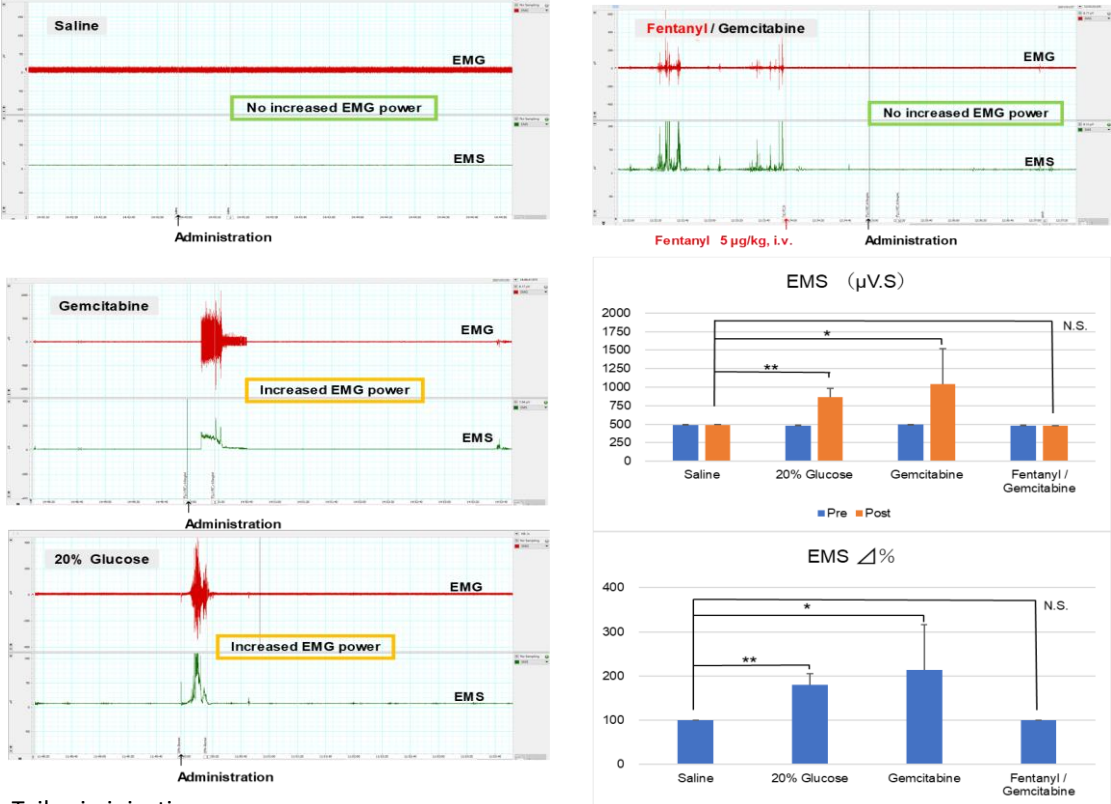


Result

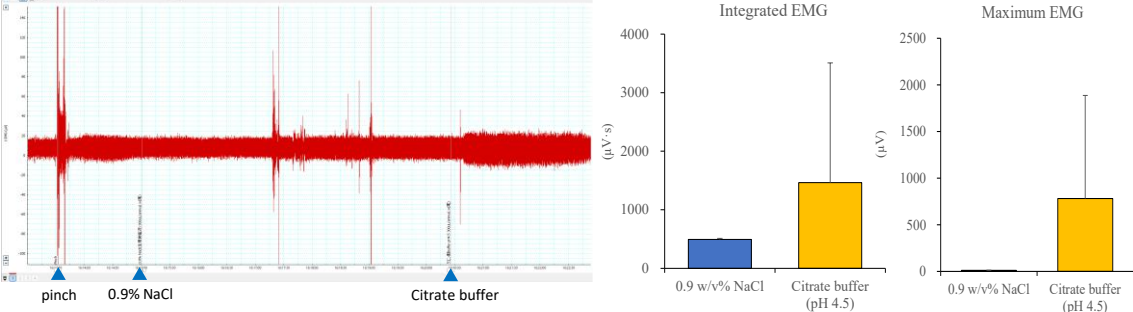
Subcutaneous injection



Femoral circumflex artery injection



Tail vein injection



Conclusion

The results of this study suggested that the pain during injections can be quantified in preclinical studies, and it was considered to be a useful evaluation system. There is a high possibility that this test method can be applied to the evaluation of vascular pain, and it is currently under investigation. In addition, the present study was some modifications with reference to the method of Ami¹⁾ et al.

1). Nozomi Ami et al, The use of rat spinal reflexes to quantify injection pain, European J of Pharmaceutical Sciences, 74(2015), 36 39

