

**Summer Training at
Zydus Cadila Healthcare Ltd, Ahmedabad
(April 3 to June 2, 2017)**

**Study of Therapy Outcomes When IA Hyaluronic Acid Administered alone
or with Steroids in Osteoarthritis**

**By
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**Under the guidance of
Dr. Sandeep Narula**

**MBA Pharmaceutical Management
2016-2018**


School of Pharmaceutical Management
**The IIHMR University, Jaipur
2017**

CERTIFICATE

This is to certify that **Saurabh Parihar** has undergone his summer training at **Zydus cadila Healthcare Ltd** from **21st April to 31st May 2017**.

The candidate himself completed the project assigned to him during summer training. His approach to the project was sincere and proactive. This summer training is in partial fulfillment of the course requirement recommended for the award of MBA in pharmaceutical Management.

I wish her success in all his future endeavors.



Col (Dr.) Ashok Kaushik
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TO WHOMSOEVER IT MAY CONCERN

This is to certify that **Mr. Saurabh Parihar** from **Indian Institute of Health Management Research, Jaipur** has successfully completed his training from **21st April to 31st May 2017** in our Organization. During his training, he underwent practical training on project titled **"Study therapy outcomes when IA hyaluronic acid administered alone or with steroids in OA"**.

During his training, we found him very sincere, hardworking, co-operative and full of enthusiasm.

We wish him all success in his future endeavours.

For, CADILA HEALTHCARE LTD

AMIT AJMERA
DIVISION HEAD

Place → Ahmedabad

Date → 08.06.2017

ACKNOWLEDGEMENT

The satisfaction and euphoria that accompany the successful completion of the project would be incomplete without the mention of the people who made it possible.

First of all, I express my sage sense of gratitude and indebtedness to **Mr. Amit Ajmera, Zydus Cadila Healthcare Ltd.** I would like to extend my sincere and heartfelt thanks to sir for providing me an opportunity to learn and develop professionally.

I would also like to express my deep sense of gratitude to **Mr. Mauleshpatel, Manager of Osteoarthritis sales division, Zydus Cadila Healthcare Ltd.** I am greatly indebted to him for providing his valuable guidance at all stages of the internship, his advice, constructive suggestion, positive and supportive attitude and continuous encouragement, without which it would have not been possible to complete the project.

To place on record, I owe a debt of gratitude to **Dr. Sandeep Narula, Associate Professor, IIHMR University** for grooming me and for the inspiration needed to work with dedication and motivation throughout as an Intern at Zydus Cadila Healthcare Ltd.

I hope that I can build upon the experience and knowledge that I have gained and make a valuable contribution towards the industry in coming future.

Last but not the least I am also thankful to all those who have directly or indirectly rendered help in completion of my summer internship.

SAURABH PARIHAR

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Abbreviations:

- 1) **WHO**– World Health Organization
- 2) **IA**– Intra Articular
- 3) **HA**– Hyaluronic Acid
- 4) **DALYs**– Disability adjusted life years
- 5) **NCE**– New Chemical Entity
- 6) **NSAIDS**– Non-steroidal anti-inflammatory diseases
- 7) **OA**– Osteoarthritis

Executive Summary

Osteoarthritis is caused due to loss articular cartilage thats leads to gradual loss of synovial fluid. It can affect any joint but is most common in the knee and hip.

At present many treatments are available in the markets decrease loss of articular cartilage within synovial joints causing decrease in cushioning and pain of bones. Current treatments like NSAIDS, opioids analgesics, viscosuppliments or advance treatments like knee replacement surgery are emerging. To further improve pharmacological interventions and therapeutical choices in the field, improvement of knowledge is very necessary.

The project assigned was “Market research of IA Hyaluronic acid using alone or with steroids”

With objective: -

- Study of Therapy Outcomes When IA Hyaluronic Acid Administered alone or with steroids in Osteoarthritis:

The project was carried out in 3 stages: -

- ✓ First stage was to carry out secondary research on osteoarthritis and mainly aims to hyaluronic acid i.e. viscosuppliment along with steroids and their therapy outcomes.
- ✓ Second stage was preparation of questionnaire after that validation is occur by meeting with orthopaedicians and conducting the survey.
- Stage 2 was carried out by meeting with orthopaedist or orthopaedic surgeons of three cities. These cities were selected according to hyaluronic acid consumption. It includes three segments are following:

Segments	Cities
High	North Rajasthan
Medium	South Gujarat
Low	North Gujarat

- ✓ The final stage was to move ahead with data analysis and conclusion.

Company Profile



Mission

Zydus cadila is dedicated to life...

