DOI: 10.55522/jmpas.V13I3.6466 **ISSN NO. 2320 – 7418**

International peer reviewed open access journal

Journal of Medical Pharmaceutical and Allied Sciences

Journal homepage: www.jmpas.com CODEN: JMPACO

Research article

Evaluation of the results of treatment of primary knee osteoarthritis using intra-joint synolis VA injection

Tran Trong Duong[1], Tran Thai Phuc*[2], Park Sung Jong[3], Vu Hai Nam[4]

[1] Faculty of Medicine, Dai Nam University, Vietnam
[2] Faculty of Nursing, Thai Binh University of Medicine and Pharmacy, Vietnam
[3] I-Medicare General Clinic, Vietnam
[4] 30-4 Hospital, Ministry Public of Security, Vietnam

Corresponding author: Tran Thai Phuc, ✉ trangiatbvn@gmail.com **Orcid Id**: https://orcid.org/ 0000-0002-2251-9757
Faculty of Nursing, Thai Binh University of Medicine and Pharmacy, Vietnam

Received - 08-11-2023**, Revised** - 17-01-2024, **Accepted** - 28-01-2024 **(DD-MM-YYYY)**

Refer This Article
Tran Trong Duong, Tran Thai Phuc, Park Sung Jong, Vu Hai Nam, 2024. Evaluation of the results of treatment of primary knee osteoarthritis using intra-joint synolis VA injection. Journal of medical pharmaceutical and allied sciences. V 13 - I 3, Pages- 6285 – 6290. Doi: https://doi.org/10.55522/jmpas.V13I3.6466

ABSTRACT

Evaluate the results and unwanted effects of intra-articular injection therapy of hyaluronic acid combined with sorbitol in the treatment of primary knee osteoarthritis. Subjects and methods: Prospective, interventional, controlled study with longitudinal follow-up on 101 patients with 151 knee osteoarthritis stages II and III according to Kellgren and Lawrence, divided into 2 groups: intervention group. Inject 1 tube of Synolis VA 80/160mg into the damaged knee joint, the control group was treated with oral medications Mobic, Viatril S.

VAS, WOMAC scores, knee flexion amplitude in the intervention group improved significantly starting from week 4 and continued until week 12, statistically significantly better than the control group ($p< 0.01$). After 12 weeks of treatment, the VAS score decreased from 5.28 to 1.24, the rate of moderate/severe pain decreased from 100% to 6.8%, 39.2% had no pain, the overall WOMAC score decreased from 36.46. down to 12.27, the knee joint flexion amplitude increased by 19.46 ± 11.84 degrees, the rate of satisfaction and very satisfaction was 92.3% ($p<0.01$). No serious unwanted effects were encountered, 28.4% of knee joint tightness after injection, 12.2% of post-injection pain within 12-24 hours, 4.1% of joint effusion. Conclusion: Intra-articular injection therapy of hyaluronic acid combined with sorbitol has a fast pain relief effect, improves knee joint mobility better than the control group and is safe.

Keywords Primary Knee Osteoarthritis, Synolis VA, Hyaluronic Acid, Sorbitol.

INTRODUCTION

Osteoarthritis is a disease that damages all components of the joint, in which the main damage is to the articular cartilage. According to the World Health Organization, osteoarthritis accounts for 10-15% of the population over 60 years old, causing disability for 10 million women and 6.5 million men each year1. Current treatment methods still have many limitations. Hyaluronic acid (HA) is the main ingredient that determines the viscosity and elasticity of joint fluid, fights inflammation, reduces pain and protects joint cartilage. According to studies, in degenerative joints, there is a significant decrease in the concentration and molecular weight of HA, causing pain and limited movement. Applying HA treatment to patients with knee osteoarthritis for more than 40 years has proven effective in reducing pain and improving joint mobility through many studies[2, 3]. However, HA is easily destroyed by free radicals found in degenerative joints. Sorbitol is a powerful free radical scavenger, incorporating a high concentration of HA (20mg/ml) 2 MDa in Synolis VA slime, forming a dense network of Hydrogen bonds that help stabilize the complex, to eliminate radicals. freely so that HA stays longer in the joint[4, 5]. Some authors around the world have conducted research and shown good effectiveness in treating knee osteoarthritis[6, 7]. Therefore,

we research this topic with two goals: Evaluate the treatment results of hyaluronic acid combined with sorbitol therapy in the treatment of primary knee osteoarthritis and comment on unwanted effects of this therapy.

