# Cover letter

## Comparison between the Analgesic Effectiveness of Virtual Reality and Topical Anesthesia: A Clinical Study

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## Aim

The aims of the study are to compare the analgesic and anxiety control effectiveness of virtual reality (VR) and topical anesthesia (TA) gel during administration of local anesthesia in adult dental patients, and to determine which approach the patients preferred to reduce pain of dental injections.

The null hypothesis was that there will be no significant difference between the effect of virtual reality compared to that of topical anesthesia gel in reducing pain during administration of local anesthesia injections in adult dental patients.

## Materials and method

The study was performed in accordance with the Declaration of Helsinki. Twenty-one adult volunteers visiting the Riyadh Elm University dental hospital participated in the study, with an age range from 22 to 59 years. The procedures were explained to the volunteers in detail and an informed written consent form were signed by each participant. IRB Approval no. RC/IRB/2019/321 was obtained from the Research Center at Riyadh Elm University, Riyadh, Saudi Arabia.

The study was conducted according to the design of split-mouth randomized controlled double-blinded trials Each participant was randomly allocated to first receive the conventional injection technique under the influence of either *topical anesthesia* or *virtual reality* at the area of the upper second premolar on one side; and then the other procedure on the contralateral tooth after an average of a 10-minute interval. Since it was a split-mouth design, each participant served as his/her own control.

## Sample Power Calculation

Sample power was calculated using the G-Power sample power calculator (Universtat Kiel, Kiel, Germany). Given the split mouth study design, an effect size of 0.75 (high effect size) was assumed and for a power of 0.95, the total number of participants was determined as 21.

## The inclusion criteria

- Class I of the American Society of Anesthesiologists (ASA) as approved by the ASA House of Delegates on October 15, 2014; aged 18 and above, both genders.
- Participants are in good general health, take no medications, and have no contraindications to the use of local anesthetic.
- The ability to understand oral and written instructions.

**Protocol for Injection of Local Anesthetic Solution**

The injection was made with 1.8 ml Xylocaine 20mg/ml (DENSPLY Pharmceutical, USA); (adrenaline: 1:100.000), delivered in cartridges using a 27 - gauge short needle (0.4 x 25 mm, C-K jet) and sterile non-aspirating syringe.

The anesthetic solution was administered into the buccal sulcus of the treated tooth following a standard technique (Handbook of Local Anesthesia, 2013). The syringe was held parallel with the long axis of the tooth while the tissue was pulled out. The needle was inserted in the mucobuccal fold above the apex of the tooth at $45^{o}$ with buccal cortical plate of the bone and with the gauge facing the bone. A few drops of local anesthetic solution were deposited immediately before the needle entered the tissue. After 2 to 3 seconds, the needle was advanced apically until the bone was reached and the rest of the solution was administered at a slow rate over approximately 1 minute. The needle was then withdrawn gently and slowly.

**Procedure with Topical Anesthesia Gel (TA)**

For each participant, the pulse rate was recorded prior to the procedure using an FDA approved pulse oximeter (SantaMedical SM-165 Fingertip Pulse Oximeter, China). The injection site was dried and isolated using a cotton roll and a small quantity of the topical anesthesia Iolite 20% benzocaine (Dharma Research , Miami, USA) anesthetic gel was applied using the end of an applicator stick directly at the site of penetration for 15 seconds and then left for 2 minutes to ensure effectiveness (Handbook of Local Anesthesia, 2013). All the time periods were calculated using Clock App timer available on an iPhone device. The injection of anesthetic solution was performed according to the standard technique mentioned above. After the injection, the pulse rate was recorded a second time.

**Procedure with Virtual Reality (VR)**

For each participant, the pulse rate was recorded prior to the procedure using an FDA approved pulse oximeter (SantaMedical SM-165 Fingertip Pulse Oximeter, China). The virtual reality standalone headset used in the study was the 128 GB Oculus Quest® (Facebook Inc. USA). The device was loaded with the animated short movie 'Henry' (Oculus Story Studio, USA) and then properly adjusted around the patient's head and in front of her/his eyes. The volume level was controlled and interpupillary distance (IPD) was adjusted by each participant after providing brief instructions. The movie was played for some time prior to administration of the injection to enable the participant to interact and get involved with the scene. The next step comprised of guiding the patients to turn their heads and adapt with the dentist's instructions while watching the movie. The injection of anesthetic solution was performed according to the standard technique mentioned above while the participants continued watching the VR movie. After the injection, the pulse rate was recorded a second time.

