Biochemical and Pain Comparisons Between the Laser Lancing Device and Needle Lancets for Capillary Blood Sampling: A Randomized Control Trial

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Background and Objectives: Patients around the world use a lancing device to perform self-monitoring of blood sugar (SMBG). However, there are always fears of needles and pain. Therefore, less painful devices are being developed. The purpose of this study was to compare the usefulness and safety of a laser lancing device (without a needle) to a conventional needle lancet (with a needle) for capillary blood sampling.

Study Design/Materials and Methods: A total of 40 healthy subjects were enrolled in the study. Capillary blood was collected from a laser lancing device (without a needle) and a conventional needle lancet (with a needle) on opposite fingers, the choice of which was randomly selected. The laser lancing device (LMT-3000) uses a 2940 nm monopulse laser, a radiation field of 350 μm, laser energy of 210 mJ, and a 3.7 V battery. One week later, capillary blood was obtained by switching the devices and fingers. The biochemical measurements and pain were compared between the two groups. Puncture pain was measured on a pain scale from 0 to 10.

Result: All patients were tested with both a laser lancing device and a conventional needle lancet. In the biochemical analysis, the blood glucose level was 103.21 ± 17.20 mg/dl in laser lancing device group and 102.25 ± 22.44 mg/dl in the conventional needle lancet group, and there were no significant differences between the two groups ($P = 0.940$). The pH, CO_2, O_2, lactate and hematocrit levels of the blood were no significant differences between the two groups. In the first trial, the median pain score (interquartile range) of patients using laser lancing device was 2.0 (1.0–3.0), whereas it was 2.5 (2.0–4.0) in patients using a conventional needle lancet ($P = 0.029$). In the second trial, one week later, the median pain score in the laser lancing device group was 2.5 (1.0–4.0), whereas it was 3.5 (2.25–5.0) in the conventional needle lancet group ($P = 0.001$). The difference in pain scores between the first and second trials was significant in the conventional needle lancet group ($P = 0.007$), but not in the laser lancing device group ($P = 0.150$).

Conclusion: There was no difference in biochemical results between the laser lancing device group and the conventional needle lancet group. The laser lancing device demonstrated comparatively lower pain than the conventional needle lancet. Lasers Surg. Med. © 2020 Wiley Periodicals LLC

Key words: lancet; glucose measurement; pain; needle; laser

INTRODUCTION

Self-monitoring of blood glucose (SMBG) in the management of diabetes plays a key role in many large-scale outcome studies, acting as an important contributor to results. SMBG has many proven benefits, such as helping to achieve hemoglobin A1c (HbA1c) targets, minimizing glucose variability, and predicting severe hypoglycemia [1-3]. In an epidemiological cohort study, SMBG was also reported to be associated with decreased diabetes-related morbidity and all-cause mortality, in type 2 diabetes [4].

Despite the importance and accessibility of SMBG, adherence to prescribed testing regimens is poor for many patients. A number of barriers to SMBG adherence have been described including demographic, biological, and psychosocial factors [5]. Among the psychosocial impediments, environmental factors such as inconvenience, cost, and pain have been reported to be the most important. Blood glucose measurement typically requires a painful finger prick; however, of the many barriers to SMBG, pain is one impediment that can be readily addressed by technology.

Lancets are a tool for blood collection designed 30 years ago. They have a long thick needle, which is used to

Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.
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puncture the finger and are still being used. In the case of conventional metal needle lancets, many fear using the needle due to pain or fear of blood sampling. In addition, advanced countries have also encountered difficulties, such as infections and pain due to needles, and waste disposal after their use. A typical stainless needle lancet has a diameter of 0.3–0.8 mm and penetrates 0.7–1.3 mm, with the depth of the penetration directly related to the level of pain [6]. Although the extent of tissue injury and pain are less from punctures by thinner and shorter needles, very small-sized needles yield less blood volume, which may not be sufficient for the glucose measurement. In addition, "needle phobia" surrounding needles, syringes, intravenous therapy, and medical devices can seriously compromise medical care [7-14]. In 2008, a device that uses laser pulses that can be collected through small holes outside the skin was first introduced [15]. Laser have been shown to have a significant benefit of reducing the risk of contamination by removing mechanical contact. In addition, the short pulsed laser was able to reduce tissue trauma produced by conventional metal lancets and greatly reduce pain.