SUBJECTS AND METHODS

Research subjects

101 patients treated at the I-Medicare General Clinic (Hanoi, Vietnam) from October 2022 to July 2023, were diagnosed with primary knee osteoarthritis according to the criteria of American College of Rheumatology ACR 1991, stage II and III according to Kellgren_Lawrence classification, VAS ≥ 4 points, no fluid or small effusion (<5mm) on knee ultrasound and accepted to participate in the study.

Patients with contraindications to intra-articular knee injections (joint and systemic infections, coagulation and bleeding disorders, severe liver failure, severe kidney failure, uncontrolled diabetes), and knee osteoarthritis were excluded from the study. secondary (after trauma, rheumatoid arthritis, gout...), or corticosteroid injections within 1 month, hyaluronic acid within 6 months or platelet-rich plasma or stem cells or surgical intervention at the knee joint. Stop steroid anti-inflammatory drugs 7 days before the study.

METHODS

- Research design: Prospective study, intervention, longitudinal follow-up, with control group.

- Sample selection and sample size: convenient sampling, 101 qualified patients, divided into 2 groups:

+ Intervention group: 52 patients (74 joints), each joint received 1 injection of Synolis VA 80mg/ 160mg, took Mobic 7.5 mg 1-2 tablets/day when in pain, maximum 15 days/session, Viatril-S 1500mg/day for 3 months.

+ Control group: 49 patients (77 joints) treated with Mobic 7.5mg 1 - 2 tablets/day when in pain, maximum 15 days/session, Viatril-S 1500mg/day for 3 months.

- Evaluate treatment results according to the VAS pain scale, the distribution ratio of VAS pain levels, the WOMAC index, knee flexion angle measurements at times T0 (before treatment), T1, T4, T8 and T12 (after treatment 1, 4, 8 and 12 weeks), satisfaction level after 12 weeks. Unwanted effects were recorded and managed at any time during the 12 weeks of follow-up.

Data processing

SPSS 20.0 statistical software, using statistically significant differences when $p < 0.05$.

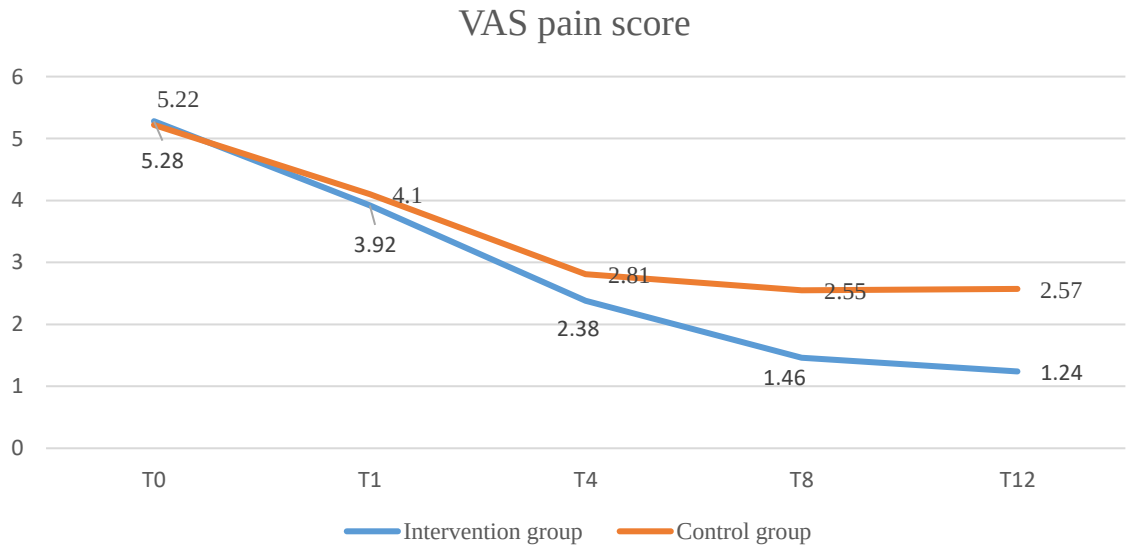
RESULTS

Table 1: General characteristics of research subjects

Characteristics		Intervention group n= 52 patients	Group certificate n= 49 patients	Total n= 101 patients	p
Ages (year)		62.98 ± 10.84	62.35 ± 9.77	62.67 ± 10.29	> 0.05
sex		Female (90.4%)	Female (79.6%)	Female (85.1%)	> 0.05
BMI (kg/m^2)		23.22 ± 2.41	23.61 ± 2.56	23.41 ± 2.48	>0.05
Job	intellectual worker	22 (42.3%)	15 (30.6%)	37 (36.6%)	>0.05
	Manual workers	30 (57.7%)	34 (69, 4%)	63 (63.4%)	
Stage	II	52joints (70.3%)	55joints (71.4%)	107joints (70.9%)	> 0.05
	III	22joints (29.7%)	22joints (28.6%)	44 joints (29.1%)	
Duration of illness (years)		5.30 ± 5.01	6.31 ± 5.80	5.81 ± 5.43	> 0.05

