A single-blind, Randomized, Single-centre Study to Investigate the Characteristics of Different Personal Lancets on Blood Volume and Perceived Pain in Patients with Diabetes Mellitus

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ABSTRACT

Introduction
Randomised controlled trial is a specific type of scientific experiment, and the gold standard for a clinical trial. RCTs are often used to test the efficacy or effectiveness of various types of medical intervention within a patient population. RCTs may also provide an opportunity to gather useful information about adverse effects.

In recent years the performance and accuracy of self-monitoring blood glucose (SMBG) devices have been closely watched by regulatory agencies and medical professionals. Mainly, because every day thousands of patients with diabetes lance their fingers many times in order to perform self-monitoring of their blood glucose values.

Material and methods
Male and female subjects with diabetes type I or II being in good physical and mental health were enrolled in the study. Female subjects were allowed to participate in this study only if they were not pregnant in self reporting. In total 60 diabetic patients were enrolled in the study. The primary objective of this study was to determine and to compare the amount of capillary blood volume collected after a single lancing of the fingertip. In addition, also the perceived pain during the lancing procedure was determined and compared between the lancets.

Results
The average blood volumes obtained with Droplet® personal lancet 33G and Glucoject® personal lancet 33G used in cooperation with Droplet® lancing device, Microlet® 2 lancing device and Glucoject® lancing device were in each case higher than 4 µl except for one puncture. In 50% of pricks the obtained average blood volume was higher than 6 µl. Bleeding time was up to 2 minutes. The study results have also shown that in case of majority of patients the received blood sample volume has been higher than 0.5 µl with a total effectiveness rate of 91.67%. Perceived pain was evaluated as a secondary efficacy variable. The pain perception was measured after each prick. 5 minutes (+/- 1 minute) after pricking the subject noted in his/her worksheet intensity of the perceived pain.
Material and Methods

**Study design**

The study has been conducted with the highest respect for the individual participants in accordance with the requirements of this Clinical Trial Protocol and also in accordance with the following:

- World Health Organization (WHO) Declaration of Helsinki (sixth revision 2008)
- CH Harmonized Tripartite Guideline for Good Clinical Practice
- Respective local laws and regulations

The study was positively evaluated/reviewed by the Bioethics Committee at the Regional Medical Chamber in Krakow, Poland.

The primary objective of this study was to determine and to compare the amount of capillary blood volume collected after a single lancing of the fingertip. The pain perceived during the lancing procedure was determined and compared between the lancets. The primary endpoint of this study was capillary blood volume produced during each lancing. The pain perceived was regarded as secondary endpoint.

This was a single blind, randomized, single-centre study in male and female patients with Diabetes mellitus type I or type II. The subjects came to the medical site on the scheduled day for 2-3 hours. After they have signed the informed consent form, they were randomized to one of the ten different finger rotation sequences. Thereafter the finger pricking (three times) was conducted in a standardized fashion. Shortly after the last pricking the CRF was checked for completeness, dated and signed by the investigator or designee and the subject was released. After the completed screening and randomization procedure the lancing procedure was performed.

Finger pricking was undertaken in a standardized fashion and performed by the same investigator or designee. Before the start of the lancing procedure the volunteers were washing their hands with soap under warm water for around 1 minute.
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1 minute to stimulate blood flow and to achieve constant temperature.

Firstly, the middle finger of the left hand (L3) was massaged 3 times from the hand towards the puncture site, then lanced and 5 minutes (+/- 1 minute) later patient was asked to rate the pain intensity during the procedure.

Secondly, the ring finger of the left hand (L4) was massaged 3 times from the hand towards the puncture site, then lanced and 5 minutes later the pain was rated.

Thirdly, the middle finger of the right hand (R3) was massaged 3 times from the hand towards the puncture site, then lanced and again 5 minutes later the pain was rated.

This sequence was followed for all subjects using the lancets as assigned by the randomization list.

Thereafter the completion status was entered in the CRF and the investigator releases the subject from the study. All blood samples taken from subjects were destroyed immediately after measuring of blood volume.

In total 60 subjects were enrolled and each subject had three fingers pricks with a different lancets [5]. Overall, 10 different lancets were investigated, three per subject which leads to 18 capillary blood volume and pain measurements per lancet type.

Study population

Male and female subjects with diabetes type I or II were enrolled in the study. Female subjects were allowed to participate in this study only if they were not pregnant in self reporting.

In total 60 diabetic patients were enrolled in the study.

The investigator was obliged to ensure that all patients being considered for the study meet the inclusion and exclusion criteria. The investigator or his/her deputy was also determined to promote compliance to inclusion/exclusion criteria for the duration of the study day. In blindness or poor visibility cases all study instructions were read by a care or accompanying person to the subject (Table 1).

Statistical analysis

All recorded and derived variables are presented using standard procedures (depending on the underlying distribution: for continuous data, sample size, mean, standard deviation (SD), minimum, median and maximum and upper and lower quartile; for categorical data, sample size, absolute and relative frequency).

