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Relation of Age with the Temporomandibular Joint Internal Derangement Stage and Its Improvement After Nano-fat Injection

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Abstract

Background Temporomandibular joint (TMJ) internal derangement is multifactorial, and many studies show that the patient's age influences internal derangement and its response to treatment. **Objectives** This study proposed to investigate the relation of age with the stage of internal derangement and its improvement after nano-fat injection. **Materials and Methods** Thirty-eight temporomandibular joints for twenty patients were included. All involved patients were previously diagnosed with internal derangement (ID) depending on Wilkes classification clinically and radiographically, ID stages II, III, IV, and V were included. Nano-fat was used as an injection in superior joint space. The evaluation was done depending on pain assessment using a visual analogue scale and measuring maximum mouth opening in the pre-injection phase, one month, three months, and six months after injection. Paired T-Test were used to compare the continuous variables and Pearson Correlation to show age and stage relation. P–value less than 0.05 was considered significant**. Results** Patients' mean age was 29.75 years. The most frequent stage of TMJs was stage III (n=23 joints), followed by stage II (n=9 joints), stage IV (n=5 joints), and stage V in one joint. The (r = .324*) between patient age and stage of ID. All age groups show significant improvement after injection, unlike stage IV, and V groups. They showed insignificant improvement in mouth opening in all follow-up appointments. **Conclusion** Internal derangement can affect persons of any age. The severity of ID increases with age. According to the study results, the nano-fat injection is safe, reduces the TMJ pain, and is free from noticeable complications MMO in different age groups and stages II, III, IV, and V of ID in varying degrees.

Keywords: Age; Stage; Internal Derangement; Nano-fat; TMJ.

Introduction

Temporomandibular joint disc derangements or ID are functional-related disturbances in which the articular disc is crucial. Hey, and Davies defined ID in 1814 as "a localized mechanical fault interfering with the smooth action of a joint" (Moturi, 2021). ID is the second most frequent type of temporomandibular disorder after

myofascial pain syndrome and represents an abnormal disc position that adversely affects the internal structures (Kumar et al, 2021). The most frequent patient complaints are pain, reduced maximum mouth opening (MMO), and clicking (Abdulmaged & Lateef, 202; Ali et al, 2023). Numerous etiological explanations have been proposed to clarify the occurrence of ID. Trauma seems to be the most frequent reason for disc derangement. Trauma comprises acute injuries, such as blunt blows to the jaws, and chronic trauma, such as habits (Warburton, 2021). Joint ligament laxity also has been reported to be associated with disc derangement (Boboc et al, 2022). Bruxism has been linked to compressive overloading leading to the generation of highly reactive oxidative radicals that degrade proteoglycans, hyaluronic acid, and collagen. Such changes in the joint lubrication system increase intra-articular friction and prevent the joint from gliding smoothly, which seems to relate to disc derangement (Chang et al, 2018; Alhussien & Ryhan, 2017). Moreover, many studies suggested wide disciplinary in the age distribution of ID, revealing that patient age may influence ID pathogenesis and clinical course (Valesan et al, 2021). A widely accepted clinical staging system for disc displacement is the Wilkes Classification, which emphasizes severity and chronicity (Han & Lieblich, 2022). Wilkes defined five stages with clinical and radiographic features of ID. Stage I is represented by clicking without pain and disc displacement anteriorly with reduction. Stage II involves locking with reduced disc displacement and clicking with occasional pain (Derwich et al, 2020). In Stage III, moderate pain, long-lasting locking, joint tenderness, limited motion, disc displacement with or without reduction, and degenerative changes do not occur in this stage. Stage IV features limitation in mouth opening with chronic pain, no clicking with degenerative bony changes, and non-reducible disc displacement (Silva et al, 2021). Stage V refers to crepitus, fluctuating pain, painfully limited function, advanced degenerative bony changes, severe disc deformity, and non-reducible anterior disc displacement (Tapan et al, 2023). The main goals of ID management are identifying and controlling the underlying causes, reducing functional load, decreasing inflammation, and allowing adaptive articular remodelling; this can lead to pain reduction, improvement of mandibular motion, and resuming function (Warburton et al, 2022). The intra-articular injection is one of the most popular minimally invasive treatment modalities for ID (Wadhokar et al, 2022). Adipose tissue can undergo mechanical degradation, reducing its particle size and producing nano-fat products that are simple to inject. Nano-fat is considered one of the richest reservoirs of adipose-derived stem cells. Many studies approve of its role in tissue regeneration as well as remodelling ability which has been found in plastic surgery applications, healing of joints, and some ligament-tendon diseases (Quintero Sierra et al, 2023; Al-Chalabi et al, 2018; Jeyaraman et al, 2021). This study aimed to investigate the relation between age and stage of ID and evaluate improvement after nano-fat injection according to age and stage.