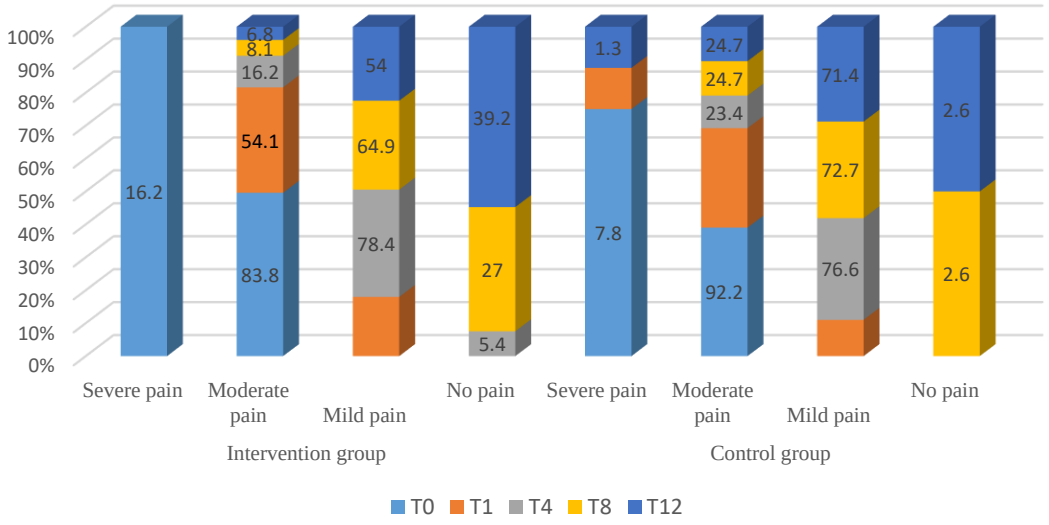
Comments There were no differences in anthropometric indicators, occupation, and disease duration disease stage before treatment between the 2 study groups with p>0.05.

Chart 1: Changes in VAS scores of the 2 groups at the time of the study



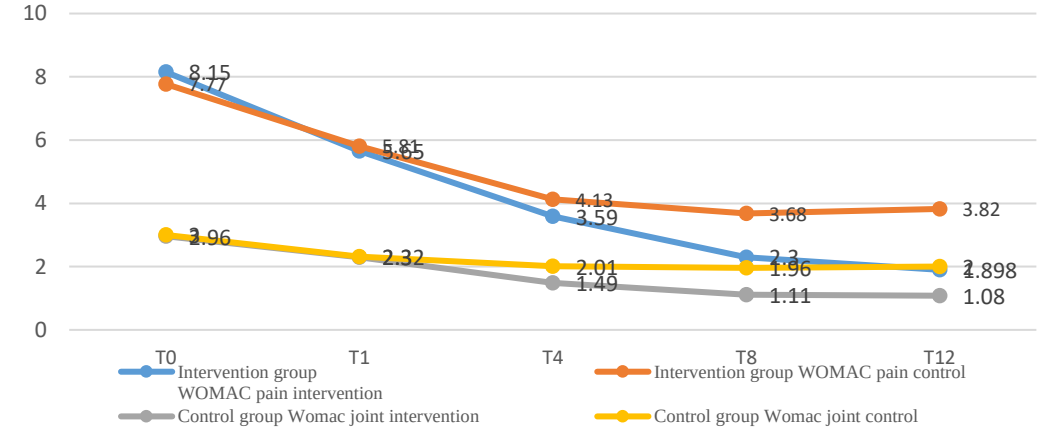
Comments Average VAS pain score of 2group gradually decreases from time T0 to T12. At thetime points T4, T8 and T12, VAS scores of the groupintervention had a more significant improvement than the control group,statistically significant with p<0.05.