Due to these well-known drawbacks, we developed a new laser lancing device (LMT-3000) without a needle. The purpose of this study was to compare the usefulness and safety of the laser lancing device (without a needle) to conventional needle lancet (with a needle) for capillary blood sampling.

MATERIALS AND METHODS

Study Subject

Forty healthy volunteers (34 females and 6 males; mean age 33.9 years, range 22–48 years) participated in this study. Forty patients were screened. The screen failure was zero, a total of forty patients were enrolled (Fig. 1).

The study was conducted at a tertiary hospital from March 2018 to June 2018.

Sample Size

To determine the number of study subjects needed for this study, a calculation was performed with statistical power $(1-b)$ of 0.85, a significance level of (a) 0.05, an intermediate effect size of 0.25, and a correlation coefficient between repeated measures (r) of 0.50 in repeated measures analysis of variance using the G*Power 3.1.7 program. As a result, 38 people were required for the experiment. Anticipating dropouts, 40 individuals were finally analyzed in this study.

Ethical Considerations

After obtaining approval (DKUHIRB 2017-10-008-011) from the Dankook University Hospital Institutional Review Board, suitable subjects were selected and written informed consent was obtained from each subject. This study was performed following the guidelines of the Declaration of Helsinki.

Study Design

This study was designed to be a randomized and cross-matched paired study design. To reduce the selection bias, blood sampling using the laser lancing device and the conventional needle lancet was performed on the same but opposite finger in the same order on both hands (first trial). One week later, the blood sampling was performed by cross-matching the finger tested in the first trial. That is the same finger, but the device and order of blood sampling were reversed compared to the first trial. (Second trial) (Fig. 1).

The primary outcome was blood biochemical analysis results (especially focused on blood glucose) between the laser lancing device and conventional needle lancet. The secondary outcome was the patient's pain score between the laser lancing device and conventional needle lancet, which we assessed based on patient interviews after the punctures.

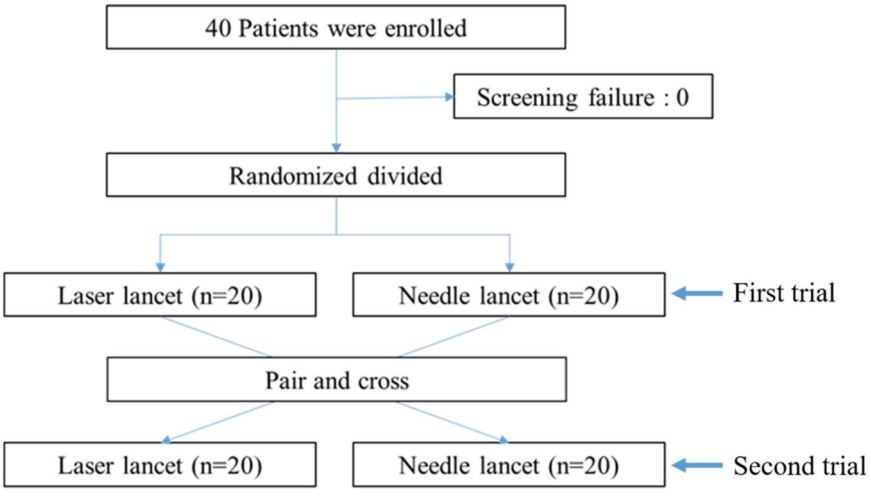

Fig. 1. Study flow.