Materials and Methods

This prospective observational clinical study was performed between December 2021 and December 2022 and approved ethically by the Research Ethics Committee of the College of Dentistry, University of Baghdad. This study included 20 patients with 38 TMJs (single joint affected in 2 patients and both joints affected for 18 patients) who suffered from TMJ internal derangement from those attending the oral and maxillofacial department of the College of Dentistry. Each participating patient who had signed informed consent was provided with their datasheet. Both males and females were involved in this study (4 males and 16 females). All patients involved in the study were previously diagnosed with TMJ internal derangement using the Wilkes classification using Cone Beam Computerized Tomography (CBCT). All those patients had no previous response to conservative management with different modalities for at least (3-6) months.

Criteria of the study

- **Inclusion criteria**
- Patients with frequent pain of the TMJ with limited mouth opening did not respond to conservative management.
- Patients with Joint noises.
- Wilkes classification of TMJ internal derangement involving Stages II, III, IV, and V.

Exclusion criteria

- Patients on anticoagulant medications.
- Patients with facial asymmetry (condylar deformity).
- Patients with previous surgery to the TMJ.
- Patients with infection of the TMJ region.
- Patients who had metabolic diseases.

Variables and Assessments

The following parameters were used to evaluate the ID in the pre-injection and the 6-month follow-up post-injection.

A. Pain Assessment using the visual analogue scale (VAS), a self-reported measure of pain, ranging from 0 to 10, in which 0 represents no pain, and 10 represents excruciating pain.

B. Maximum Mouth Opening was measured pre-injection and post-injection. It represents the distance between the incisal edge of the maxillary central incisor to the incisal edge of the mandibular central incisor on the midline when the mouth is opened widely by using a millimetre ruler.

The pre-injection phase

started with history-taking, which included personal information, medical history, chief complaint, any history of trauma, previous TMJ surgery, or nonsurgical treatment. After history taking, the extra-oral clinical examination included inspection for any swelling, deformation, facial asymmetry, deviation of the chin or reduced mouth opening, and palpation of TMJ to identify pain and tenderness. Palpation of masticatory muscles was performed to eliminate the probability of myofascial pain syndrome. The measurement of MMO considered the inter-incisal distance in which the patient was asked to further open wide despite the pain, and the normal range is 40–45 mm. Following the extra-oral examination, the intraoral clinical examination was performed. The essential evaluation criteria were the centric relation, overjet, overbite, and Angle's classification for occlusion. CBCT was taken to exclude any TMJ pathology or if there is a dental cause of pain and to assess any osseous changes.

Injection phase

The operative technique was done with complete aseptic conditions under local anaesthesia for 11 patients and under general anaesthesia for 9 patients.

