How to Cite:
Moussa, M. S., Elhasan, M. F. A., & Abdullah, A. A. B. (2022). Effectiveness of electromyography guided botulinum toxin injection and dextrose prolotherapy in recurrent TMJ dislocation (radiographic and clinical study). *International Journal of Health Sciences*, *6*(S6), 3610–3620. https://doi.org/10.53730/ijhs.v6nS6.11501

Effectiveness of electromyography guided botulinum toxin injection and dextrose prolotherapy in recurrent TMJ dislocation (radiographic and clinical study)

Moataz Soliman Moussa
BDS, 2009G MSc, 2018G, Faculty of Dental medicine, Al-Azhar University (Cairo, Boys)

Mohsen Fawzy Abo Elhasan
Department of Oral and Maxillofacial Surgery, Faculty of Dental Medicine, Al-Azhar University, Assuit, Egypt

Abdel Aziz Baiomy Abdullah
Department of Oral and Maxillofacial Surgery, Faculty of Dental Medicine, Al-Azhar University, Assuit, Egypt
*Corresponding author email: abdelazizbaiomy@azhar.edu.eg
Orcid: https://orcid.org/0000-0002-5446-2820

***Abstract*---**Objectives: This study was conducted to assess effectiveness of dextrose prolotherapy, Electromyography (EMG) Guided Botulinum Toxin – A (BTX-A) Injection, and combination between them in treatment of recurrent TMJ Dislocation cases. Subjects and methods: This current study was carried out on 60 adult patients suffering from recurrent TMJ Dislocation. The patients divided equally into three groups, Group I: 20 patients were treated with EMG guided BTX-A injection. Group II: 20 patients were treated with dextrose prolotherapy. Group III: 20 patients were treated with combination of EMG guided BTX-A injection and dextrose prolotherapy. The clinical evaluation preoperatively and postoperatively (at 1week , 3 months , 6 months) included visual analog scale of TMJ pain, maximum mouth opening (MMO), and frequency of luxations . Radiographic evaluation using MRI was done preoperatively, and at 6 months. The collected data were then statistically analyzed. Results: best results were recorded in group III compared with other groups; at all intervals of study with significant reduction of pain score, and frequency of luxations beside to improvement of MMO measurements. Conclusion: the combination of EMG guided BTX-A injection and dextrose prolotherapy is a promising

treatment in recurrent TMJ dislocation cases. It achieved the best therapeutic results with simplicity, and safety manner compared with each treatment maneuver alone.

***Keywords*---**EMG guided injection, TMJ dislocation, botulinum toxin type A, dextrose, visual analogue scale.

Introduction

A common condition among patients is recurring dislocation of the temporomandibular joint (TMJ), which can happen when they laugh or yawn normally. Mandibular condyle displacement from the glenoid fossa and anterior locking of the articular eminence are symptoms of anterior TMJ dislocation. As a result, the mouth cannot be closed without pain. TMJ dislocation classified depending on the onset and frequency of dislocation to acute, chronic recurrent or subluxation or according to the direction of dislocated condyle to superior, medial, lateral, anterior or posterior dislocation which can occur bilateral, or unilateral (1). Several techniques have been advocated for the treatment of chronic TMJ dislocation. These techniques divided into noninvasive methods and invasive methods including sclerosing agent or autogenous blood injection into TMJ which aimed to induce fibrosis to limit the condylar movement but with drawbacks of unexpected reduction of mouth opening (4-6). Despite being an intrusive treatment for dystonia, botulinum toxin type A injection is a reasonably conservative choice. Because injection into the lateral pterygoid muscle (LPM) is simple and may be performed in outpatients with minimal difficulties, it can be utilized as a first strategy (5).

In TMJ dislocation, the target muscle is the lateral pterygoid with or without concomitant injection into the masseter muscle as they is involved in spasm during dislocation (6). Authors recommended also injection of the anterior fibers of the temporalis muscles, as the vector of pull of these fibers may serve to contribute to protrusion of the mandible and a predisposition to condylar dislocation (6,7). Regenerative injection therapy is another name for proliferation therapy, or "Prolotherapy." A non-pharmacological irritant solution, such as dextrose, is injected into the area of the tendons or ligaments during prolotherapy, and it is believed that this causes an inflammatory process that deposits new fibers to strengthen the lax tendons or ligaments and may even encourage the release of local growth factors (8). In order to compare the effectiveness of dextrose prolotherapy and EMG guided BTX-A injection in the treatment of recurrent dislocation, either alone or in combination, was the goal of the current study.