Inclusion Criteria

The inclusion criteria were:

(1) Healthy adult patients who needed blood sampling.
(2) Those who could participate for the entire period of the clinical trial.
(3) Those who could collect blood on the same finger of both hands.
(4) Those who fully understood the nature of the test and the risks involved in taking the test, were able to communicate with the researcher, and able to maintain compliance.
(5) Those who decided to participate and signed written informed consent after listening to an explanation of the purpose, methods, and likely effects of the clinical trial.

Exclusion Criteria

The exclusion criteria were:

(1) HIV infected persons.
(2) Subjects to be tested for hemophilia and blood coagulation disorders, such as thrombocytopenia.
(3) Blood-fearing patients.
(4) Those who could not collect blood on the same finger of both hands.
(5) Those who participated in other clinical trials within 90 days from the screening date.
(6) In addition to the above, if the researcher considered it difficult to perform the clinical trial based on medical judgment.

Research Procedure

First puncture trial. The finger and blood sampling device (laser lancing device or conventional needle lancet) were randomly selected. Capillary blood sampling was performed on the selected finger with the selected device and the blood biochemical factors were measured. Immediately after the measurements, capillary blood sampling and biochemical factors were measured using the other lancing device on the opposite finger. For example, if the right fourth finger was sampled with a laser lancing device, the left fourth finger was sampled with a conventional needle lancet.

Second puncture trial. The second puncture trial was performed 7 days after the first puncture trial. Capillary blood sampling was performed on the same finger in the first trial with the opposite device and blood biochemical factors were measured. Immediately after the measurements, capillary blood sampling and biochemical factors were measured using the other lancing device on the opposite finger.

Evaluation of Pain

The evaluation of pain during blood sampling was performed using a numeric rating scale (NRS) from 0 to 10. Completely painless was given 0 points and the most extreme pain was given 10 points. The patients rated their pain immediately after blood sampling.

Medical Devices

Laser lancing device. The laser lancing device (LMT-3000) was used for clinical testing (Fig. 2). This device uses a 2940 nm mono-pulse laser, a radiation field of 350 μm, laser energy of 210 mJ, and a 3.7 V battery. For patient safety, the laser exposure time was very short (below 1/10,000 second). The average diameter of the puncture was 0.5 mm, and the penetration depth was 0.6–0.9 mm.

For the puncture and capillary blood sampling, the patient's fingertip was cleaned with an alcohol swab and wiped with sterile gauze, and the lancing was performed by a physician.

To prevent contamination, a disposable protection cap was placed on the laser irradiation part of the device before capillary blood sampling. This cap prevents infection at the puncture site and prevents blood contamination of the device and damage to the laser irradiation area (Fig. 3B). Once used, the protection cap is not reused. Also, to prevent safety accidents caused by lasers during storage, the device does not operate unless the grip sensor is gripped correctly (Fig. 3A). And the push sensor of the

