AUTOLOGOUS CONDITIONED SERUM INTRAARTICULAR INJECTIONS FOR TEMPOROMANDIBULAR JOINT OSTEOARTHRITIS TREATMENT: LITERATURE REVIEW AND CASE REPORT

Torres-Hortelano JM, Romero-García A, Rodríguez-Ramírez de Arellano T, Torres-Rubio A.

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Alicante

INTRODUCTION

- Arthrosis or osteoarthrosis of the temporomandibular joint (TMJ-OA) is a degenerative disorder involving the joint and is the most common non-inflammatory disease of the TMJ, characterized by deterioration of articular tissue with concomitant osseous changes in the condyle and/or articular eminence[(1)]. The biological linkage between the progressive degeneration of the articular cartilage of the TMJ and the occurrence of orofacial pain is still largely unknown. For this reason, clinical treatments of TMJ-OA are focused, in a first stage, on the relief of orofacial pain with Symptom Modifying OsteoArthritis Drugs - **SMOADs** (e.g. analgesic medications, NSAIDs, steroid injections or Symptomatic Slow Acting Drugs for Osteoarthritis) and finally, if the pain continues, in a surgical intervention.

- Which the aim to optimize conservative management and avoid or delay surgical intervention, recent studies suggest to use Disease Modifying OsteoArthritis Drugs - **DMOADs** in order to maintain the cartilage homeostasis of the synovial joints and shift the metabolic status from catabolic to anabolic using intra-articular injections with, for example, Hyaluronic Acid (HA)[(2)], Platelet Rich Plasma (PRP) or Plasma Rich in Growth Factors (PRGF)[(3)], Autologous Conditioned Serum (ACS)[(4)] or stem cells[(5)].

MATERIAL AND METHODS

- A systematic review of the relevant literature performed by us seems to confirm that autologous intra-articular therapies with **ACS**, rich in growth factors (e.g. TGF-ß, IGF-1, etc) and anti-inflammatory cytokines (e.g. Interleukin-1 Receptor Antagonist - IL-1Ra), or **PRGF**, mainly rich only in growth factors, show clinical improvements in TMJ-OA patients. Therefore, strong evidence-based data are needed to identify the best ACS/PRGF preparation protocol (e.g., platelet concentration, timing and volume for injection, combination with arthrocentesis, etc) according to the physiological conditions and clinical diseases of the patients (e.g., inflammatory-degenerative disorders, arthralgia, closed lock, other internal derangements, etc)[(6)].

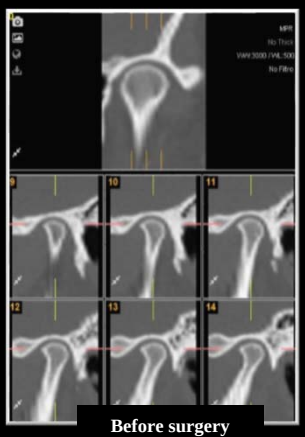
Platelet-rich plasma for the treatment of temporomandibular joint osteoarthrosis

Study	Type of study	Aspects related to PRP			Study design				Assessments	Results
		Centrifugation	Injections interval	Volume (ml)	Grade/Diagnosis of OA	Treated (N)	Controls (N)	Analyzed paramenters		
Machon 2013[1]	Prospective Pilot study	Single 1500 rpm (6 min)	2 injections biweekly	1	Wilkes stage IV	10 PRP	10 HA 10 controls	VAS MIO	3 months	PRP superior to HA
Cömert 2015[2]	Prospective Controlled Randomized	Single 1000 rpm (10 min)	5 injections monthly	1	Clinical and CBCT evaluation (DC/TMD; axis I group IIIb)	18 PRP (32 joints)	12 controls (15 joints)	VAS MIO CBCT	12 months	PRP showed benefit
Giacomello 2015[3]	Prospective	Single 580g (8 min)	2 injections monthly	1.5-2	Imaging findings (orthopantomography and MRI)	13 PRGF-Endoret	None	VAS MMO	1 (after 2nd injection) and 6 months	PRP showed benefit
Hegab 2015[4]	Prospective Controlled Randomized	Single 3200 rpm (12 min)	3 injections weekly	1	Imaging findings (radiography or MRI)	25 PRP	25 HA	VAS MVMO	1, 3, 6 and 12 months	PRP superior to HA
Cömert 2016[5]	Prospective Controlled Randomized	Single 1000 rpm (10 min)	5 injections monthly	1	Clinical and CBCT evaluation (DC/TMD; axis I group IIIb)	18 PRP (32 joints)	13 HA (17 joints)	VAS MIO	12 months	No difference between PRP and HA
Fernández-Sanromán 2016[6]	Prospective Controlled Randomized	Single 580g (8 min)	Single injection	8	Wilkes stage IV	42 PRGF-Endoret	50 controls	VAS MMO	3, 6, 12, 18 and 24 months	PRP showed benefit at 6 and 12 months No difference at 18 and 24 months

