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- **The Methodological Question Being Addressed**

- How will healthy young Japanese subjects respond to experimental pain and can the response be reversed by oxycodone

- **Introduction**

Pain is the most common health problem in human. However, because of lack of the reliability of the animal models and the psychological, pathophysiological and cultural nature of pain itself, it is often a challenge to assess the efficacy of pain medicine in the drug developments.

It is well known that the experience of clinical pain differs across ethnocultural groups and also many studies have shown different sensitivities to the experimental pain in different ethnicities. However, most studies have been conducted in western countries, and nearly no literature is found to demonstrate the validity of using experimental pain model in healthy Japanese subjects.

In this study, we planned and performed a clinical research on the purpose of pain evaluation using the cold pressor test (CPT) in healthy young Japanese subjects.

- **Methods**

The CPT was used as an experimental pain model. The water temperature was maintained at 4°C using a low-temperature thermostatic water bath (Thomas Kagaku, Japan).

A randomized, double-blind, placebo-controlled, 2-group 2-period cross-over study in healthy young Japanese male volunteers was conducted at SOUSEIKAI, Japan.

The CPTs were performed at pre-, 1, 2, 5, and 8 hours after the Oxycodone or placebo administration.

Oxycodone or placebo were administered orally once on the 1st day of the 1st and 2nd period.

Pain latency and Pain tolerance were measured by the investigators during the tests based on the subject's response.

Pain intensity was recorded by each subject by rating it via Visual Analogue Scale (VAS), Numeric Rating Scale (NRS), and the Short Form McGill Pain Questionnaire (SF-MPQ-2) after each CPT.

The clinical research was reviewed and approved by SOUSEIKAI Hakata Clinic IRB.

- **Results**

- We were able to produce both consistent and safe experimental pain in healthy Japanese volunteers by using the CPT, and confirmed that it is possible to investigate the pain using VAS and NRS.
- Both on the VAS and NRS, the Cumulative Odds Ratio (Oxy/Plc) were below 1 for all the time points from 1 hr to 8 hrs, which indicated that the Oxycodone suppressed the cold pressor-induced pain in healthy Japanese volunteers.
- We were also able to evaluate the psychological aspects of the cold pressor pain using the Japanese version of the short-form McGill Pain Questionnaire.
- The Oxycodone suppressed the cold pressor pain, shown by the Cumulative Odds Ratio (Oxy/Plc) being below 1 for 11 items out of 13 items in the SF-MPQ-2.

- **Conclusions**

It is possible to produce and evaluate experimental pain in healthy volunteers using the CPT in healthy Japanese male volunteers.

The CPT can be useful to measure the analgesic properties of new drug candidates for pain in early phase clinical studies without compounding effects in Japanese subjects.

Additional research to determine the validity of other types of analgesic medicines will be followed in Japanese subjects.