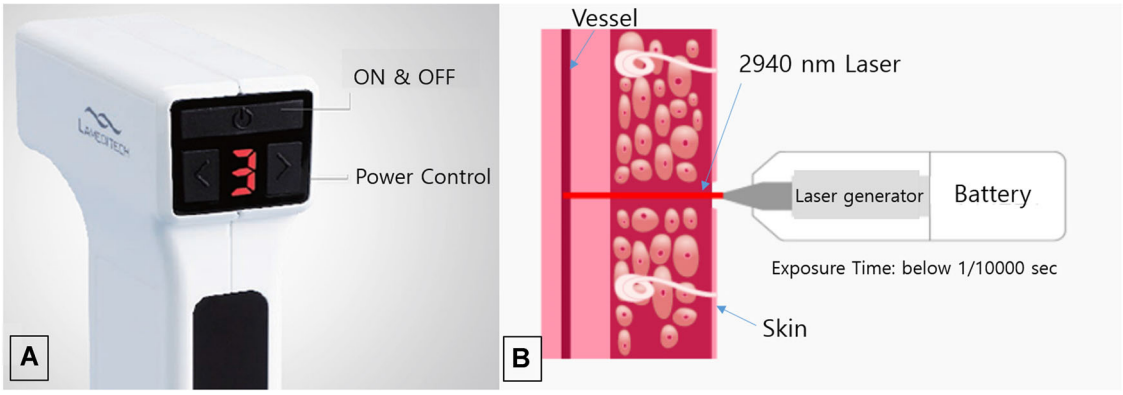

Fig. 2. Laser lancing device. (**A**) Approximate appearance of laser lancing device, there have an on/off button and power control button. (**B**) Schematic figure of working of laser lancing device.

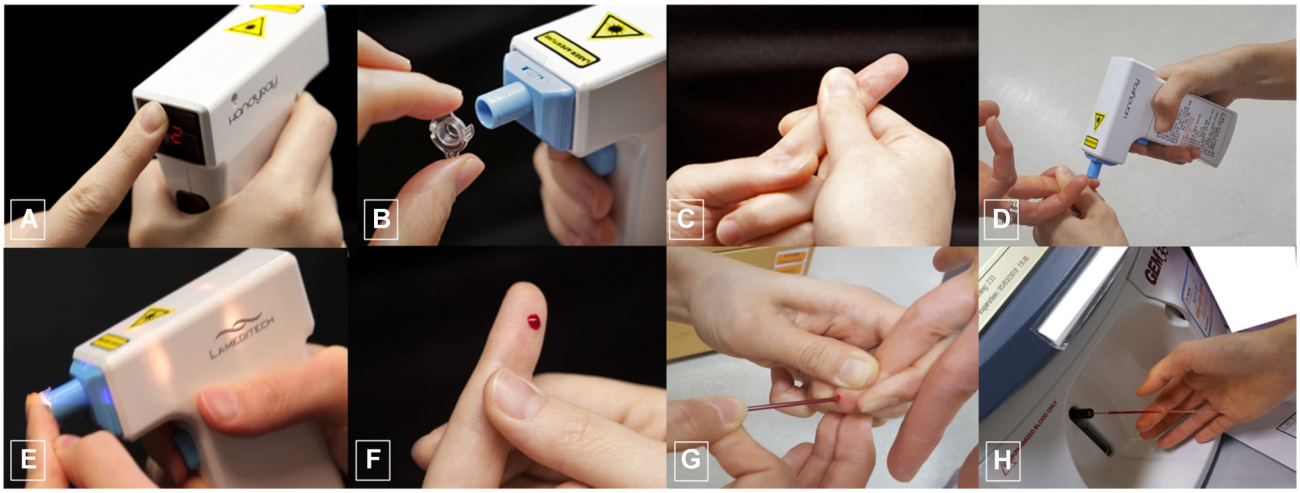

Fig. 3. Working of laser lancing device. (**A**) Power on (button push), (**B**) using one-time protection cap, (**C**) preparation of the puncture finger, (**D**) target finger placed in front of the laser lancing device opening, (**E**) firing on the target finger, (**F**) check the blood, (**G**) blood collection by capillary tube, (**H**) blood gas analysis.

laser irradiation area is operated only when close contact is made to the blood sampling site (Fig. 3E).

The patients could see the laser lancet before lancing. After touching the fingertip, the operator pressed the shot button to irradiate the skin. Blood sampling was collected by laser irradiation (Fig. 3).

Conventional needle lancet. A disposable manual needle lancing device named "LANZO" was used. The name of conventional needle lancet is "CareLance," which was made out of a 28-gauge needle (Fig. 4A). The disposable needle lancet was loaded into the holder and the depth control knob was adjusted. After placement on the blood sampling area, the button was pressed to lance the skin and the blood was collected.