A. Nanofat harvesting

The planned donor site for fat harvesting was the sub-umbilical abdomen region for all patients; a small incision was made in this region, whereas the patient was supine. Tumescent Solution, which consists of 490 ccs of normal saline, 10 ccs of 2% lidocaine, and 1 cc of 1:1000 adrenaline vial, was prepared and infiltrated through the incision into the donor site by using an infiltration cannula 2.5mm in diameter connected to a 60-cc disposable syringe. The infiltrated solution should cover all included areas. A firm grip was required to lift the tissues as the infiltration cannula was aimed at the most profound plane to avoid an inadvertent puncture of underlying fat tissues. After waiting 10 minutes for the tumescent solution effect, fat was picked by the harvesting cannula 3.0 mm internal diameter connected to a 60-cc disposable syringe. The harvested cannula was inserted slowly through an incision previously done, then under gentle negative pressure by pulling back the syringe plunger and moving the harvesting cannula in a different direction within the infiltrated area. After harvesting about 20cc of fat for processing, the harvesting cannula was removed from the syringe and secured. The collected fat was washed with a saline solution several times until the fat became clear without blood and fluids. Finally,

the collected pure fat was processed according to the protocol of Tonnard et al. (Yang et al, 2021). Fat was mechanically emulsified by moving the fat between two 60-cc syringes connected by an anaerobic Luer-to-Luer fat transfer adapter with an inner diameter of 2.4,1.4, and 1.2 mm in an ordered manner. Thirty passes were done between two disposable syringes for each size of the adapter to ensure degradation. The processed fat changed into an emulsion with a whitish appearance and filtered through transfer mesh to remove the connective tissue remnants that would block the fine needles. 1.5 cc taken in a 5-cc disposable syringe; the prepared nano-fat was ready for injection.

B. The technique of nano-fat injection
Approximately 10 mm anterior and 2 mm inferior to a canthal-tragal line drawn with a marker pen between the lateral canthus and the apex of the tragus. The maximum concavity of the fossa and the articular eminence was palpated to confirm the injection site. In this position, a 23-gauge needle was inserted into the upper compartment of the TMJ. After aspirating to ensure no blood in the syringe, the upper joint space was injected with 1.5 cc of nano-fat, as illustrated in Figure (1).

Post-injection phase
Post-injection care includes applying a cold pack during the first few hours after injection; the patients were instructed to take a soft diet only and return to a regular diet after one month. The clinical assessment of ID for each patient during the follow-up phase was planned to be continued after one month, three months, and six months using the same pre-injection parameters.

Statistical Methods
The data was analysed using Statistical Package for Social Sciences (SPSS) version 25. The data are presented as mean, standard deviation, and ranges. Frequencies and percentages present categorical data. Paired t-tests were used to compare the continuous variables in pre-injection and post-injection and Pearson correlation. A level of P – value less than 0.05 was considered significant.

Results
This study included 20 patients, with 38 TMJs diagnosed with internal derangement. The patient's ages ranged from 15 to 61 years with a mean of 29.75 years and standard deviation (SD) of ± 11.04 years, and more than half of the study patients, 11 (55%) aged ≥ 30 years, and the remaining nine patients (45%) aged < 30 years. Regarding sex, there were 16 females (80%) vs. 4 males (20%) with a male-to-female ratio of 1:4. Concerning the side of TMJs, 18 (90%) patients presented with both joints affected, while 2(10%) patients presented with single joints either left or right joint. The most frequent stage of TMJs was stage III in 23 joints (60.5%), followed by stage II in 9 joints (23.7%), stage IV in 5 joints (13.2%), and stage V in one joint (2.6%) as shown in Table (1). There is a significant positive correlation (r = .324*, P= 0.03) between patient ages and stages of ID. For statistical purposes, patient ages were divided into two groups (< 30 and ≥ 30), and the stages were divided into two groups as well (II, III as one group and IV, V as the second group); the mean VAS score for pain significantly decreased (P < 0.05) compared to that pre-injection regarding age and stage of TMJs after one month, three months, and six months of injection as shown in Tables (2,3, 4) and Figure (2). While comparison of MMO means according to age and stage showed that after nano-fat injection, the MMO significantly increased than that pre-injection among patients aged < 30, ≥ 30 years, with stages II and III. No statistically significant difference (P ≥ 0.05) was found in MMO mean with TMJ stages IV and V, as shown in Tables (5,6, 7) and Figure (3).

