Study Title: A Randomized, Double-Blind Study of the Efficacy of Steroid Supplementation After Temporomandibular Joint Arthrocentesis

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Protocol

1. Title:

A Randomized, Double-Blind Study of the Efficacy of Steroid Supplementation After Temporomandibular Joint Arthrocentesis

2. Investigator(s):

Principal Investigator: Charles G. Widmer, D.D.S., M.S.
Co-Principal Investigator: M. Franklin Dolwick, D.M.D., Ph.D.
Sub Investigator: Daili Diaz, D.M.D.

3. Abstract:

Temporomandibular joint disorders are common and poorly understood in terms of etiology and pathogenesis. These disorders are multifactorial in origin including physical and psychosocial aspects; however, there is little understanding as to how much each of these components are associated with a particular diagnosis and subsequent treatment outcome of temporomandibular joint disorders. There is also a paucity of information regarding the relative effectiveness of different therapies for the treatment of patients with temporomandibular joint disorders. The identification of the least invasive and most efficacious therapy is vital to proper management of these patients with temporomandibular joint pain. The purpose of this study is to establish the relative efficacy of TMJ arthrocentesis with normal saline versus adjunctive steroid injection using standard pain and physical measures that are recorded before and after treatment. Patients enrolled into the study will be examined and treated at the Department of Oral and Maxillofacial Surgery. At the first appointment, they will be examined following standard procedures to determine if they would potentially benefit from the TMJ arthrocentesis procedure. If the patient meets the inclusion criteria for the study and with their informed consent, they will be required to complete a questionnaire about their physical and pain symptoms and undergo a standardized clinical exam. At the next appointment, the patients will undergo the standard clinical protocol for TMJ arthrocentesis with either only normal saline or normal saline with adjunctive steroids (triamcinolone acetonide). Follow-up appointments will be at 2 weeks, 6 weeks and 12 weeks where the pain VAS and clinical exam will be completed.

4. Background:

Temporomandibular joint (TMJ) disorders are considered to be the most common facial pain conditions that health professionals encounter each year and are probably the least understood in terms of etiology and pathogenesis of the disorders. As such, management of these disorders is poorly standardized and non uniform. One modality that has emerged in recent years is temporomandibular joint arthrocentesis and is a procedure that involves joint lavage using physiologic solutions. This lavage is commonly performed with normal saline or Lactated Ringers solution and may be followed with or without adjunctive steroids (depending upon the training of the practitioner). Although there are multiple case

reports and experimental trials that have confirmed the efficacy of the TMJ arthrocentesis procedure, there are few studies that have established the efficacy of adjunctive steroids in this procedure and no studies specifically studying the use of the steroid triamcinolone acetonide. This particular steroid has been found to be particularly effective in patients with Juvenile Rheumatoid Arthritis involving the temporomandibular joint (Stoll, et al, 2012). Therefore, the purpose of this study is to evaluate the efficacy of TMJ arthrocentesis with or without steroid supplement on well-defined patient populations that have pain in the temporomandibular joint. Information collected will include pain and physical determinants which will be compared pre and post TMJ arthrocentesis with and without the use of adjunctive triamcinolone. By conducting this study we hope to determine the need of adjunctive steroid use with TMJ arthrocentesis for TMJ pain.

5. Specific Aims:

To compare the resting and functional pain levels in patients with temporomandibular joint pain before and after temporomandibular joint arthrocentesis with placebo or temporomandibular joint arthrocentesis with steroid supplementation.

6. Research Plan:

Subjects will be recruited from patients referred to Dr. Frank Dolwick for potential temporomandibular joint arthrocentesis of one temporomandibular joint. Determination of a potential subject into the study will be made at the consultation visit (1st visit) by Dr. Frank Dolwick (co-PI) based on the medical history, response to a questionnaire, and inclusion and exclusion criteria. Each qualifying patient will be provided an explanation of the study by the Principal Investigator in the Oral and Maxillofacial Surgery clinic (by review of the Informed Consent Form) and a copy of the Informed Consent Form will be provided at the end of the consultation. The second scheduled visit is the TMJ arthrocentesis procedure and Informed Consent will be obtained at the beginning of the appointment if the patient has decided to participate in the study. The interval between the consultation and clinical procedure appointments is usually 1-4 weeks and this interval will allow the patient to decide if they would like to participate in the study. If the patient has decided not to participate, the normal clinical procedure for TMJ arthrocentesis will be pursued. Re-evaluation of the subject in the study will occur at 2, 6 and 12 weeks and will consist of filling out a questionnaire and a brief physical exam. The questionnaire and physical exam will be administered by the Principal Investigator while the co-PI and sub-Investigator will perform the TMJ arthrocentesis procedure and the supplementation of the placebo or steroid.