Blood biochemical analysis. Blood biochemical analyses were performed on a GEM3500 system (A Werfen Company, Bedford, MA). After puncture with a device (laser or needle), a maximum of 150 µl of blood was collected using capillary collection tubes. Blood was collected using a capillary phenomenon by contacting the tubes with the puncture area. To collect sufficiently, gently rubbed the finger to help blood collection. Immediately afterward, the amount of blood collected was calculated through the length of blood collected in the tube, and pH, CO_2, O_2, lactate, hematocrit, and glucose levels were measured using an automatic analyzer (Fig. 1). The results of the blood biochemical analyses were compared between the two devices.

Safety analysis. To confirm the safety of the blood collection site, the first puncture area was examined at the second visit, and the state of the second puncture area was examined over the phone a week later.

Data Analysis

IBM SPSS for Windows v21.0 (IBM Corp., Armonk, NY) was used for all data analyses. The characteristics of the

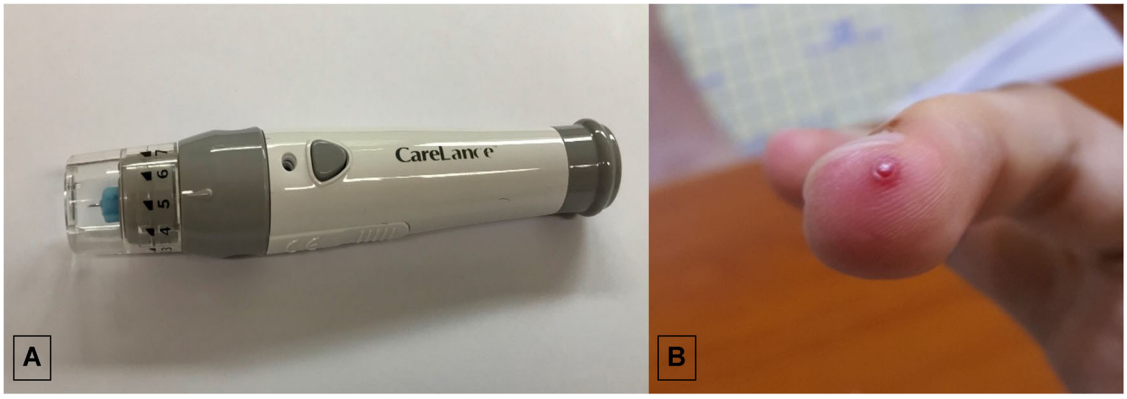

Fig. 4. (**A**) Needle lancet used as the control device, (**B**) one granuloma was seen after use of the laser lancet.

experimental and control groups were analyzed with real numbers, percentages, and mean and standard deviations. The Student t test was used to compare the characteristics of the experimental and control groups and to determine the homogeneity of the research variables. The Wilcoxon signed-ranked test was used to compare the pain scores of both groups.

RESULTS

Subject Characteristics

All blood sampling was successful on the first attempt. The total number of participants was 40. There were 34 females and six male patients with a mean age of 33.92 ± 6.64 years. The mean height was 163.53 ± 7.53 cm and the mean weight was 61.87 ± 11.21 kg. As this study was a cross-matched paired study design, the sex ratio, age, height, and weight of both groups were the same. In the conventional needle lancet group ($n = 40$), systolic BP was 125.7 ± 18.3 mmHg, diastolic BP was 77.4 ± 12.3 mmHg, the heart rate was 80.3 ± 23.9/min, the body temperature was 36.5 ± 0.2°C, and the number of follow-up days was 14.14 ± 2.08. In the laser lancing device group ($n = 40$), systolic BP was 123.2 ± 14.6 mmHg, diastolic BP was 71.3 ± 8.6 mmHg, the heart rate was 86.6 ± 13.9/min, the body temperature was 36.6 ± 0.1°C, and the number of follow-up days was 14.03 ± 2.22. There was no significant difference in any of these parameters. The demographic and clinical characteristics of subjects are summarized in Table 1.