Table (1): General characteristics distribution of the study sample.

General characteristics	No.	Percentage (%)
Age		NO.20 Patients
< 30	9	45
≥ 30	11	55
Sex		
Male	4	20
Female	16	80
Side		
Unilateral	2	10
Bilateral	18	90
Stage	NO. 38 TMJs	
II	9	23.7
III	23	60.5
IV	5	13.2
V	1	2.6

Table (2): Comparisons of mean VAS scores for pain before and after one month of nanofat injection according to age and stage.

Characteristics	VAS Score of Pain		P-Value
	Pre-injection Mean ± SD	PIM1 Mean ± SD	
Age			
< 30	8.62 ± 1.84	3 ± 3.29	0.003
≥ 30	6.08 ± 3.05	1.08 ± 2.02	0.001
Stage			
II & III	7.46 ± 2.62	1.71 ± 2.58	0.001
IV & V	6.67 ± 3.20	2.50 ± 2.07	0.001
PIM1:postinjection month1, SD: standard deviation			

Table (3): Comparisons of mean VAS scores for pain before and after 3 months of nanofat injection according to age and stage.

Characteristics	VAS Score of Pain		P-Value
	Pre-injection Mean ± SD	PIM3 Mean ± SD	
Age			
< 30	8.62 ± 1.84	1.50 ± 2.13	0.001
≥ 30	6.08 ± 3.05	1 ± 2.11	0.001
Stage			
II & III	7.46 ± 2.62	1.43 ± 2.22	0.001
IV & V	6.67 ± 3.20	0.66 ± 1.03	0.003
PIM3:postinjection month 3, SD: standard deviation			

Table (4): Comparisons of mean VAS scores for pain before and after 6 months of nanofat injection according to age and stage.

Characteristics	VAS Score of Pain		P-Value
	Pre-injection Mean ± SD	PIM6 Mean ± SD	
Age			
< 30	8.62 ± 1.84	0.75 ± 1.84	0.001
≥ 30	6.08 ± 3.05	0.66 ± 1.61	0.001
Stage			
II & III	7.46 ± 2.62	0.68 ± 1.53	0.001
IV & V	6.67 ± 3.20	0.1 ± 0.01	0.002
PIM6:postinjection month 6, SD: standard deviation			

Table (5): Comparisons of MMO mean before and after 1 month of nanofat injection according to age and stage.

Characteristics	MMO		P-Value
	Pre-injection Mean ± SD	PIM1 Mean ± SD	
Age			
< 30	23.11 ± 4.93	32.88 ± 6.86	0.002
≥ 30	32.01 ± 9.59	40.09 ± 8.19	0.025
Stage			
II & III	28.81 ± 9.51	38.28 ± 6.91	0.001
IV & V	24.66 ± 4.50	31 ± 12.42	0.121
PIM1:postinjection month1, SD: standard deviation			

Table (6): Comparisons of MMO mean before and after 3 months of nanofat injection according to age and stage.

Characteristics	MMO		P-Value
	Pre-injection Mean ± SD	PIM3 Mean ± SD	
Age			
< 30	23.11 ± 4.93	34 ± 6.20	0.001
≥ 30	32.01 ± 9.59	40.81 ± 7.26	0.002
Stage			
II & III	28.81 ± 9.51	39.15 ± 5.91	0.001
IV & V	24.66 ± 4.50	31.66 ± 12.01	0.078
PIM3:postinjection month3, SD: standard deviation			

Table (7): Comparison of MMO means according to age and stage, before and after 6 months of nanofat injection.