Subjects and Methods

The 60 adult participants (23 male and 37 female) in this study were chosen from the outpatient clinic, oral and maxillofacial surgery department, faculty of dental medicine, Al-Azhar University (Assuit), and had bilateral recurrent TMJ dislocation as determined by clinical and radiographic evaluation. The study extended through two years from MAY 2020 to MAY 2022. All patients were

informed about the study and signed a consent form. Ethical approval was obtained from Al- Azhar University ethical committee. This study followed the Declaration of Helsinki on medical protocol and ethics.

Inclusion Criteria

The patients' ages ranged from 20 to 50. All patients participated in this study were complaining of bilateral TMJ dislocation for a minimum of 6 months and had previously failed therapy using conservative measures. Preoperative MRI showed there was no articular cartilage degeneration, disc displacement, or osteoarthritis in any patients. It was identified that the patients had unilateral or bilateral condyles anterior to the eminence with their mouths in the open position

Exclusion criteria

Any patients suffering from degenerative joint disease, musculoskeletal, neuromuscular disorders, cardiovascular, bleeding disorders, breathing difficulties, pregnant and lactating women, patients with a history of taking regular drugs as opioid, muscle relaxants, calcium channel blockers, immunosuppressive drugs or aminoglycoside antibiotics or hypersensitivity to any botulinum toxin preparation, dextrose, human albumin or sodium chloride excluded from this study.

Grouping

The patients divided randomly into three equal groups according to the type of injected material. Group I: 20 patients injected with BTX-A guided by EMG in the Masseter, Temporalis & *Lateral* Pterygoid muscles through an extraoral approach as a study group. Group II: 20 patients had intra-articular injection with 2ml of 25% dextrose solution at superior space of capsule and 1ml pericapsular as a study group. Group III: 20 patients injected with combination of EMG guided BTX-A injection in the Masseter, Temporalis & Lateral Pterygoid muscles and intra-articular injection with 2ml of 25% dextrose solution at posterior superior space of capsule and 1ml pericapsular as a study group.

Sample size calculation

based on mouth opening, using a sample of 60 people divided into 3 groups, a one-way ANOVA research has a power of 81 percent. This power is based on a non-central F test with a 0.05 threshold of significance. Subject counts for the group are 20, 20, and 20. According to the other theory, the group means are 33, 36, and 37. Under the null hypothesis, the group means are all the same. The replies' average standard deviation is 4.1.

Arthrocentesis procedures

The skin surface of the preauricular area was disinfected with povidone-iodine surgical scrub solution. Then auriculotemporal nerve block was made using 0.3 to 0.5 ml of 2% lidocaine with 1/20000 Levonordefrin anesthetic solution. All patients underwent arthrocentesis using two plastic syringes 20ml each; one was

inflow and the second outflow needle. According to Nitzan (9), the canthal-tragus line was utilized to define the points of needle insertion. A point was designated 10 mm in front of the tragus and 2 mm below the canthal-tragus line to serve as the location of insertion of the first needle employed as an inflow needle. A second point was indicated to serve as the place of insertion of the second needle utilized as an outflow needle. This point was 20 mm in front of the tragus and 10 mm below the canthal-tragus line (i.e. 10 mm anterior to the former one). A 20-guage needle was inserted at the marked first point (10 mm in front of the tragus and 2 mm below the canthal-tragus line) and another one in the second marked point (20 mm in front of the tragus and 10 mm below the canthal-tragus line). The patients were asked to open and close the mouth during the procedure to help outflow of the injected ringer lactate (Fig .1 A&C).

Articular Injection: (10, 11)

Articular injection was made with 2ml of 25% dextrose solution at superior space of capsule and 1ml pericapsular as following steps: After arthrocentesis, access to the superior joint space was attained by asking the patient to close the anterior teeth on a small bite block or 1cm thickness of dental cotton rolls which enables translation of the mandibular condyles down the anterior slope of the glenoid fossa. The point of needle insertion was marked on the skin with indelible pencil midway between tragus of ear and posterior aspect of condyle (at site of inflow needle of arthrocentesis). The syringe needle was directed superiorly and anteriorly towards the apex of the glenoid fossa into the superior joint space until contact of the needle with the periosteum was reached. 2ml of 25% dextrose solution was gradually injected in the superior joint space. The needle then withdrawn 5mm and the remaining 1.0 ml were gradually injected in pericapsular zone (Fig.1B).