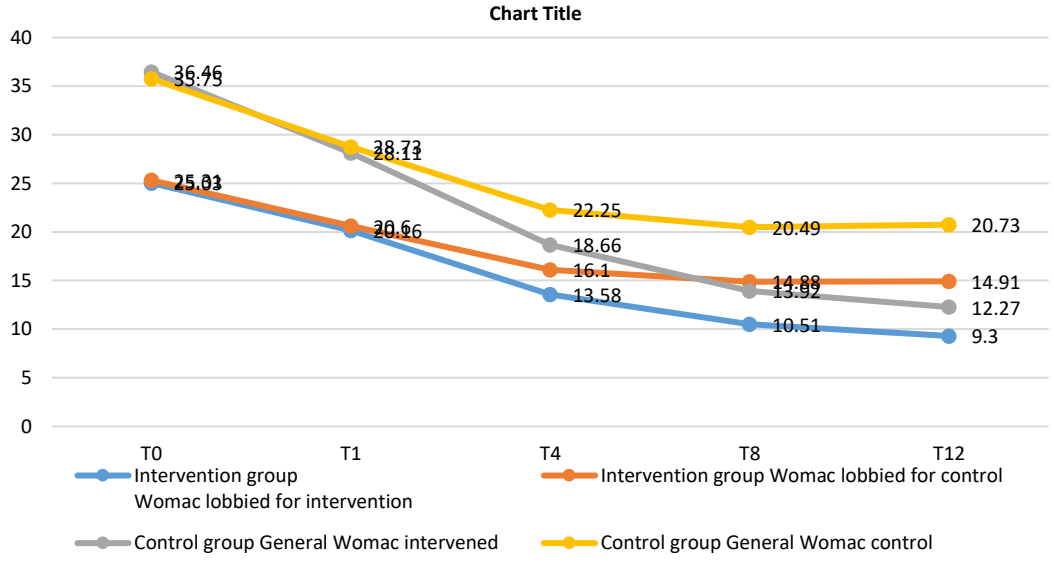
Figure 2: VAS pain level of 2 groups research at different times



Comments The distribution of pain levels between the 2 groups before and 1 week after treatment was not statistically different (p>0.05). At times T4, T8 and T12, the ratio of severe/moderate pain gradually decreased. , slight/no pain increases. The intervention group had a more significant improvement than the control group with p < 0.05.

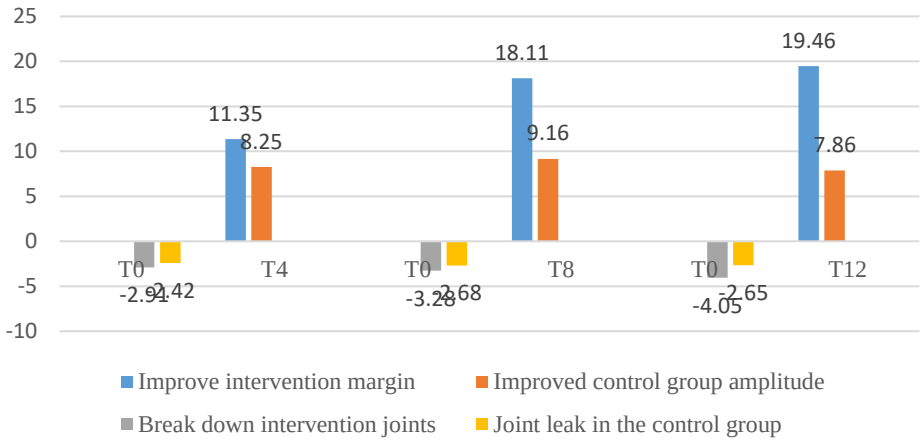
Figure 3: WOMAC pain, stiffness, mobility and general index of the 2 groups





Comments General WOMAC scores, pain, stiffness and mobility did not differ between the 2 groups (p > 0.05) at the beginning of treatment and after 1 week of treatment (T0, T1). After 4, 8 and 12 weeks of treatment, WOMAC pain, stiffness, and mobility and general scores of the intervention group were statistically significantly lower than the control group with p < 0.05.

Figure 4: Improvement in range of motion and joint leak breaking time of the 2 groups



Comments after 4 weeks of treatment, knee flexion range of motion and joint leakage time improved and continued to improve after 8 weeks and 12 weeks of treatment in both groups, in which the intervention group had an improvement. Improved more than the control group, the difference was statistically significant with p < 0.05.

