Effect of topical lidocaine in the oral and facial regions on tactile sensory and pain thresholds

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A B S T R A C T

Objective: The aim of the present study was to examine the effect of lidocaine application to the face, tongue and hand on sensory and pain thresholds of symptom-free subjects.
Design: Eighteen females (mean age 25.7 years, range 22–38) participated. Using Semmes-Weinstein monofilaments, the tactile detection threshold (TDT) and the filament-prick pain detection threshold (FPT) were measured on the cheek skin (CS), tongue tip (TT) and palm side of the thenar skin (TS). Subjects were tested in 2 sessions at a 1 week interval in randomised order. Lidocaine (session A) or placebo gel (session B) was applied for 5 min. The TDT and FPT were measured before and after application.
Results: The TDT at all sites in session A significantly increased after 5 min, but a significant session effect on the TDT was only found at the TT ($P < 0.01$). On the other hand, there were significant session effects on the FPT at all sites ($P < 0.01$).
Conclusion: These results indicate that the pain threshold (FPT) is more susceptible to local anesthetics than the sensory threshold (TDT), but further study is needed to use topical lidocaine for the control of oral and facial pain in the clinic.

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1. Introduction

The general dentist and dental specialist treat patients with pain on a daily basis. Orofacial pain is pain perceived not only in the oral cavity and face, but also in the jaw and head (De Leeuw, 2008; Sessle, 2005; Sessle, Lavigne, Lund, & Dubner, 2008). In treating orofacial pain conditions, oral drugs such as nonsteroidal anti-inflammatory drugs (NSAIDs), acetaminophen, antidepressants, anticonvulsants and opiates are effective, but adverse effects may be problematic (Ito et al., 2015; Kimura et al., 2012; Nagashima et al., 2012). So, simple and effective approaches without significant adverse effects would be promising, and topical therapies would offer the promise of such a treatment (Watson, 2005). In fact, some studies suggested the efficacy and safety of topical lidocaine for the treatment of neuropathic pain such as postherpetic neuralgia (PHN) and trigeminal neuralgia (TN) (Kanai

et al., 2009; Niki, Kanai, Hishi, & Okamoto, 2014). Topical clonazepam therapy has been used for the management of burning mouth syndrome (BMS), and BMS has been considered to be neuropathic pain condition as has also atypical odontalgia (AO) (Amos, Yeoh, & Farah, 2011; Clark, 2010; De Laat, 2010; Gremeau-Richard et al., 2004; List, Leijon, Helkimo, Oster, & Svensson, 2006; List, Leijon, & Svensson, 2008; Patton, Siegel, Benoliel, & De Laat, 2007).

Recently, we have been using topical lidocaine as the initial treatment for patients with BMS as well as AO, PHN and TN in the clinic (Okayasu, Ayuse, Oi, 2013; Okayasu & Ayuse, 2013; Okayasu & Ayuse, 2014). Although there are some expert opinions stating that topical lidocaine may be helpful for the management of such orofacial pain conditions and that it has been used in clinical settings on a trial-and-error basis (De Laat, 2010; Okayasu et al., 2013; Okayasu & Ayuse, 2013; Okayasu & Ayuse, 2014; Patton et al., 2007), there is not sufficient objective evidence.

Consequently, the aim of the present study was to examine the effects of lidocaine application to the face and tongue on tactile sensory and pain thresholds of symptom-free subjects using quantitative sensory testing (QST) as used previously (Okayasu, Oi, & De Laat, 2009; Okayasu, Oi, & De Laat, 2012; Okayasu, Komiyama

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et al., 2012;; Okayasu, Komiyama, Ayuse, & De Laat, 2014). We added the hand skin as the measuring point as a corresponding control site, and examined the effects of lidocaine application to the hand as well as the face and tongue.

2. Materials and methods

2.1. Subjects

Eighteen healthy volunteers (18 women, mean age 25.7 years, range 22–38) participated. Based on the clinical feature that women are affected more than men in orofacial pain conditions (De Leeuw, 2008; Sessle et al., 2008), all subjects were females asymptomatic for pain in the head and neck. As a previous study indicated that pain thresholds were lower in the menstrual phase, women were not tested during their menstrual phase and smokers were excluded (Isselee, De Laat, Bogaerts, & Lysens, 2001; Isselee, De Laat, De Mot, & Lysens, 2002). Informed consent was obtained from all participants. The institutional Ethics committee of Nagasaki University Graduate School of Biomedical Sciences approved the study (No. 1502).

The subjects were seated comfortably upright in a dental chair. Using Semmes-Weinstein monofilaments with 20 different diameters (Premier Products, Kent, WA, USA) following psychophysical methods (Jacobs et al., 2002), the tactile detection threshold (TDT) and the filament-prick pain detection threshold (FPT) were measured 1) on the cheek skin (CS) overlying the central part of the right masseter muscles midway between the upper and lower borders and 1 cm posterior to the anterior border, 2) at the anterior tip of the tongue (TT) on the midline, and 3) on the skin overlying the palm side of the right thenar muscle on the point connecting the longitudinal axis of the thumb and index finger (Thenar Skin: TS).