**Patient Input**

After each procedure was performed (TA or VR), the participants were asked to evaluate the degree of pain that they experienced using the Wong-Baker Faces Pain-rating Scale (W-BFPS). Official permission was issued from the Wong-Baker FACES Foundation.

Additionally, each participant was also asked to state his/her preference of delivery system for future injections.

**Risk of bias**

To avoid the risk of bias, the following were considered:

- All participants were blinded to the order of the technique to be used.
- Both procedures were coded and blinded to the one who did the analysis.
- Both types of procedures were performed in one session by the same operator to avoid an inter-operator variability influence.
- Special attention was given to keep the syringe out of their line of sight.
- Regarding communication with the participants, the words (*injection shot*, *pain*, and *hurt*) were not used to avoid increasing stress or fears.

***Statistical Analyses***

The normality of the heart rates observed was calculated and was observed to be within acceptable limits of Kurtosis and Skew. Therefore, parametric tests were used to analyze differences in heart rate. Given the subjective nature of Wong-Baker faces pain-rating scale (W-BFPS), non-parametric tests were used to analyze differences in W-BFPS.

The paired *t test* was used to compare the heart rates of the individuals between the two methods. The Wilcoxon Sign rank test was used to compare the W-BFPS between the two methods. The spearman's correlation was used to check the association between W-BFPS and heart rate for each procedure. All tests were performed at $p<0.05$.

**Results**

**Analysis of the Descriptive Statistics**

The sample comprised of 21 participants (10 male, 11 female) aged between 25 to 55 years of age.

The heart rates of the participants were normally distributed during each procedure (Table 1). This necessitated the use of parametric statistics for the analysis of heart rate.

**Table 1: Overview of Heart Rates before and after each procedure**

| | N | Minimum | Maximum | Mean | Std. Deviation | Skewness | | Kurtosis | |
|---|---|---|---|---|---|---|---|---|---|
| | Statistic | Statistic | Statistic | Statistic | Statistic | Statistic | Std. Error | Statistic | Std. Error |
| Heart Rate Before (with VR) | 21 | 64.00 | 101.00 | 77.7143 | 9.64957 | .878 | .501 | .675 | .972 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Heart Rate After (with VR ) | 21 | 61.00 | 93.00 | 75.9048 | 8.53173 | .240 | .501 | -.518 | .972 |
| Heart Rate Before (with TA) | 21 | 62.00 | 109.00 | 80.4286 | 12.35950 | .465 | .501 | .269 | .972 |
| Heart Rate After (with TA) | 21 | 64.00 | 102.00 | 79.0000 | 10.02497 | .705 | .501 | .317 | .972 |

In order to measure the impact of procedure on heart rate, the heart rates before and after the procedure were compared. It was observed that for both procedures the mean heart rate after the procedure was slightly lower than mean heart rate before the procedure (Table 2). However, the paired t test showed that the difference between the heart rate before and after treatment were not significantly different (Table 3).

**Table 2: Heart rate before and after the treatment for each type of procedure**

| | | Mean | N | Std. Deviation | Std. Error Mean |
|---|---|---|---|---|---|
| With VR | Heart Rate Before | 77.7143 | 21 | 9.64957 | 2.10571 |
| | Heart Rate After | 75.9048 | 21 | 8.53173 | 1.86178 |
| | Heart Rate Before | 80.4286 | 21 | 12.35950 | 2.69706 |

| | | | | | |
|---|---|---|---|---|---|
| With TA | Heart Rate After | 79.0000 | 21 | 10.02497 | 2.18763 |

**Table 3: Significance of difference in heart rate before and after giving the injection for each type of procedure**

| | | Paired Differences | | | | | t* | Sig. (2-tailed) |
|---|---|---|---|---|---|---|---|---|
| | | Mean | Std. Deviation | Std. Error Mean | 95% Confidence Interval of the Difference | | | |
| | | | | | Lower | Upper | | |
| With VR | Heart Rate Before - Heart Rate After | 1.80952 | 4.02019 | .87728 | -.02044 | 3.63949 | 2.063 | .052 |
| With TA | Heart Rate Before - Heart Rate After | 1.42857 | 6.20138 | 1.35325 | -1.39426 | 4.25141 | 1.056 | .304 |

* Calculated using the paired t test Differences are not statistically significant

The patients recorded lower heart rates while in VR than in Topical anesthetic as mentioned earlier. This was true both before and after the dental injections. However, the paired *t test* found the differences to be statistically insignificant both before and after dental injections. While when gender differences were observed it was seen that the females had a higher heart rate compared to the males in each of the four situations. It was observed that these differences were statistically significant for TA-before, VR-before and VR-after (Table 4).