Characteristics	MMO		P-Value
	Pre-injection Mean ± SD	PIM6 Mean ± SD	
Age			
< 30	23.11 ± 4.93	35.44 ± 6.63	0.001
≥ 30	32.01 ± 9.59	42.36 ± 6.93	0.001
Stage			
II & III	28.81 ± 9.51	40.78 ± 5.97	0.001
IV & V	24.66 ± 4.50	31 ± 11.41	0.067
PIM6:postinjection month 6, SD: standard deviation			

Discussion

According to age distribution, ID can affect persons of any age, as shown in our study results, which concur with many studies (Blanco-Rueda et al, 2023). The prevalence of ID is significantly higher in young and middle-aged adults from the second to the fourth decade, and this age group coincides with the age group of our study (Kulkarni et al, 2020). The more significant peak in the occurrence of symptoms is seen around 20 and 40 years which accounts for the increased prevalence in this age range, while in advancing age, signs and symptoms become less or undetectable, so accordingly, prevalence is inversely proportional to age (Alhussien, & Ryhan, 2017; Ryan et al, 2019). Bruxism is regarded as a causative factor which is found in 87.5% of patients with ID and TMJ pain; the highest prevalence of bruxism is between the ages of 20 and 50, which coincide with the age where ID is most prevalent (Van Praag, 2019). In older age, the low prevalence may be attributed to the ID course in a significant percentage of persons is highly affected by environmental factors that become less with aging (Ohrbach et al,2021). The disparity in results may be because many questionnaires and examinations are better tailored to the adult population, unlike children, who often need help understanding some of the questionnaires and can be confused by the examinations (Ryan et al, 2019). In the present study, the most frequent stage of TMJ was stage III, followed by stage II; these are the most prevalent forms of TMJ disc displacements. This finding comes in agreement with the studies. Pain and jaw limitation, primarily present in these stages, often impact daily function, psychosocial well-being, and quality of life, making these patients seek treatments (Rafaat & Shalan, 2020). Furthermore, the results of our study show that the severity of ID increases with age since there is a significant positive correlation between them, which goes in line with the Nagihan Koç study, which concludes that older patients may have more common findings of osseous changes, such as condylar and articular erosion, osteophytes and joint space narrowing, these represent the advanced stages of ID (Koç, 2020). With age, the average adult articular disc has little to no cell division or cell death, and it does not appear that there is an available supply of progenitor cells to replace chondrocytes that do die since the chondrocytes are distinct cells that may be subject to aging-related alterations. These contributing factors all line up with the findings of this study, which

demonstrated increased severity of ID with increased age (Alzahrani et al, 2020). Both age groups show the same response at all times of follow-up, a significant decrease in pain, and a significant increase in MMO happened; these results coincide with many studies that reported the same effect for nano-fat intra-articular injection (Mahmmood & Shihab, 2019). The ability of nano-fat to improve symptoms is due to its anti-inflammatory and immunomodulatory properties. Moreover, adipose stem cells multilineage can produce adequate functioning cells with good proliferative and differentiating abilities to heal damaged tissue (La Padula et al, 2023). Recently, stem cell therapy has gained significance due to its abundance, availability, and accessibility, Mesenchymal stem cells are multipotent progenitor cells that can differentiate into numerous lineages and self-renew (Chen et al, 2021). Regarding the evaluation of TMJ-stages response, all stages show a significant pain reduction in all follow-up times. According to MMO, stages II and III respond significantly after injection, unlike stages IV and V, since the improvement was insignificant in these stages in MMO in all follow-up times. This may be attributed to irreversible, non-reducing disc position in the advanced stages of ID, since in these stages stickiness of the disc to the condyle may occur causing limitations that cannot be easily resolved (Han & Lieblich, 2022). Limitations of this study in their small sample size and short follow-up period.

Conclusions

Internal derangement can affect persons of any age. The severity of ID increases with age. According to the study results, the nano-fat injection is safe, reduces the TMJ pain, and is free from noticeable complications MMO in different age groups and stages II, III, IV, and V of ID in varying degrees.

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