AAO Foundation Award Final Report

Type of Award: Biomedical Research Award

Name of Principal Investigator: Sunjay Suri

Title of Project: Integrated role of Orthodontics in the Multidisciplinary Diagnosis and Management of children with Temporomandibular Joint involvement in Juvenile Idiopathic Arthritis

Period of AAOF Support: 07-01-14 to 06-30-15 NCE till 12-31-15

Amount of Funding: USD 25,000

Summary/Abstract

This project aimed to comprehensively study the role of orthodontics in diagnosis and treatment of temporomandibular joint involvement in children affected by Juvenile Idiopathic Arthritis (JIA), and derive clinical practice recommendations based on a collaboration of specialists who routinely provide care for children affected by JIA, based in a tertiary-care university affiliated teaching hospital. There were 5 specific aims in this project and a summary for each specific aim of the project is included below:

Response to the following questions:

1. Were the original, specific aims of the proposal realized?

All 5 specific aims were realized. A summary is described in the detailed report below.

2. Were the results published? If not, are there plans to publish? If not, why not?

A paper prepared from specific aim 5 is under review by the AJODO. An MSc Orthodontics thesis that resulted from that specific aim was published. Other papers and clinical practice guidelines are being prepared for submission to peer reviewed journals.

AAOF support was and will be duly acknowledged in all publications emanating from this project.

3. Have the results of this proposal been presented? If so, when and where? If not, are there plans to do so? If not, why not?

The following presentations included findings that emanated from this project:

a) 'The orthodontist's role in diagnosis and management of temporomandibular joint arthritis in Juvenile Idiopathic Arthritis.' S. Suri. Doctor's session lecture at the 115th Annual

Session of the American Association of Orthodontists, San Francisco (May, 2015).

b) 'Effects of orthodontic appliances on diagnostic quality of MR images of the head.' D. Zhylich, S. Suri, B. Tompson, W. Lou, M. Shroff, P. Krishnan, P. Muthusami, A. Doria, T. Rayner-Kunopaski. at Charley Schultz Resident Scholar Program at the 115th Annual Session of the American Association of Orthodontists, San Francisco (May, 2015).

c) 'Effects of Orthodontic Appliances on Diagnostic Quality of MR Images of the Head.' Zhylich D, Suri S, Tompson B, Lou,W, Shroff M, Krishnan P, Muthusami P, Doria A, Rayner Kunopaski T. at "Latest Advances in Canadian Orthodontic Research" 67th Annual Session of the Canadian Association of Orthodontists, Victoria (September, 2015).

d) I will be including results from the completed study in my Doctor's session lecture on 'Orthodontic diagnosis and management of temporomandibular joint involvement in Juvenile Idiopathic Arthritis' at the 116th Annual Session of the American Association of Orthodontists, Florida (May, 2016).

AAOF support was and will be duly acknowledged in all of these presentations.

4. To what extent have you used, or how do you intend to use, AAOF funding to further your career?

There are very few funding sources for clinical research studies and therefore, AAOF funding is of immense value in making many such clinical research projects possible that otherwise may suffer due to lack of resources available to conduct them. In my studies which have been supported by the AAOF, funds have helped to pay for remunerating research associates and assistants, equipment, covering costs for expensive imaging such as magnetic resonance imaging, and costs related to publication and dissemination of findings as well as for participation in conferences. The true measure of an academician's career is the quality of their work published in peer reviewed scholarly journals and presentation in scientific conferences. I sincerely appreciate AAOF funding that supports my research endeavors and strengthen the quality of work to allow meeting high standards.

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Integrated role of Orthodontics in the Multidisciplinary Diagnosis and Management of children with Temporomandibular Joint involvement in Juvenile Idiopathic Arthritis

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Clinical Research Coordinator: Nicole Sidhu

Overview and broad description of study subjects and clinical material

The subject material for the studies and specific aims 1 through 4 described in this report is based on 102 patients with JIA, who I have examined and/or treated over a 5.5 year period at the Hospital for Sick Children, Canada, from 2010 till 2015. These children were referred by the department of Pediatric Rheumatology at the hospital. For studying skeletodental characteristics related to JIA, longitudinal chart notes and observations were made from diagnostic records over several longitudinal clinical examinations, however, each patient was registered as a unique subject so that there were no double inclusion of the same individual.