Inclusion criteria:
Female
18 – 80 years of age
TMJ Arthralgia
TMJ Myalgia
TMJ sounds
History of at least 6 weeks use of appliance therapy

Exclusion criteria:
Contraindication to sedation including pregnancy or medical history
History of previous TMJ procedure including arthrocentesis, arthroscopy or arthrotomy
History of steroidal injection in TMJ
History of trauma to TMJ
TMJ pain greater than 3 years
History of narcotic drug use on a scheduled basis
Current active infection

Procedures

Patients will be evaluated at the consultation appointment (1st appointment) to determine contraindications to the sedation/TMJ arthrocentesis procedure and to evaluate the potential benefit of the TMJ lavage procedure. These procedures are no different than those that would be conducted on patients referred for this procedure (see Fig. 1 for comparison of normal clinical procedures to the procedures that are proposed in this study). At this first appointment, patients that qualify for the study will be asked to participate and will be informed of the study's procedures and risks. Patients will not be asked to sign the informed consent until the beginning of the second appointment. If the patients decide to participate, they will again review the study procedures and risks and then sign the informed consent. The patient will then be randomized to one of two treatment groups: (1) TMJ arthrocentesis with lavage solution (placebo) supplementation in the upper joint space; or (2) TMJ arthrocentesis with steroid supplementation (20 mg triamcinolone acetonide) in the upper joint space. The clinical procedure in this study is exactly the same as the normal clinical procedure for TMJ arthrocentesis. The patient will be evaluated for a potential pregnancy and a pregnancy test will be administered and a negative response will be confirmed if there is any ambiguity in the patient's history. The patient will be sedated using fentanyl and midazolam, prepped, draped and a local anesthetic (3% mepivacaine) will be used to anesthesize the temporomandibular joint region. Two needles will be placed in the upper joint space and the joint will be lavaged with 100 cc of Ringers Lactate solution. Depending on the group that the patient is randomly assigned, either additional Ringers Lactate solution (placebo) or triamcinolone acetonide (steroid) will be infused into the upper joint space. The needles will then be removed and a bandage will be placed over the needle sites. The patient will be seen for standard questionnaire and physical exam evaluations at 2, 6 and 12 weeks post-arthrocentesis.