Drug Preparation

100 U Botox (Neuronox, Al Mottahdoon Pharma, Egypt) vial was diluted in 1.0 mL sterile, preservative-free 0.9% sodium chloride solution to give a solution of 10 IU/0.1 mL. To ensure that all the powder dissolved in the solution to be a clear colorless solution free of particles. The prepared solution was used immediately.

EMG Guided Injection: (6, 7)

Preoperatively EMG was made for Masseter, Temporalis & Lateral Pterygoid muscles to assess muscles activity and define trigger points. The EMG study was done for all patients by using an audio-amplified EMG machine (Clavis by Dantec Dynamics Ltd, Royal Portbury, Bristol, UK) portable device at neurophysiology unit of the neurology department, Al-Zahra University Hospital (Egypt ,Assuit). Electrical activity of muscles was recorded by using the concentric probe. Insertion activity, amplitude, duration, and recruitment of motor unit action potential (MUAP) were recorded. Then EMG guided BTX-A injection was performed through extra-oral approach after application of topical antiseptic agent (povidone-iodine). Muscles were injected by insulin syringe attached to 27-gauge Teflon coated (lumen electrode 50 x 0.45 mm) monopolar needle with dual action specifically engineered for Botox injection and EMG study (Fig.1D&E) to

confirm needle placement within the muscle at hyper active point (trigger point). The correct needle tip placement assured by positive EMG activity with contralateral jaw movement against resistance and no EMG activity at rest. 0.2 mL (20 IU) of reconstituted drug injected as a bolus injection into Lateral Pterygoid muscle and 0.3 mL (30 IU) of drug in each of Masseter and Temporalis muscles.

Post-operative instructions

The patients were instructed to eat soft diet and avoid wide mouth opening, ice application after injection and anti-inflammatory drugs for 2 weeks. Acetaminophen was prescribed for pain control after injection if needed.

Patient evaluation

- ***Clinical evaluation***
  All patients were subjected to clinical examination included pain severity, maximal mouth opening (MMO), and frequency of luxations. The patients subjectively assessed their TMJ pain intensity on palpation using the verbal analog scale (VAS; scale 0 - 10), and the maximal interincisal mouth opening (MMO) was clinically measured in millimeters. Moreover, frequency of luxations (number of locking episodes per month) was assessed just before the injection procedure, one, and three months after the injection.
- ***Radiographic evaluation***
  All of the patients were scanned by MRI before injection, and 6 months after injection to assess position of condyle and articular disk. MRI was carried out with a 1.5T, MR scanner (Gyroscan Intera Master; Philips Healthcare, Eindhoven, The Netherlands) and a dedicated, circular polarized transmit and receive TMJ coil. The MRI protocol included bilateral sagittal oblique proton density images of the right and left sides in both the closed mouth (maximum intercuspation) and maximum open mouth positions. The data were collected on a 240 X 167 matrix, with a field of view of 15 cm giving a pixel size of 0.625 X 0.9 mm. With the patient in a supine position, 12 parasagittal slices were obtained for each TMJ by using a turbo spin-echo proton density sequence (TR of 1500 ms, echo time of 30 ms), number of excitations was 4.00 with 3 mm slice thickness. MR images were corrected to the horizontal angulation of the long axis of the condyle.

Statistical analysis

The quantitative data were presented as mean & standard deviation. Accordingly, Repetitive One-Way ANOVA test was used to compare between different follow up records. On the other hand, comparison between three groups was performed by using One Way ANOVA test followed by Tukey`s Post Hoc test for multiple comparisons. The P value considered significant if $P < 0.05$

Fig 1. Clinical photographs showing A, Arthrocentesis in case of G II. B, Injection of 25% dextrose solution in case of G II. C, Arthrocentesis in case of G I . D, EMG guided BTX-A injection at Masseter muscle .E, Extra-oral EMG guided BTX-A injection at Lateral Pterygoid muscle

Results

Pain score

Comparison between all groups revealed significant difference as $P < 0.05$ at each follow up period. preoperatively G III was significantly the lowest while there was insignificant difference between G I & G II / after 1 week postoperatively & after 6 months post operatively there was a significant difference between all groups as GI was significantly the highest while GIII was significantly the lowest/ after 3 months postoperatively GI was significant the highest while there was in significant difference between G II & G III) (table 1).