The average age of the subjects was 12.1 $\pm$ 4.0 yrs at the time of the orthodontic assessments. Also included as part of the essential diagnostic examinations were Magnetic Resonance (MR) examinations of the TMJ's in order to include the findings from the MR examinations closest to the orthodontic examination. The time difference between the MR examinations and orthodontic assessment for the study cohort described above was -0.2 $\pm$ 0.6 yrs. It is clarified here that when I conducted the clinical orthodontic examinations, I did not access the MR imaging before or during my examination in order to remain blinded to the findings in the MR images.

At the time of the main orthodontic examination included, which was the basis of the comparative study with the MRI gold standard, the occlusal observations in the included 102 subjects were as follows:
Overjet: 3.4 $\pm$ 2.0 mm
Overbite: 1.8 $\pm$ 2.5 mm
Maximal incisal opening (including the overbite): 43.4 $\pm$ 5.9 mm
Molar relationships: Class I: 51.6%, Class II: 44.2%; Class III: 4.2%

The constitution of this broader sample with respect to the different kinds of JIA was as follows:

Oligoarticular arthritis: 39 (14M, 25F), mean age at orthodontic assessment: 11.5 $\pm$ 3.9 yrs.
Polyarticular arthritis: 45 (6M, 39F), mean age at orthodontic assessment: 12.7 $\pm$ 4.1 yrs.
Psoriatic arthritis: 7 (2M, 5F), mean age at orthodontic assessment: 10.2 $\pm$ 4.8 yrs.
Enthesitis related arthritis: 11 (5M, 6F), mean age at orthodontic assessment: 12.9 $\pm$ 2.2 yrs.

Specific Aim 1: What are the short and long term treatment burdens of TMJ involvement in JIA?

For this specific aim, 69 patient charts of children with JIA with TMJ involvement were included. These were then categorized according to their JIA diagnosis. In this population, the sub-groups were: polyarthritis (n=31), oilgoarthritis (n=27), enthesitis related arthritis (n=7) and psoriatic arthritis (n=4). Burden of JIA medical treatment was assessed by examining age of diagnosis, medication regime and number of intra-articular steroid injections. Overall, NSAID and antirheumatic drugs (most commonly methotrexate), leflunomide, sulfasalazine, embrel and humira were used. Patients were prescribed a systemic corticosteroid in the form of prednisolone for a flare up of the arthritis, which was usually tapered off once the arthritis was in remission.

In this study, the average age at which JIA diagnosis was made was 6 years of age, with the youngest patient being 1 year old whilst the eldest was 15 years. In this cohort, 78% of patients had been prescribed some form of NSAID therapy. A large percentage of patients received disease modifying antirheumatic drugs (DMARDs) with methotrexate being the most commonly prescribed. Of these patients, 77% of patients at some point received methotrexate in comparison to 21% for leflunomide and 4% for sulfasalazine. Due to difficulty tolerating methotrexate, 36% of patients required a proton pump inhibitor. In cases where DMARDs were insufficient in controlling the arthritis, a biological agent such as enbrel or humira was prescribed, which occurred in 19% of patients. It was found that 19% of patients were prescribed a systemic corticosteroid in the form of prednisolone for a flare up of the arthritis, which was usually tapered off once the arthritis was in remission. Intraarticular steroid injections were used with varying frequencies based on type of arthritis and activity of disease. Further details of these burdens based on the sub-groups are included in a manuscript being prepared for submission to a peer reviewed journal and not discussed here for brevity and to respect the blind peer review process.

Specific Aim 2: What are the characteristics of the skeleteodental malocclusions and manifestations of TMJ effects that are revealed in the orthodontic clinical and functional assessment?

The following features were revealed in the orthodontic assessment:
Decreased mouth opening
Swing of the mandible to the more severely affected side
Cant of the occlusal plane towards the affected side
Progressive angulation of the mandibular incisor crowns to the less affected side
Progressive condylar erosion.