Each subject undertook two sessions at a 1 week interval in randomised order. A 2% lidocaine gel (AstraZeneca, Osaka, JAPAN) was applied for 5 min (session A) at the CS, TT and TS simultaneously. A placebo gel (Weltec, Osaka, JAPAN), similar in appearance to the lidocaine, was administered in an identical manner (session B). The area covered by gel at the CS, TT and TS was a circle 1 cm across, and the amount of gel was approximately 0.2 g. The TDT and FPT were measured before and after each application.

The number of the filaments (1.65–6.65) corresponds to a logarithmic function of the equivalent forces of 0.0045–447 g. Each filament size is marked with the resultant force and these values are used in the descriptive statistics, which enables easier comparison of thresholds as reported previously (Jacobs et al., 2002).

2.2. Tactile detection threshold

At first, TDT was examined. The subjects were instructed to close their eyes during the whole test procedure and to raise their hand as soon as they felt touch or tactile detection on the test site. The filament was applied vertically to the test site and slowly the force level was increased until the filament bowed. The time needed to bow the filament was standardized to approximately 1.5 s. The stimulus was maintained for approximately 1.5 s and then removed in 1.5 s. Quick applications and bouncing of the filaments were avoided. At each site, the test started with the number (No.) 4.74 filament. If the subject raised his/her hand, this was considered a positive response, and the next filament applied was one step lower (No. 4.56). This procedure was repeated with decreasing filament diameters until the subject no longer felt touch and tactile detection. This was considered a negative answer. Again, the filament with a higher force level was applied. This procedure continued until five positive and five negative peaks

were recorded and the threshold (TDT) was calculated as the average of these values. If the subject still had a positive response while applying the lowest fiber (No. 1.65), this pressure was considered the threshold. Two "blank" (placebo) trials were performed after peaks 5 and 10. During these control trials, the filament did not make contact with the tissue. If the subject reported a positive answer, the test was discontinued and the subject was questioned about what kind of stimulus was perceived. The whole procedure was explained again to the subject and afterwards the test was restarted (Jacobs et al., 2002; Komiyama and De Laat,2005; Komiyama, Gracely, Kawara, & De Laat, 2008; Okayasu et al., 2009; Okayasu, Oi et al., 2012; Okayasu, Komiyama, Yoshida, Oi, & De Laat, 2012; Okayasu et al., 2014; Svensson et al., 2011).

2.3. Filament-prick pain detection threshold

After the TDT measurements, the FPT was examined. The stimuli were applied in the same way as for the TDT, but the subjects were instructed to keep their eyes open and to raise their hand as soon as they felt pain in the test area. If the subject had no positive response for the thickest fiber (No. 6.65), this value was recorded as the threshold. No placebo stimuli were applied. There was a time lag of 3 min between the measurements on a same site in order to avoid sensitization.

Pain intensity of the FPT (the lowest stimulus intensity that the subject perceives as painful) was also assessed on a numetric rating scale (NRS) where 0 cm indicates 'no pain' and 10 cm indicates 'worst pain imaginable' (Jacobs et al., 2002; Komiyama & De Laat, 2005;; Komiyama et al., 2008; Okayasu et al., 2009; Okayasu, Oi et al., 2012; Okayasu, Komiyama et al., 2012; Okayasu et al., 2014; Svensson et al., 2011).

2.4. Statistical analysis

The mean values and standard error of the mean of TDT and FPT were calculated. Data were not normally distributed, and the differences in mean threshold values between various sites were analyzed using Wilcoxon-Mann-Whitney test. Wilcoxon-matched pair test was performed to test the effects of the session and condition as reported in previous publications (Jacobs et al., 2002; Okayasu, Komiyama et al., 2012; Okayasu et al., 2014). The significance was accepted at $P < 0.05$.

3. Results

As previously, no significant difference could be found between the right and left testing sites (Jacobs et al., 2002; Okayasu et al., 2014), and consequently we selected the right CS and TS as a single value for the CS and TS.

First, we compared the pre-TDT, FPT and NRS at three different sites: CS, TT and TS. Since there were no significant differences in the pre-TDT, FPT and NRS between session A and session B, the pre-

Table 1
Tactile sensory and pain thresholds.

	CS	TT	TS
pre-TDT	2.73 ± 0.48	2.10 ± 0.16[**]	2.59 ± 0.38
pre-FPT	5.77 ± 0.52	5.33 ± 0.37[**]	5.81 ± 0.43
pre-NRS	2.0 ± 1.3	2.4 ± 1.2	2.0 ± 1.2

Data are expressed as mean ± standard error of the mean.
TDT, tactile detection threshold; FPT, filament-prick pain detection threshold. NRS, numetric rating scale; CS, cheek skin; TT, tongue tip; TS, palm side of the thenar skin.
The values of TDT and FPT indicate log force.
[**] $P < 0.01$ vs CS and/or TS.