Mouth opening

Results revealed a significant difference as $P < 0.05$ at all follow up periods except preoperatively as $P > 0.05$. after 1 week postoperatively GIII was significantly the lowest while there was insignificant difference between GI & GII / after 3 months postoperatively GI was significantly the highest while there was insignificant difference between G II & GIII / after 6 months postoperatively GIII was significantly the lowest while GII was significantly the highest) (table 1).

Frequency of luxations

Results revealed a non significant difference at preoperative24 Hs and at 1 week postoperatively intervals as $P > 0.05$. While at 3 and 6 months, there is highly significant difference between groups as $P < 0.05$. Where, the lowest number of luxations was showed in G III followed by G II then G I (table 1). Regarding to relative improvement in the frequency of luxation (decrease number of luxation of TMJ), groups II and III showed significant improvements at all intervals of study compared with G I. Although, there were highly significant difference between both groups at last day of study. This was presented in the percentages of the improvement which higher in G III than G II at last day of the study.

Table 1
Comparison between all groups regarding pain score, and MMO records,and frequency of luxations at Pre- operative 24 h, 1 week P.O., 3 months P.O. & 6 months P.O

	PRE- OPERATIVE		1 WEEK P.O.		3 MONTHS P.O.		6 MONTHS P.O.	
	M	SD	M	SD	M	SD	M	SD
Pain score								
Group I	7.270 a	0.383	6.030 a	0.527	4.710 a	0.393	3.600 a	0.353
Group II	7.080 a	0.492	5.090 b	0.574	3.570 b	0.411	2.770 b	0.359
Group III	6.420 b	0.646	4.130 c	0.353	3.430 b	0.298	2.240 c	0.250
P value	0.002*		< 0.0001 *		< 0.0001 *		< 0.0001 *	
Mouth opening								
Group I	48.230 a	1.374	43.020 a	1.658	41.000 a	1.417	36.260 ab	1.099
Group II	47.580 a	1.572	44.62a	2.082	39.300 b	1.889	36.780b	1.397
Group III	47.190 a	1.485	40.230 b	1.893	37.80 b	1.698	35.050 a	0.882
P value	0.29		< 0.0001 *		0.001*		0.007*	
Frequency of luxations								
Group I	11.78 a	2.01	11.020 a	1.658	9.26 a	1.417	8.71 a	1.099
Group II	12.02 a	1.572	10.62a	2.082	7.30 b	1.889	5.18b	1.397
Group III	11.17 a	1.485	10.230 b	1.893	5.80 b	1.698	2.04 a	0.882
P value	0.31		0.23		< 0.0001 *		< 0.0001 *	

M: mean SD: standard deviation *Significant difference as P < 0.05

Radiographic results

Postoperative MRIs of all patients (taken with the open – mouth position) at 6 months showed that highly significant improvement in position of condyle during opening in G II and III than G I with no difference between G II and G III in radiographic presentation. Where, they revealed that the condyle was either at the apex of the eminence or posterior to it. Although, 3 months postoperative MRIs of all patients presented that early reduction of condyle with articular disc to normal position during open mouth position in G III than G II (Fig. 2)

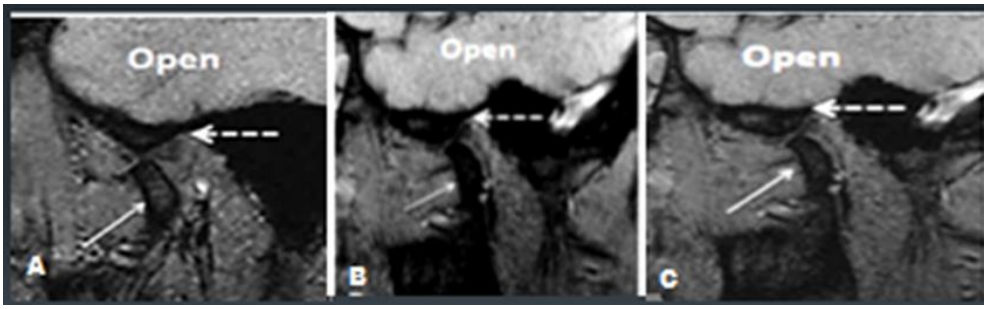

Figure 2. MRI images of the left TMJ in 3 groups at 6 months after treatment. A. Open-mouth position in case of G I, B. Open –mouth position in case og G II, C. Open –mouth position in case of G III. Continuous arrows pointed to site of condyle and dashed arrows pointed to articular eminence

Discussion

Condyle dislocation (or hypermobility) of TMJ is one of the most frequent TMJ disorders in humans. In the case of hypermobility, the condyle reaches a position in front of the articular tubercle at wide mouth opening, which can be caused by abnormalities in the shape of the joints, by ligament looseness or by reduced muscle tension (12). There have been reports of therapeutic intra-articular injections into the superior joint space of viscoelastic solution, steroids, anti-inflammatory medicines, and local anaesthetics (4-6,13). There is no definite consensus regarding superiority of any treatment modality over the other. The present study was atrial to assess effectiveness of dextrose prolotherapy and EMG guided BTX-A muscular injection each one alone or in combination in treatment of recurrent TMJ dislocation.