**Table 4 – Differences in Heart Rate according to Gender for each procedure**

| | Gender | Mean | Std. Deviation | t* | Sig |
|---|---|---|---|---|---|
| Heart Rate Before (VR) | Male | 73.4000 | 6.09554 | -2.117 | 0.048** |
| | Female | 81.6364 | 10.82841 | | |
| Heart Rate After (VR) | Male | 73.9000 | 6.62403 | -1.102 | 0.311 |
| | Female | 77.7273 | 9.92059 | | |
| Heart Rate Before (TA) | Male | 74.9000 | 9.65459 | -2.118 | 0.048** |
| | Female | 85.4545 | 12.77782 | | |
| Heart Rate After (TA) | Male | 74.1000 | 7.29459 | -.2.369 | 0.029** |
| | Female | 83.4545 | 10.35725 | | |

**Differences are significant at p<0.05

A paired t test comparing the change in heart rate per procedure with the gender of the participants, showed no significance for both genders.

The patient's experience of pain with each group was measured using Wong-Baker Faces Pain-rating Scale (W-BFPS). The Wilcoxon Sign Rank test showed that while 10 of the 21 participants had a higher W-BFPS with TA when compared to VR, 5 of the 21 reported a worse experience with VR when compared to TA. There were six individuals who reported the same experience with both procedures (Table 5). These differences were however not significant (Z=1.662, sig= 0.096)

**Table 5: Comparisons and Ranking of W-BFPS**

| | | N | Mean Rank | Sum of Ranks | Z* | Sig |
|---|---|---|---|---|---|---|
| W-BFPS - VR<br>W-BFPS – TA | Negative Ranks | 5[a] | 6.50 | 32.50 | 1.662 | 0.096 |
| | Positive Ranks | 10[b] | 8.75 | 87.50 | | |
| | Ties | 6[c] | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| | Total | 21 | | | | |

a. W-BFPS - TA < W-BFPS – VR

b. W-BFPS - TA > W-BFPS – VR

c. W-BFPS - TA = W-BFPS – VR

*calculated using the Wilcoxon Sign Rank test

Differences are not statistically significant

In contrast to the heart rate and W-BFPS reading of pain level, when patients were asked which method they preferred, a significant majority (Chi square = 14.124, p=0.021) reported that they preferred the VR to Topical Anesthesia (Fig 1).