Biochemical Analysis

Biochemical analysis was performed on all participants. The blood test results are shown in Table 2. The blood sampling amounts were 140.63 ± 28.05 μl and 145.50 ± 9.85 μl ($P = 0.71$). The blood pH was $7.4\ 3 \pm 0.03$ and 7.41 ± 0.03 ($P = 0.11$). The blood CO_2 was 37.89 ± 3.29 mmHg and 39.55 ± 3.42 mmHg ($P = 0.18$). The blood O_2 was 79.21 ± 14.79 mmHg and 73.35 ± 8.45 mmHg ($P = 0.36$). The blood glucose levels were 103.21 ± 17.20 mg/dl and 102.25 ± 22.44 mg/dl ($P = 0.94$). The blood lactate levels were 1.69 ± 1.10 mmol/L and 1.71 ± 1.03 mmol/L ($P = 0.73$) and the hematocrit was $44.57 \pm 6.26\%$ and $43.95 \pm 5.28\%$ ($P = 0.90$). There was no difference between the laser lancing device and conventional needle lancet groups.

Puncture Pain Results Comparing Laser Lancing Device and Conventional Needle Lancet

In the first trial, the median pain score (interquartile range) in the laser lancing device group was 2.0 (1.0–3.0), and it was 2.5 (2.0–4.0) in the conventional needle lancet group ($P = 0.029$). In the second trial, 1 week later, the median pain score in the laser lancing device was 2.5 (1.0–4.0), whereas it was 2.5 (2.25–5.0) in the conventional needle lancet group ($P = 0.001$) (Fig. 5). The difference in pain scores between the first trial and the second trial was significant in the conventional needle lancet group ($P = 0.007$), but not in the laser lancing device group ($P = 0.150$) (Table 3).

Complication

A complication was noted in the second trial with laser lancing device (granulation at the puncture site in 1/80 samplings (1.2%) (Fig. 4B). Granulation was treated with laser according to the opinion of dermatologist and was removed completely. This might have been caused by a lack of post-puncture care. There were no complications in the needle lancet group.

DISCUSSION

In this study, the laser lancing device significantly reduced pain compared to the conventional needle lancet. It is very important and of clinical significance to reduce the pain of blood sampling for self-glucose monitoring. Needle pain and phobia are substantial concerns for patients who experience distress while giving or receiving injections or experiencing skin punctures [16]. Among the many difficulties and problems encountered by diabetic patients, the daily experience of pain and soreness of the finger cannot be underestimated. Although the pain itself may not be a serious medical condition, it is indirectly associated with complications in diabetic patients. A patient's reluctance to test blood glucose levels due to the fear of puncture pain is a well-known cause of poor compliance. In a study by Humphrey et al. [17], high levels of distress were apparent

TABLE 1. Patient Characteristics

Patients	Laser lancing device (Mean ± SD) ($N = 40$)	Conventional Needle lancet (Mean ± SD) ($N = 40$)	P
Age (years)	33.92 ± 6.64	33.92 ± 6.64	NA
Male/female	6/34	6/34	NA
Height (cm)	163.53 ± 7.52	163.53 ± 7.52	NA
Weight (kg)	61.87 ± 11.21	61.87 ± 11.21	NA
Systolic BP (mmHg)	123.20 ± 14.63	125.74 ± 18.34	0.624
Diastolic BP (mmHg)	71.34 ± 8.64	77.37 ± 12.28	0.485
Heart rate (rate/min)	86.55 ± 13.90	80.26 ± 23.90	0.392
Body temperate (°C)	36.58 ± 0.11	36.47 ± 0.18	0.896
Follow-up (days)	14.14 ± 2.08	14.03 ± 2.22	0.701

BP, blood pressure; NA, not available; SD, standard deviation.