In our study 2ml of 25% dextrose solution was gradually injected in the superior joint space which has been considered to be an essential site for interventional treatment of recurrent dislocation. The needle then withdrawn 5mm and the remaining 1.0 ml were gradually injected in pericapsular zone this is in the same direction with Kilic et al (14) . Although Zhou et al (15) recommend single site of injection in posterior articular tissue. In the present study, the therapeutic dose of BTX-A for masseter, temporalis& lateral pterygoid injection was 50 U ipsilateral muscles. This is in opposite direction with Karacalar et al (16) who chose to inject LPM only with 12.5 U. Explanation of this in our study we inject other muscles and response for BTX-A depends on mass of injected muscles. In our study, the post-injection period was unremarkable, with the exception that 10 patients complained of discomfort and increasing pain during the first week and only two patients' nasal speech symptoms went away during the second week. After three cases of BTX-A injection for the treatment of recurrent TMJ dislocation, Martnez et al. (17) noted the same adverse effect as a result of the drug's diffusion into nearby muscles.

All patients of this study tolerated the TMJ prolotherapy injection well without serious complications and this was in consistence with the findings of Refai et al., (18). On the other hand, although Zhou et al., (15) agree with our findings of no serious complication, they reported one case of fainting and they related this to

the patient anxiety. In this study, discomfort after injection of dextrose prolotherapy was recorded in VAS for each follow up periods for all patients, the patients experienced mild to severe pain at first 2- 3 days post injection which was controlled by acetaminophen (Paracetamol) and resolve spontaneously after 1 week post injection. In our study the maximal mouth opening showed decrease after prolotherapy injection for both groups II &III with better results in group III. This is in consistence with the finding of Refai et al., (18) who reported significant decrease in maximal mouth opening in all patients during the different follow up periods. This may be due to injection in additional two sites (superior capsular attachment and inferior capsular attachment). On the other hand this was in contrast to the results achieved by Zhou et al., (14) who reported that the maximal mouth opening show insignificant reduction but patients who were given bilateral injections described a temporary decrease in maximal mouth opening during the first week which was recovered within one month.

In the present study 75% of all patients were satisfied with the results after single injection as there was improvement regarding dislocation frequency with better results in group III. The present study revealed that pain intensity was lower in group III patients who received the combination between BTX-A and 25% dextrose injection after TMJ arthrocentesis; pain records reach the lowest values at the following intervals: one week, 3 months and 6 months in comparison with group II patients who received 25% dextrose injection only after TMJ arthrocentesis and group I patients who received BTX-A that recorded higher values at the same intervals. Regarding to frequency of luxation, both groups II &III showed high percentages of improvement (decrease number of luxation) at last day of the study with highly significant difference between both groups and group I at last day of study with superiority for group III. These results may be explained by direct action of dextrose on articular tissue combined with decrease hyperactivity of muscle leading to repair of retrodiscal area with tightness of capsular wall. Therefore, the third group that was injected with the combination of 25% dextrose prolotherapy and EMG guided BTX-A injection achieved the best results because it combined the advantages of each group, and this is what was shown by the results of the statistics and the follow-ups of the patients. This explanation goes parallel with studies of Kahn et al (7) and Tanaka E (19) who pointed to role of hyperactivity of Lateral Pterygoid and other masticatory muscle in induce TMJ hypermobility disorder. Also, this matched with report of Hakala (8) about regenerative role of dextrose in TMJ dislocation treatment.

Conclusion

In conclusion, the results of this study appeared to show the beneficial effects of combination of EMG guided BTX-A injection with 25% dextrose injection after TMJ arthrocentesis in patients with recurrent TMJ dislocation, with improvements in both pain relief and function.

Conflict of interest

There are no conflicts of interest.