Table 2: Patient satisfaction after 12 weeks of treatment

Level	Intervention group (n=52 patients)	Control group (n=49 patients)	p
Unsatisfied	4 (7.7%)	21 (42.9%)	< 0.01
Satisfied	28 (53.1%)	26 (53.1%)	
Very pleased	20 (38.5%)	2 (4.1%)	
LIKERT points medium	6.92 ± 1.49	4.82 ± 1.50	

Comments After 3 months of treatment, the rate of satisfied and very satisfied patients in the intervention injection group was statistically higher than the control group with p<0.01.

Table 3: Unwanted effects of Synolis (n=74 joints)

Characteristic	Quantity	Ratio (%)
Pain after injection(lasts 12- 24 hours)	8	10.8
Tightness after injection	20	27.1
Joint effusion	3	4.1
Joint infection	0	0
Headache, dizzy	0	0
Anaphylaxis	0	0

DISCUSSIONS

In the treatment of knee osteoarthritis, hyaluronic acid has lubricating, elastic, friction-reducing effects and stimulates the proliferation of articular cartilage cells and articular cartilage matrix through the CD44 receptor, anti-inflammatory, and pain-relieving [8]. Therefore, hyaluronic acid injection therapy is proven to reduce pain, fight inflammation, restore joint cartilage and improve knee joint mobility. In our study, we showed that the VAS score had a clear improvement at all-time points and the pain relief effect of Synolis VA was quite early. The average VAS score of the 2 groups at T0 was 5.25 ± 1.00, with no difference (p > 0.05). Immediately after 1 week of treatment, the intervention group's VAS score decreased significantly from 5.28±1.08 to 3.92±1.21 with statistical significance (p<0.05) (Chart 1).

The distribution of pain levels also varies a lot. Before treatment, 100% of patients had severe and moderate pain, the intervention group had a rate of severe pain 16.2%, 7.8% higher than the control group (P > 0.05). From T1 to T12, the proportion of patients with severe/moderate pain gradually decreased and mild pain/no pain increased. After 12 weeks of treatment, only 6.8% of the intervention group had moderate pain, no joints had severe pain, 39.2% had no pain, a statistically significant improvement compared to the control group with p < 0.01 (Figure 2).

In 2013, J. Heisel and C. Kipshoven studied 1,147 patients with stage I-IV knee osteoarthritis who received 3 injections of hyaluronic acid combined with sorbitol (GO-ON matrix). The results after 6 months were 56.5% reduction in pain level from (2.61 ± 0.80) to (1.07 ± 0.86). The proportion of patients with severe/very severe pain increased from 56.2% to 5.9%, no pain/mild pain increased from 6.8% to 67.1% [6].

The WOMAC scale (Western Ontario and McMaster Universities Arthritis index) is used to evaluate the effectiveness of treatment in reducing pain, stiffness and improving mobility. The higher the score, the more severely damaged the knee joint is. In our study, the WOMAC pain, stiffness, mobility, and general scores gradually decreased after the first week of treatment until week 12. The intervention group showed a clear improvement in the WOMAC score starting from week 12. 4th day after treatment, continuing until week 12, statistically significantly lower than the control group ($p < 0.05$). Specifically after 12 weeks of treatment, WOMAC pain decreased from 8.15±2.00 to 1.89±1.80, WOMAC stiffness decreased from 3.00±1.68 to 1.08±0.99, WOMAC Movement decreased from 25.31±7.49 to 9.30±6.03, overall WOMAC score decreased 24.19±6.73. Thus, Synolis VA injection has the effect of improving the motor function of the rapidly degenerative knee joint after 4 weeks and lasting up to 12 weeks after treatment (Figure 3). Similar to the results of author Pham Thi Bich Ngoc (2019) on 76 patients with stage II and III knee osteoarthritis injected with Regenflex Bioplus, the overall WOMAC score decreased from 38.68 to 11.6 points [9]. In 2016, M. Bausani studied 15 patients with severe knee osteoarthritis stages III and IV who received 3 injections of Synolis VA 2ml. After 52 weeks of treatment, WOMAC pain score decreased from 13.60 to 7.67, WOMAC stiffness score decreased from 6.3 to 3.20.

Range of motion of the knee joint is also a criterion to evaluate treatment effectiveness. In our study, at T0, the intervention group's knee flexion angle measurement was 107.70 ± 17.27, lower than the control group's 113.83 ± 16.24, a statistically significant difference. $p<0.05$. The intervention group's knee flexion amplitude improved more than the control group at times T4, T8 and T12 ($p<0.01$). After 12 weeks, the knee flexion angle measurement increased by 19.46 (± 11.84) degrees. Joint leak destruction time also decreased by -4.05 (±1.10) minutes ($p<0.01$) (Chart 4).

