Statistical Analysis Plan

Official title: Efficacy of platelet- and extracellular vesicle-rich plasma in the treatment of chronic postoperative temporal bone cavity inflammations

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Statistical analysis was performed by the principal investigator. We used the computer program Microsoft Excel for Mac (versions 16.9.0-16.36) to record and edit the survey data, and the computer program SPSS (angl. Statistical Package for the Social Sciences, version 23, IBM Corp., Armonk, New York, USA) for statistical analysis. The difference between the groups was defined as statistically significant if the probability of rejecting the null hypothesis was greater than 95% ($p < 0.05$).

1. Statistical analysis of continouous variables

To compare the differences between the two groups of independent continouous numerical variables (e.g. the comparison between PVRP and the control group), we first determined the outliers in groups. Outliers were defined as values greater than 1.5 times the length of the boxplot (i.e., the length of the box without the whiskers). We then determined the distribution in the groups using the Shapiro-Wilk test. At p-value (p) <0.05, the distribution was considered as non-normal. If there were no outliers in both groups and the distribution was non-normal, we used an independent samples t-test. The homogeneity of the variances between the groups was checked by the Levene test. If the variances were different (i.e., heterogeneous) between groups ($p < 0.05$), we used an independent samples t-test, adapted for the case of violation of the homogeneity of variances. If the of variances were homogeneous, we used a normal independent samples t-test. Descriptive t-test statistics for independent samples were described with mean (M), standard deviation (SD), and 95% confidence interval (95% CI), and the statistical signicifance was defined by the value of test statistics (t) at degrees of freedom and with p-value (p).

If outliers and / or a non-normal distribution were present in at least one of the two independent groups with continuous numerical variables, the groups were analysed with the Mann-Whitney U-test. Data transformation or elimination of outliers was not used due to significant impact on results. We first compared the shape of distributions in both groups; if the shapes were similar, we compared the medians with the Mann-Whitney U-test. Descriptive statistics of the Mann-Whitney U-test were presented with median (Mdn) and statistical characteristics with the value of Mann-Whitney test statistics (U), standardized test statistics (z) and p-value (p).

To compare the differences between four groups of dependent and two groups of independent continuous numerical variables (eg comparison of COMQ-12 questionnaire scores between the four check-ups and at the same time between PVRP and the control group) we checked the assumptions for using two-way mixed analysis of variance, i.e., two-way mixed ANOVA). We first determined the outliers, the shape of the distribution, and the homogeneity of the variances in all groups. In the absence of outliers, normal distribution, and homogeneity of variances, the homogeneity of covariances was analyzed by the Box M-test. At $p > 0.05$, the covariances of the groups were homogeneous, so the sphericity was determined by the Mauchly test. Since

sphericity was taken into account at a value of p> 0.05, a two-way mixed analysis of variance with post-hoc testing was performed in the final analysis. Descriptive statistics of two-way mixed analysis of variance were presented with mean (M) and standard error (SE), and the statistical characteristic with the value of test statistics F at degrees of freedom (in parentheses), with p-value and with effect size measure (partial $\eta 2$ at p > 0.05).

To compare the differences between at least four groups of dependent continuous numerical variables (eg comparison of the surface area between four check-ups), we first tested the assumptions for using one-way repeated measures ANOVA. Outliers, shape of distributions, and sphericity were determined in all groups. If the assumption of sphericity was met, we performed a standard one-way analysis of the variance with repeated measures, and when the assumption of sphericity was violated, we performed a Greenhouse-Geisser correction of the one-way analysis of the variance of repeated measures by determining the epsilon (ε) value. We then identified the differences between the pairs of groups by post-hoc analysis using the Bonferroni correction. Descriptive statistics of one-way analysis of the variance of repeated measurements were described with mean (M), standard deviation (SD) and 95% confidence interval (95% CI), and statistical significance with the value of test statistics F at degrees of freedom (in parentheses), with p -value and with a measure of the effect size (partial $\omega 2$ at p> 0.05).

2. Statistical analysis of dichotomous variables

To compare the differences between the two groups of independent dichotomous variables (e.g. gender differences between PVRP and the control group), we used the Fisher exact test for samples of size < 5 and the $\chi 2$ test of homogeneity for samples of size > 5. The McNemar test was used to compare the differences between the two groups of dependent dichotomous variables (e.g., the presence of bacteria in the postoperative temporal bone cavity at the first and at the third check-up). Descriptive statistics of the analysis of dichotomous variables were presented with a percentage and statistical significance with p-value.