The other main findings of this study showed that joint sounds and crepitations and/or pain were less consistently detected. Lateral excursions toward the less affected side were restricted more frequently due to impaired translation, but this was less consistent and not necessarily diagnostic in many subjects when compared with MR findings. Children with polyarticular disease were generally affected more significantly with respect to these findings, however the findings were surprisingly severe in many children with oligoarthritis. Further details of these findings are included in a manuscript being prepared for submission to a peer reviewed journal and not

discussed here for aforesaid reasons.

Specific Aim 3: How do different components of the orthodontic clinical and functional assessment compare with detection of TMJ inflammation and arthritic changes revealed in the MR assessment?

A total of 102 MRI examinations of 102 subjects for the broad study sample described in the introduction was the source of gold standard diagnosis for this comparative assessment. MR examinations had been conducted and reported by staff radiologists who specialized in body and musculoskeletal imaging. Their reports were assessed to extract diagnoses of:

i) Synovitis, ii) disc thinning, fragmentation and abnormalities, iii) Condylar flattening, iv) Condylar erosions, v) Bone marrow edema within the condyles and finally vi) TMJ effusion

Several clinical orthodontic examination components were analyzed, and results compared with findings from the MRI examination. Detailed results have been provided to the AAOF, but are not disseminated here for brevity of this report and since they are part of a manuscript for submission for publication to respect the sanctity of the blind peer review process.

Specific Aim 4: What are the consequences of specific interventions such as intraarticular injections on TMJ inflammation and intraarticular disc?

The characteristics and progression of disc fragmentation was explored in this specific aim. A retrospective longitudinal cohort design was followed in which MRI findings from before the TMJ intra-articular steroid injections, and subsequent imaging till approximately 18 months from the intra-articular steroid injections were explored to study their potential association and effects on the disease and the joint. Presence of synovitis, condyle flattening and erosion, joint effusion and disc characteristics, were studied on MRIs acquired before and after TMJ steroid injections. Of the sample, 35 subjects who had at least one TMJ intra-articular Corticosteroid (IACS) injection were isolated. The 18 month time point for longitudinal follow up was chosen to allow sufficient time to have passed to arrive at definitive conclusions regarding disc outcomes. All MRI's had been reported by staff radiologists who are specialized in TMJ imaging. In total, 60 joints were injected in the 35 subjects included, and the average follow up was 1.82 yrs. Details of results have been submitted to the AAOF but not discussed here for aforesaid reasons of brevity and to respect the peer review process of manuscript submission. .

Specific Aim 5: Which routinely used fixed orthodontic appliances cause minimum artifacts on magnetic resonance (MR) images?

The influence of four common fixed orthodontic appliances on artifact formation and diagnostic quality of head MR images produced by a 3 Tesla MR scanner was studied. i) Stainless steel brackets, ii) ceramic brackets, iii) a combination of ceramic brackets and steel molar tubes, and iv) multistranded steel mandibular lingual retainers were embedded into custom made Essix® trays for each of 10 adult subjects. Head MR scans of nine regions were acquired for each subject wearing these trays with the embedded appliances. Sagittal T1-weighted, axial T2-weighted, axial gradient-recalled, axial diffusion-weighted, non-contrast axial MR angiography

and axial fluid-attenuated inversion recovery (FlAIR) MR sequences were included. Two neuroradiologists evaluated image distortions and diagnostic qualities of the 13860 acquired images. It was found that images were affected by appliance, head region and MR sequence. We concluded that head MR images are differentially affected by the presence of orthodontic appliances. The appliance, region imaged and MR sequence need consideration before imaging patients wearing different fixed orthodontic appliances.

From the results of this study, we have drafted clinical practice recommendations for use in hospital and imaging centers for subjects with the types of fixed orthodontic described above. For example, for 3T MRI; none of the appliances listed above need to be removed for MRA, FlAIR, and T2 sequences; steel brackets and tubes need to be removed for T1, GRE, and DWI; ceramic brackets do not need to be removed; steel molar tubes need to be removed for GRE and DWI; steel lingual retainer does not need to be removed.