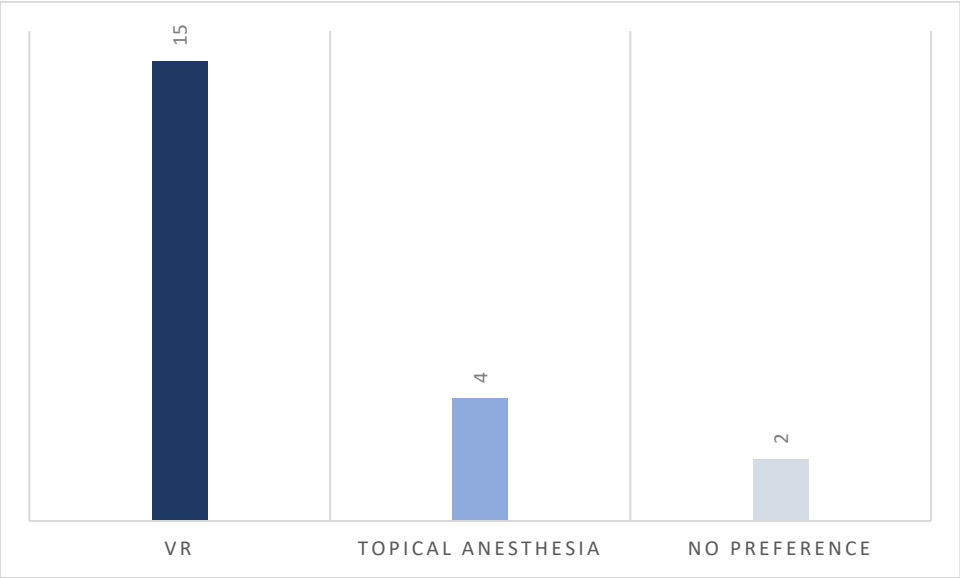


**Fig 1:** Stated preference of procedure by the population

# INFORMED CONSENT FORM FOR PATIENT

This Informed Consent Form is for men and women who attend dental clinic at Riyadh Elm University and who we are inviting to participate in research titled **Comparison between the Analgesic Effectiveness of Virtual Reality and Topical Anesthesia: A Clinical Study**

## Part I / Information sheet

I am Dr May Almugait, working for the dental clinic at Riyadh Elm University. We are doing research on effectiveness of virtual reality (VR) in local dental anesthesia. I am going to give you information and invite you to be part of this research. You do not have to decide today whether or not you will participate in the research. Before you decide, you can talk to anyone you feel comfortable with about the research. There may be some words that you do not understand. Please ask me to stop as we go through the information and I will take time to explain.

**Purpose of the research**

The aims of the study are to compare the analgesic and anxiety control effectiveness of virtual reality (VR) and topical anesthesia (TA) gel during administration of local anesthesia in adult dental patients, and to determine which approach the patients preferred to reduce pain of dental injections.

**Type of research intervention**

This study involves doing local anesthesia twice for maxillary teeth, one with VR device, and one with topical anesthesia.

**Voluntary Participation**

Your participation in this research is entirely voluntary. It is your choice whether to participate or not. Whether you choose to participate or not, all the services you receive at

this clinic will continue and nothing will change. You may change your mind later and stop participating even if you agreed earlier.

**Procedures and protocol**

Participants will receive dental anesthetic injections bilaterally for the maxillary second premolars, within the same visit. One side will be injected under the influence of the topical anesthesia (TA) 20% benzocaine, while the other side under the influence of a virtual reality (VR) animated movie using an Oculus Quest® device. The order of procedure will be random. Heart rates will be recorded prior to and after the injections using a finger pulse oximeter. Immediately after each injection, the participants will be directed to rate their pain experience using the Wong-Baker Faces Pain-rating Scale (W-BFPS), along with choose which delivery system they preferred.

**Duration**

The research takes place over one session for almost 30 minutes.

**Side effects**

It is unlikely to have any side effects during the study.

**Risks**

If any risk appears during the process, the healthcare workers will be looking after you and the other participants very carefully during the study.

**Reimbursements**

Your participation is free. You will not be given any other money or gifts to take part in this research

**Confidentiality**

The information that we collect from this research project will be kept confidential. Information about you that will be collected during the research will be put away and no-one but the researchers will be able to see it. Any information about you will have a number on it

instead of your name. Only the researchers will know what your number is and we will lock that information up with a lock and key. It will not be shared with or given to anyone except Dr May who will have access to the information.

**Sharing the Results**

The knowledge that we get from doing this research will be published in a scientific journal. Confidential information will not be shared.

**Right to Refuse or Withdraw**

You do not have to take part in this research if you do not wish to do so. You may also stop participating in the research at any time you choose. It is your choice and all of your rights will still be respected.

**Alternatives to Participating**

If you do not wish to take part in the research, you will be provided with the established standard treatment available at the dental clinic.

**Who to Contact?**

If you have any questions, you may ask us now or later, even after the study has started. If you wish to ask questions later, you may contact Dr May at 0506195647.

**This proposal has been reviewed and approved by the research center in the university and given this IRB approval number: IRB Approval no. RC/IRB/2019/321.**

## PART II: Certificate of Consent

I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions that I have asked have been answered to my satisfaction. I consent voluntarily to participate as a participant in this research.

Name of Participant_____

Signature of Participant _____

Date _____

**Statement by the researcher/person taking consent**

I have accurately explained the information sheet to the potential participant, and to the best of my ability made sure that the participant understands that dental injection will be made twice for him/her, one with VR and another one with TA.

I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this consent form has been provided to the participant.

Name of Researcher/ Dr May Almugait

Signature of Researcher /person taking the consent_____

Date _____