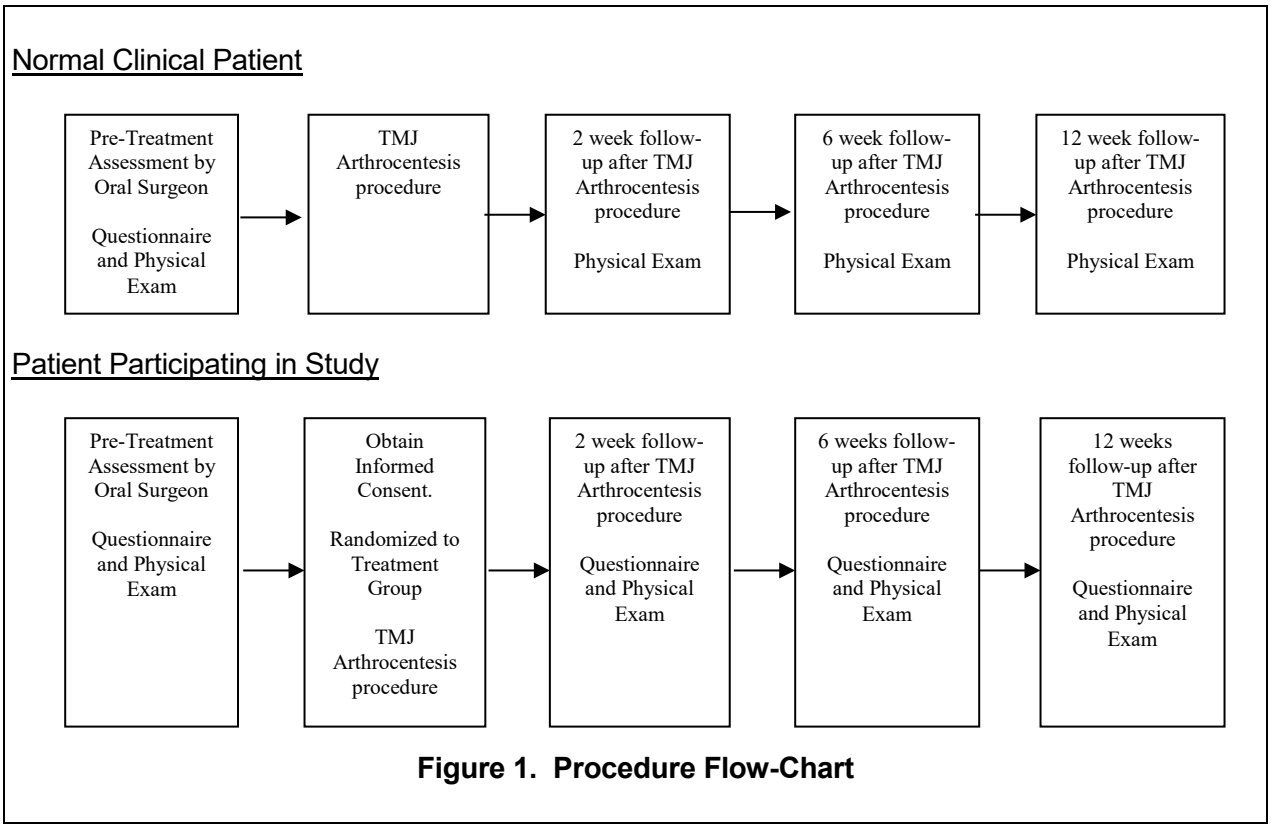

Figure 1. Procedure Flow-Chart

Data will be collected on questionnaires and clinical examination forms. These data will be transferred to a custom database for warehousing. Each subject will be evaluated for pain using a VAS measure for spontaneous pain and functional jaw pain (jaw opening and closing; TMJ loading) as the primary outcome measures. Secondary outcome measures include the following criteria: opening pattern, maximum unassisted vertical opening with pain, maximum unassisted vertical opening with pain, maximum assisted vertical opening, masticatory muscle palpation results, intraoral muscle pain results, TMJ palpation and TMJ sounds.

Power Sample Size Estimation

Power sample size estimations were based on the Visual Analog Scale (VAS) measures of pain in the two groups after TMJ arthrocentesis (steroid vs no steroid) with a difference of 10 (i.e., on a 100 mm scale, a change from 30 to 20) with a standard deviation of 8 and an alpha of 0.05. A power of 0.80 would require a sample size of 12 subjects per group while a power of 0.90 would require a sample size of 15 subjects (two way ANOVA, one between, one within, 2 groups). Therefore, a total sample size of 30 subjects should provide sufficient power to test for differences in pain levels between the two groups. We have included a potential drop-out rate of 20% (6 subjects) and have added these subjects for the total number of subjects to be recruited at 36 subjects.

Statistical Analyses

Statistical analyses will be conducted by the Principal Investigator and will consist of descriptive statistics (mean, standard deviation for parametric data; median and range for non-parametric data) and inferential statistics (two way ANOVA, 1 between (groups), 1 within (time)) using a probability level of < 0.05). Primary outcome variables are three pain variables (resting pain, 2 functional pain assays). Secondary outcome variables include palpable muscle tenderness, range of motion (no-pain limit and maximal opening with pain) and joint sounds (type, timing).

Adverse Reactions

Adverse reactions will be monitored for each patient at the time of clinical care (TMJ arthrocentesis) and for each re-evaluation appointment. Any significant adverse reaction will be addressed and treated at the time of the patient report. These findings will be noted in the database and reviewed monthly. No Data Safety Monitoring Board or oversight committee will be formed. Instead, the three investigators (PI, co-PI and sub-Investigator) will meet monthly to discuss any adverse reactions that were reported by subjects. The potential occurrence of adverse reactions is expected to be minimal based on the outcomes of the patients that have pursued these procedures in the past.

Data Confidentiality

Privacy information will only be accessible to the three participants (PI, co-PI and sub-Investigator). These data will be transferred from the data collection forms to a PDF format and will be stored on a computer that is secured by password protection and encryption (with password protection) of the files. The data collection forms will be destroyed using the existing procedure for hardcopy destruction used in the Oral and Maxillofacial Surgery Clinic.

7. Potential Discomforts and Risks:

There is no known health risks associated with completion of the questionnaires or the brief physical examination. The physical examination techniques used by the Principal Investigator during his evaluation are essentially the same as the techniques used in the standard physical exam protocol. The risk from sedation and steroid supplementation is evaluated clinically and patients are excluded based on their medical history. Pregnant females are excluded from participating in this study.

The cost of the TMJ arthrocentesis procedure with steroid/placebo supplementation is the responsibility of the study participants (or their insurer) and is considered standard therapy for the TMJ pain condition.

There is no anticipated discomfort associated with the steroid supplement. Breakthrough pain after the TMJ arthrocentesis procedure will be treated by the standard of care for this procedure.

8. Possible Benefits:

There are no known direct health benefits to the subject by this research. It is currently unclear if the addition of a steroid supplement will have a positive impact on the TMJ pain and jaw mobility over the TMJ arthrocentesis procedure. The information obtained from this study may help improve the treatment of patients with jaw joint problems in the future or may support the elimination of steroid supplementation and, thus, the risk (albeit low) of this added medication. The benefits include the potential for successful treatment of temporomandibular joint disorders with the risks being essentially the same as that of any proposed standard clinical care.

9. Conflict of Interest:

There is no conflict of interest of any investigators in this research study.