Evaluate patient satisfaction through the Liker scale. In the study, a 10-point Liker scale was used, divided into 3 levels (0-4 points: unsatisfied, 5-7 points: satisfied, 8 points: satisfied). -10 points: very satisfied). After 12 weeks of treatment, the intervention group had an average Liker score of 6.92 ± 1.49, much higher than the control group 4.82 ± 1.50 ($p < 0.01$), with 92.3% of patients satisfied and very satisfied with treatment, the difference between the control group was 59.2% with $p < 0.01$ (Table 2).

Unwanted effects of Synolis VA in 74 injected knee joints were 10.8% post-injection pain (8 joints) lasting 12 to 24 hours; 27.0% of post-injection tension (20 joints), only occurred within 30 minutes to 1 hour after injection and resolved spontaneously after the patient performed knee flexion and extension movements for 10 to 15 minutes, no patients had to use other pain relief methods, 4.1% had effusion (3 joints). In general, these are not serious side effects and do not cause patients to abandon monitoring and treatment. In particular, there were no cases of joint infection, post-injection bleeding or serious side effects (table 3). 2021 Cortet and colleagues conducted a head-to-head multicenter study between Synolis VA 80/160mg and Hylan GF-20 480mg in 202 patients with stage II and III knee osteoarthritis. After 24 weeks of treatment, 89.2% of patients in the intervention group were more satisfied than the control group ($p < 0.01$). The main unwanted effects were pain and stiffness after injection, and there were no serious side effects.

CONCLUSION

Intra-articular injection therapy of hyaluronic acid combined with Sorbitol has the effect of quickly reducing pain and improving mobility of the knee joint better than the control group in the treatment of primary knee osteoarthritis. Unwanted effects are rare and not serious.

REFERENCES

1. Zhang Y, Jordan JM., 2010. Epidemiology of Osteoarthritis. Clin Geriatr Med. 26(3), Pages 355-369. Doi: 10.1016/j.cger.2010.03.001.

2. Bannuru RR, Natov NS, Obadan IE, et al, 2009. Therapeutic trajectory of hyaluronic acid versus corticosteroids in the treatment of knee osteoarthritis: A systematic review and meta-analysis. Arthritis Care Res. 61(12), Pages 1704-1711. Doi: 10.1002/art.24925.

3. Rutjes AWS, Jüni P, da Costa BR, et al, 2012. Viscosupplementation for Osteoarthritis of the Knee: A Systematic Review and Meta-analysis. Ann Intern Med. 157(3), Pages 180-191 Doi: 10.7326/0003-4819-157-3-201208070-00473.

4. Lavet C, Badoud I, Ammann P., 2017 Hyaluronic acid/ sorbitol complex (Synolis VA) improves cartilage material properties. Osteoarthritis and Cartilage. 25, Pages S411-S412. Doi: 10.1016/j.joca.2017.02.709

5. Mongkhon J-M, Thach M,Shi Q, et al, 2014. Sorbitol modified hyaluronic acid reduces oxidative stress, apoptosis and mediators of inflammation and catabolism in human osteoarthritic chondrocytes. Inflamm Res. 63(8), Pages 691-701. Doi: 10.1007/s00011-014-0742-4.

6. Heisel J, Kipshoven C. 2013. Safety and Efficacy Findings from a Non-interventional Study of a New Hyaluronic Acid/Sorbitol Formulation (GO-ON® Matrix) for Intra-articular Injection to Relieve Pain and Disability in Osteoarthritis Patients. Drug Res. 63(09), Pages 445-449. Doi: 10.1055/s-0033-1343425.

7. Cucurnia I, Pudda A, Madonna V, et al, 2021. Patient-reported outcomes of intra articular hyaluronic acid for osteoarthritis of the knee: a prospective and multicentric case series. Musculoskelet Surg. 106(3), Pages 303-310. Doi: 10.1007/s12306-021-00698-8.

8. Akmal M, Singh A, Anand A, et al, 2005. The effects of hyaluronic acid on articular chondrocytes. J Bone Joint Surg Br. 87-B (8), Pages 1143-1149. Doi: 10.1302/0301-620X.87B8.15083.

9. Pham Thi Bich Ngoc. Evaluating the therapeutic effects of intra-articular injection therapy with hyaluronic acid (Regentflex Bio Plus) in the treatment of primary knee osteoarthritis. Master's degree thesis. Hanoi Medical University 2019.

10.