TABLE 2. Comparative Analysis of Laser Lancing Device and Conventional Needle Lancet on Biochemical Parameters

	Laser lancing device (mean ± SD)	Conventional needle lancet (mean ± SD)	*P*
Blood amount (μl)	140.63 ± 28.05	145.50 ± 9.85	0.71
pH	7.43 ± 0.03	7.41 ± 0.03	0.11
CO_2 (mmHg)	37.89 ± 3.29	39.55 ± 3.42	0.18
O_2 (mmHg)	79.21 ± 14.79	73.35 ± 8.45	0.36
Glucose (mg/dl)	103.21 ± 17.20	102.25 ± 22.44	0.94
Lactate (mg/dl)	1.69 ± 1.10	1.71 ± 1.03	0.73
Hematocrit (%)	44.57 ± 6.26	43.95 ± 5.28	0.90
Complications	Granuloma: 1 case	None	

SD, standard deviation.

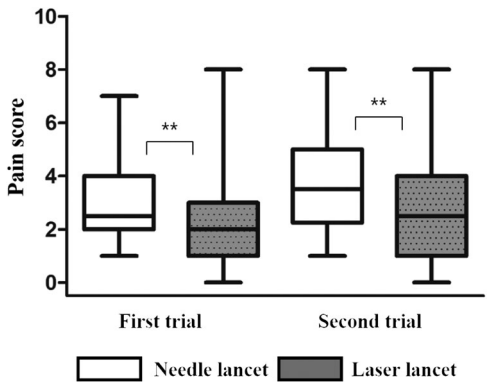

Fig. 5. Comparison of puncture pain score between laser lancing device and conventional needle. Boxes represent medians and interquartile (Q1–Q3) ranges, whiskers represent minimal and maximal values. Pain scores were compared using Mann–Whitney tests: $^{**}P < 0.05$.

during needle pricks in approximately 50% of the 223 patients in the study. Both the anticipated and actual pain of the needle prick are factors in a patient's fear of needles. The prevalence of needle anxiety in patients with diabetes was revealed in a research study completed by Howe et al. [18]. A large number of patients (40.9%) reported fear, and 22.7% reported pain with injections. A total of 8.3% of the patients in the study had high needle anxiety, with a Visual Analog Scale score greater than or equal to 5, and most of these patients had been diagnosed with diabetes within the last 5 years [19]. We can anticipate that the use of a less painful lancet, such as the laser lancing device, would reduce fear and anxiety in patients and thus, have a positive effect on diabetes management.

TABLE 3. Comparative Analysis of Laser Lancing Device and Conventional Needle Lancet on Puncture Pain

	Laser lancing device median (IQR)	Conventional needle lancet median (IQR)	*P*
First trial	2.0 (1.0–3.0)	2.5 (2.0–4.0)	0.029
Second trial	2.5 (1.0–4.0)	3.5 (2.25–5.0)	0.001
P	0.150	0.007	

IQR, interquartile range.

There are two reasons for less pain from the laser lancing device. The first is anatomically different penetration. The skin consists of the epidermis and the dermis. Underneath the epidermis, which has no blood vessels and pain nerve innervations, the dermis is divided into two layers: the papillary layer above and the reticular layer below. Typically, the superficial portion of the papillary layer is arranged into ridge-like structures, the dermal papillae, which contain microvascular and neural components that sustain the epidermis. A vascular plexus, the rete subpapillare, demarcates the lower limit of the papillary dermis [20]. The normal thickness of the epidermis of the middle fingers is about 0.3 mm, and that of the dermis 1.5 mm [21]. The papillary layer is about 0.3 to 0.4 mm thick [20]. Merkel's cells in the epidermis and Morgagni's corpuscles in the papillary layer are nerve receptors for touch sensations. The laser lancing device used in this study was a 2940 nm mono-pulse laser, with a radiation field of 350 μm and laser energy of 210 mJ. For patient safety, the laser exposure time was very short (below 1/10,000 second) and the penetration depth was 0.6–0.9 mm [15]. Therefore, the laser could hit the rete subpapillae, the superficial vascular structure of the papillary dermis, without going deeper to the reticular dermis where abundant free nerve fibers are present. By penetrating the papillary dermis only, the laser may hit nerve receptors, such as the Merkel's cells and Morgagni corpuscles, with patients feeling something like a touching sensation, instead of an unpleasant pain. The penetration depth is controlled by the laser and it is conjectured to be the reason why the tested patients consistently reported less pain.