References

1. Torres DE, McCain JP. Arthroscopic electrothermal capsulorrhaphy for the treatment of recurrent temporomandibular joint dislocation. Int J Oral Maxillofac Surg. 2012;41(6):681-9.
2. Leopard PJ. Surgery of the non-ankylosed temporomandibular joint. Br J Oral Maxillofac Surg 1987; 25: 138-48.
3. Sinclair CF, Gurey LE, Blitzer A.Oromandibular dystonia: long-term management with botulinum toxin. Laryngoscope 2013; 123: 3078-83.
4. Baur DA, Jannuzzi JR, Mercan U, Quereshy FA. Treatment of long term anterior dislocation of the TMJ. Int J Oral Maxillofac Surg. 2013;42(8):1030-3.
5. Martínez-Pérez D, García Ruiz-Espiga P. Recurrent temporomandibular joint dislocation treated with botulinum toxin: report of 3 cases. J Oral Maxillofac Surg 2004; 62: 244-6.
6. Vasquez Bouso O, Forteza Gonzalez G, Mommsen J, et al. Neurogenic temporomandibular joint dislocation treatment with botulinum toxin: report of 4 cases. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2010;109: 33–7.
7. Kahn et al. Assessing the effectiveness of botulinum toxin injections into masticatory muscles in the treatment of temporomandibular disorders. J Oral Med Oral Surg 2018;24:107-11.
8. Hakala R V. Prolotherapy (proliferation therapy) in the treatment of TMD. Craniomandibular Practice. 2005;23(4):283- 8.
9. Nitzan D.W., Dolwick M.F., Martinez G.A.: Temporomandibular Joint Arthrocentesis: A Simplified Treatment for Severe, Limited Mouth Opening. J Oral Maxillofac Surg 1991; 49:1163-7.
10. 8. Dionne R.A.: Pharmacologic Treatments of Temporomandibular Disorders. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1997; 83:134-142.
11. Stein C., Comisel K., Hainerl E.: Analgesic Effect of Intra-ArticularMorphine after Arthroscopic Knee Surgery. New Engl J Med 1991; 325:1123-6.
12. Mubashir Younis, Ajaz A. Shah, Abina Rashid. Evaluating the effect of dextrose prolotherapy on temporomandibular disorders by choosing different injection sitesa comparative clinical study. International Journal of Contemporary Medical Research 2020;7(1):A1-A3
13. Fouda AA. Change of site of intra-articular injection of hypertonic dextrose resulted in different effects of treatment. Br J Oral Maxillofac Surg 2018; 56(8):715-718
14. Antczak-Bouckoms A. Epidemiology of research for temporomandibular disorders. J Orofac Pain 1995; 9: 226–34.
15. Stein C., Hassan A.H., Lehrberger K., Giefling J., YassouridisA.: Local Analgesic Effects of Endogenous Opioid Peptides. Lancet 1993; 342:32-4.
16. 14.Cömert Kiliç S, Güngörmüş M. Is dextrose prolotherapy superior to placebo for the treatment of temporomandibular joint hypermobility? A randomized clinical trial. Int J Oral Maxillofac Surg. 2016;45(7):813819
17. Zhou H, Hu K, Ding Y. Modified dextrose prolotherapy for recurrent temporomandibular joint dislocation. Br J Oral Maxillofac Surg. 2014;52(1):63-6.
18. Karacalar A ; Yi̧lmaz N, Bilgici A ; Baş B; Akan H. Botulinum toxin for the

treatment of temporomandibular joint disk disfigurement: clinical experience . J. of Craniofac Surg: 2005, 16 (3): 476-81
19. Martínez-Pérez D, García Ruiz-Espiga P. Recurrent temporomandibular joint dislocation treated with botulinum toxin: Report of 3 cases. J Oral Maxillofac Surg 2004;62:244-6..
20. Refai H, Altahhan O, Elsharkawy R. The efficacy of dextrose prolotherapy for temporomandibular joint hypermobility: a preliminary prospective, randomized, double-blind, placebo-controlled clinical trial. J Oral Maxillofac Surg. 2011;69(12):2962-70
21. Nyandra, M., Kartiko, B.H., Susanto, P.C., Supriyati, A., Suryasa, W. (2018). Education and training improve quality of life and decrease depression score in elderly population. *Eurasian Journal of Analytical Chemistry*, *13*(2), 371-377.
22. Dwijayanti, N., Mufdlilah, M., & Suryaningsih, E. K. (2022). The role of midwives in the application of classroom services for pregnant women during the COVID-19 pandemic period. International Journal of Health & Medical Sciences, 5(3), 228-239. https://doi.org/10.21744/ijhms.v5n3.1918