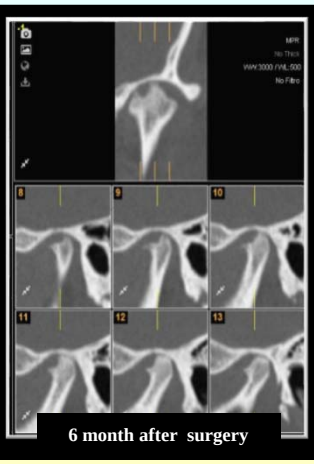
CASE REPORT

- This case report describes an unsuccessful orthognathic surgery treatment of a skeletal Class III malocclusion with mandibular prognathism and asymmetry in a 26 year old male.
- Six months after surgery the patient developed pain at left TMJ, appearing an osteoarthritic condylar destructive process in CBCT scans, which is characterized by a break in the anterosuperior outline surface and the presence of a "cup"-shaped defect.
- The case was treated conservatively with a stabilization splint and 4 intra-articular TMJ injections (1 every 3 weeks) with 2 ml of ACS-Orthokine®.
- A year later, the patient is painless, without limited ROM and a corticated outline of the superior surface of the condyle can be observed in CBCT scans.

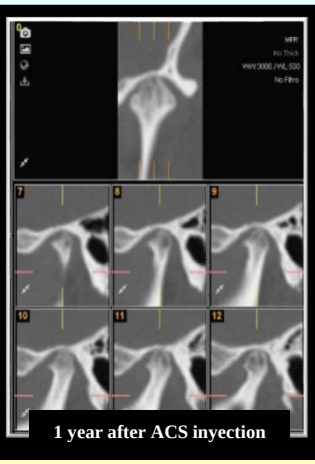
PRGF PRP	ACS (Orthokine®)
Plasma contains platelets, white blood cells, fibrinogen and growth factors.	Serum is cell-free and no clotting factors. Contains growth factors and anti-inflammatory cytokines.
Presence of anticoagulants and additives. Prior to injection is necessary platelets activation with CA^{2+} to promote the liberation of the GF.	No anticoagulants and additives but medical grade glass beads in the syringe. Is not necessary activation with CA^{2+} since GF are released during incubation.
Applied directly after processing without incubation.	Applied after incubation at 37° for 6–9 h (now studying after 1 h).
Must be prepared each time for every single injection. Frozen storage not possible because of requirement of vital platelets.	Prepared only once. Storage possible since the syringe aliquots can be stored at -20° up to 7 months.
Can not be administered with an antibacterial filter due to presence of cells.	Safer injection administered with an antibacterial filter because it is cell-free.



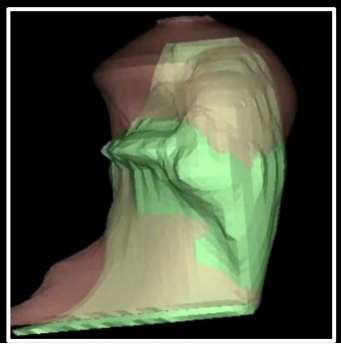
Before surgery



6 month after surgery



1 year after ACS inyection



Software superinposed CBCT scans ramu images pre (green) and post-ACS injections (red), showing bone growth in the upper condylar heat.

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