The second reason is psychological. Pain perception is influenced not only by the actual wound size but also by psychological factors. Anticipating pain is perceived as actual pain [22]. This is especially true when diabetic patients puncture the finger skin themselves. The psychological aspect of pain anticipation was considered an

important factor in measuring the pain intensity in this study. Therefore, patients in this study could see the laser lancing device before it punctured the skin, as the pain was anticipated to be less than with the control lancets.

In the study results, the pain scores of the second trials in both groups were higher than first trials. It is presumed that the subjects who experienced pain in the first trials felt more pain due to psychological anxiety during the second trials. The laser lancing device without needle would have reduced anxiety, so the increase in average pain score in the second trial increased by 0.70 in the control group, while it increased by only 0.37 in the laser lancing groups.

Another advantage of the laser lancet is that, unlike disposable needles, no infection or secondary damage occurs during storage and handling. It is free from needlestick injuries because the needle is not used and the laser exposure time is very short. Needlestick injury is the most common cause of infection, especially through blood-borne infections, such as human immunodeficiency virus and hepatitis B and C [23,24]. These infections present risks and threats, especially to healthcare workers, and products without needles have great advantages in preventing these risks.

Blood sampling with less pain can be useful clinically [25-30]. In addition to self-measuring blood glucose in patients with diabetes mellitus, it can be used for gas analysis in the intensive care unit and biochemical component analysis. As a result of present study, an average of 140.63 μl of blood was collected using laser lancet, and this blood volume is sufficient to measure metabolic parameters and HbA1c using a reported kit [31]. However, blood collection by laser devices has the potential to change the blood components. The effects of lasers can cause changes in the acid-based state, oxygenation [32], glucose [33], and viscosity in the blood. The thermal energy of the laser can change gas composition in the blood, and glucose can change when the interstitial fluid of tissue is mixed according to the blood collection method. Therefore, we compared and analyzed the glucose, pH, O_2, CO_2, and lactate levels, as well as the hematocrit, after blood sampling in both groups to confirm changes in the blood caused by laser. The results showed that the biochemical values in the laser lancing device group were not different from the conventional needle lancet group (Table 2). Changes in blood components caused by a laser are seen when exposed for a long time, and the laser lancet used in this study, with a very short exposure of 1/10,000 seconds, did not cause changes in blood components. In a study using an erbium:YAG laser by Fonseca et al. [33] there was no significant change in bicarbonate, hematocrit, and glucose in the blood, consistent with our findings. One adverse event was noted, a granuloma (0.55%), which was likely to have been caused by minor trauma and disappeared after dermatological treatment.

This study had some limitations. First, it is not a blind study. Therefore, there is a possibility of some bias for the assessment of pain. Further study using blind method is needed. Conversely, the author thinks that reducing the fear of pain due to the invisibility of the needle is an advantage for the laser lancing devices. Second, although the patients were followed for two weeks, in order to evaluate the risks and benefits of the laser lancing device, a longer follow-up study may be needed. Third, additional studies with larger sample sizes may be needed to investigate the differences among various age and sex groups. It may also be necessary to improve the reliability and applicability of the data for treating and managing patients who have used laser lancing devices. Also, we need to study the cost-effectiveness and convenience of this laser lancing device.

CONCLUSIONS

There were no blood biochemical result differences between the laser lancing device group and conventional needle lancet group. The laser lancing device demonstrated comparatively lower pain than the conventional needle lancet. This laser lancing device is intended for use by medical personnel for the collection of blood samples from patients in hospitals, laboratories, blood transfusion centers, and other medical institutions where the capillary blood is collected.

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