For sample size 18, a two-sided 95% confidence interval for a single mean extends 0.46 from the observed mean, assuming that the standard deviation is known to be 1 and the confidence interval is based on the t- statistic. In other words, for each lancet the 95% confidence interval extends around 46% of the standard deviation from the observed mean. All data for background and demographic variables were listed by subject. For these parameters summary statistics or frequency tables (race, gender, type of diabetes and skin status) were provided. Efficacy analysis was conducted for the full analysis set (FAS) population principle. All subjects who were lanced with the same lancet and had a blood volume recorded are included in the analysis for that lancet. Efficacy data (blood volume and pain) was listed by subject and lancet.

Descriptive statistics and two-sided 95% confidence intervals based on the t-statistic was
Results

Blood volume

In the study Droplet® personal lancets 33G and Glucoject® personal lancets 33G were used together with Droplet® lancing device, Microlet® lancing device and Glucoject® lancing device. Both had the depth level adjusted to the maximum (Table 2) and (Figure 1).

Pain Perception

Perceived pain was evaluated as a secondary efficacy variable. The pain perception was measured after each prick. 3 minutes (+/- 1 minute) after pricking the subject noted in his/her worksheet intensity of the perceived pain (Table 3).

Conclusion

The average blood volumes obtained with Droplet® personal lancet 33G and Glucoject® personal lancet 33G used in cooperation with Droplet® lancing device, Microlet®2 lancing device and Glucoject® lancing device were in each case higher than 4 µl except for one puncture. In 50% of pricks the obtained average blood volume was higher than 6 µl. Bleeding time was up to 2 minutes. The study results have also shown that in case of majority of patients the received blood

Table 2: Summary statistics for Capillary blood volume in µl (all available subjects)

<table>
<thead>
<tr>
<th>No</th>
<th>Lancet Type/Lancing device</th>
<th>N</th>
<th>Mean</th>
<th>STD</th>
<th>Min</th>
<th>Q1</th>
<th>Median</th>
<th>Q3</th>
<th>Max</th>
<th>LCL</th>
<th>UCL</th>
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<tbody>
<tr>
<td>1</td>
<td>HTL Droplet 33G/Bayer Microlet</td>
<td>18</td>
<td>6.9</td>
<td>6.2</td>
<td>0.3</td>
<td>1.9</td>
<td>4</td>
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<td>3.8</td>
<td>9.9</td>
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<td>2</td>
<td>HTL Droplet 33G/HTL Droplet</td>
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<td>4.7</td>
<td>5.9</td>
<td>0</td>
<td>0.6</td>
<td>2.3</td>
<td>7.4</td>
<td>22.9</td>
<td>1.7</td>
<td>7.6</td>
</tr>
<tr>
<td>3</td>
<td>Glucoject 33G/ Glucoject</td>
<td>18</td>
<td>5.9</td>
<td>6.4</td>
<td>0.3</td>
<td>1.6</td>
<td>2.9</td>
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<td>2.7</td>
<td>9</td>
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<tr>
<td>4</td>
<td>Glucoject 33G/HTL Droplet</td>
<td>18</td>
<td>4.8</td>
<td>3.9</td>
<td>0.3</td>
<td>1.9</td>
<td>3.6</td>
<td>7.1</td>
<td>14.5</td>
<td>2.9</td>
<td>6.7</td>
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</table>

N - Number of subjects, STD - Standard Deviation, Min - Minimum value, Q1 - Lower quartile, Q3 – Upper quartile, Max - Maximum value, LCL - Lower 95% confidence limit, UCL - Upper 95% confidence limit

Table 3: Summary statistics for pain rating (0 - no pain, 10 - most imaginable pain).

<table>
<thead>
<tr>
<th>No</th>
<th>Lancet Type/ Lancing device</th>
<th>N</th>
<th>Min</th>
<th>Q1</th>
<th>Median</th>
<th>Q3</th>
<th>Max</th>
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<tr>
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<td>3</td>
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<tr>
<td>3</td>
<td>Glucoject 33G/ Glucoject</td>
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<td>1</td>
<td>2</td>
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<td>5</td>
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<tr>
<td>4</td>
<td>Glucoject 33G/ HTL Droplet</td>
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<td>0</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td>8</td>
</tr>
</tbody>
</table>

N - Number of subjects; Min- Minimum value; Q1- Lower quartile; Q3- Upper quartile; Max - Maximum value

Figure 1: Capillary blood volume in µl (all available subjects).
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sample volume has been higher than 0.5 µl with a total effectiveness rate of 91.67%.

Perceived pain was evaluated as a secondary efficacy variable. The pain perception was measured after each prick [6,7]. 5 minutes (+/- 1 minute) after pricking the subject noted in his/her worksheet intensity of the perceived pain.

**Final Conclusion**

As demonstrated by the results of clinical evaluations, Droplet® personal lancets 33G type 560 and Glucoject® personal lancet 33G s type 560 manufactured by HTL-STREFA S.A. provide sufficient blood sample for personal blood glucose level measurements with minimal pain perception.

**References**