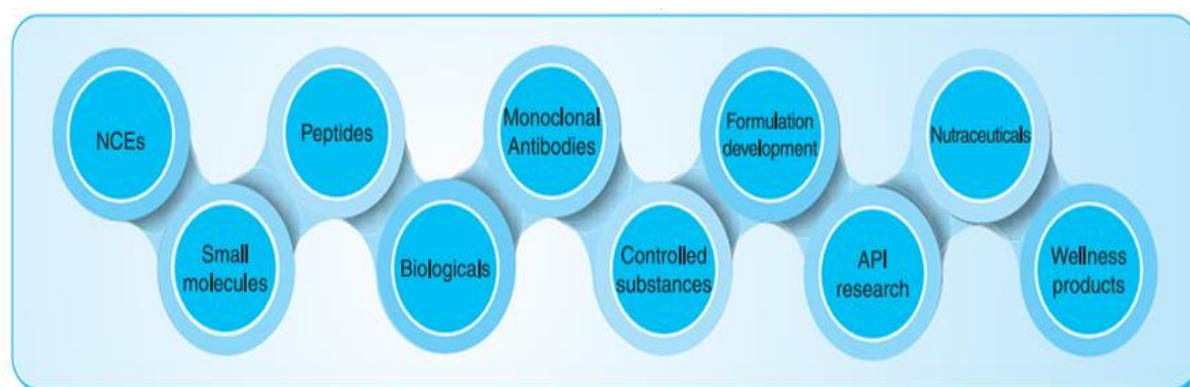
Vision

quality excellence and new pathways through innovation

The major therapeutic areas are following:

- Cancer
- Cardiovascular
- Diabetes
- Infectious Disease
- Gastrointestinal
- Respiratory agents
- Pain and inflammation associated disease
- Haematinics..... etc

Focus



Introduction

Osteoarthritis is the medical term to identify degenerative arthritis often seen with aging. However, with aging the new tissue formed is not as healthy and tends to be weaker causing gradual loss of function. As one ages, the cartilage cells produce less and less of the cushioning substance found in between the bones in a joint. The quality is also poorer. As a result, the 2 bones in the joint start rubbing against each other and this cause pain. In those patients having an inadequate response or a contraindication to these therapies and in those patients surgery is not appropriate or should be delayed, consideration may be given to the use of intra-articular steroids or intra-articular hyaluronic acid.



Hyaluronic acid and products for intra-articular use are categorized as “Biologic Devices” by the FDA with the first products gaining approval in 1997.



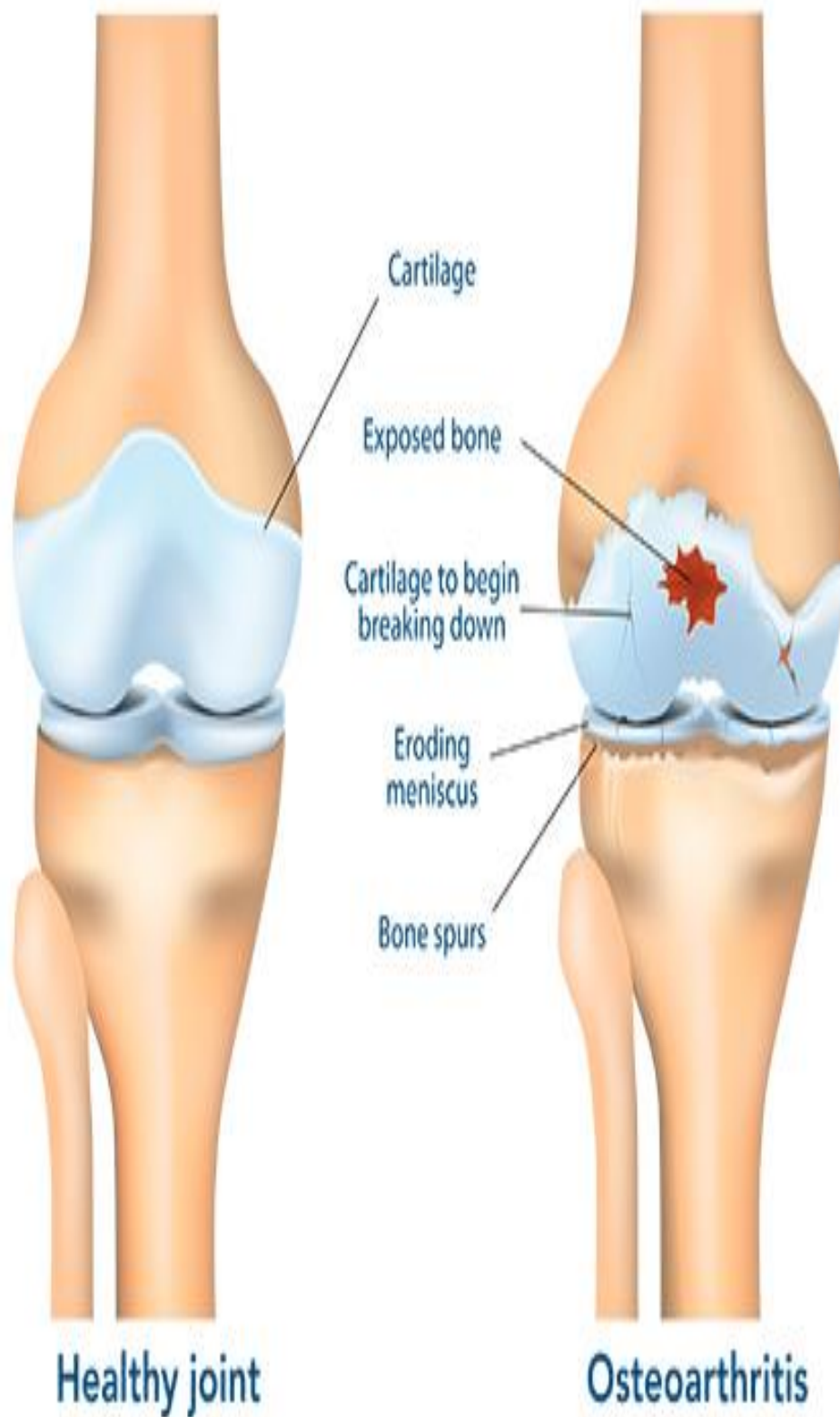
Any joint in the body may be affected. However, OA is most likely to affect the patient's:

- Hands
- Hips
- Knees
- Lower back
- Neck

Osteoarthritis has three characteristics:

- Bony growths
- Damages cartilage
- Synovitis

OSTEOARTHRITIC CHANGES OF THE KNEE



Medication

Medicines for OA are available as pills, syrups, creams or lotions, or they are injected into a joint. They include:

- ❖ **Analgesic**
- ❖ **Nonsteroidal anti- inflammatory drugs (NSAIDS)**
- ❖ **Corticosteroids**
- ❖ **Hyaluronic acid**
- ❖ **Natural and Alternatives Therapies**
- ❖ **Surgery**

Hyaluronic acid

Hyaluronan (hyaluronate, hyaluronic acid) is a disaccharide polymer produced by synovial cells. In the normal joint, HA has a molecular weight between 3.5 and 5 kDa. Many potential effects in the knee are hypothesized, including mechanical, anti-inflammatory, analgesic, effects on synovial cells and chondrocytes. In OA affected joints, the molecular weight of HA may decrease with a concomitant increase in total HA owing to more synovial fluid. Although IAHA has been proposed as therapeutic in knee OA, the mechanism of action is not defined. It has viscoelastic properties with two mechanical functions:

- 1) the fluid is more viscous and acts as a joint lubricant
- 2) the fluid becomes more elastic and acts as a shock absorber

Intra-articular hyaluronic acid (IAHA) extracted from rooster coombs, produced synthetically or fermentatively is considered a therapy that can diminish knee pain and improve function.

Objective:

- **Study of Therapy Outcomes When IA Hyaluronic Acid Administered alone or with steroids in Osteoarthritis.**

Rationale

- The study helps to determine current prescribing trend of doctors for OA. It gives idea that customer (surgeons) prescribe viscosupplements to OA patients.
- The study helps to provide customer (surgeons) prescribing viscosupplements alone or with combination with steroids for greater results.
- It can help a pharmaceutical company to make strategies and make a foothold through creative marketing so as to acquire a good market share.

Methodology

Research study design: Descriptive study design was used in this study, which involve observing, describing recording, analysing and reporting conditions that exists without alterations.

Target Population:Orthopaedicians

Sample Size: During the study only 193 respondents filled questionnaire.

Study Area: Jaipur (North Rajasthan), Surat (South Gujarat), Ahmedabad (North Gujarat).

Time Period: 3 April 2017 - 2 June 2017

Sampling Technique: The researcher used Non-Probability (convenience) sampling to get the sample size.

Instruments: The researcher main instruments for data collections were mixed ended questionnaires, semistructured interviews and secondary data collection.

Data Collection Methods: The researcher involved data collection from primary and secondary sources. The primary data was collected through questionnaires (mixed ended) and semi structured interviews.

Personal interviews gave an in depth into the information; and eliminated misinterpretation. Questionnaire had the advantage that the respondent had adequate time to respond to questions and free from bias because the respondents were guided and interviewer did not influence answers. The secondary data were obtained from published material, journals and internet sources.

Data Analysis and Presentation:

The data collected was analysed by both qualitative and quantitative methods. Quantitative technique such as percentages and frequencies were used. Tables, graphs and charts were used to present findings where applicable.

Findings:

I. How many osteoarthritis patients examine by Orthopaedicians daily?

Number of patients	Responses	% Responses
>10	53	27.46%
10-20	88	45.59%
20-30	36	18.65%
<30	16	8.2%

Table 1: Total no. of osteoarthritis patients examine daily by Orthopaedicians

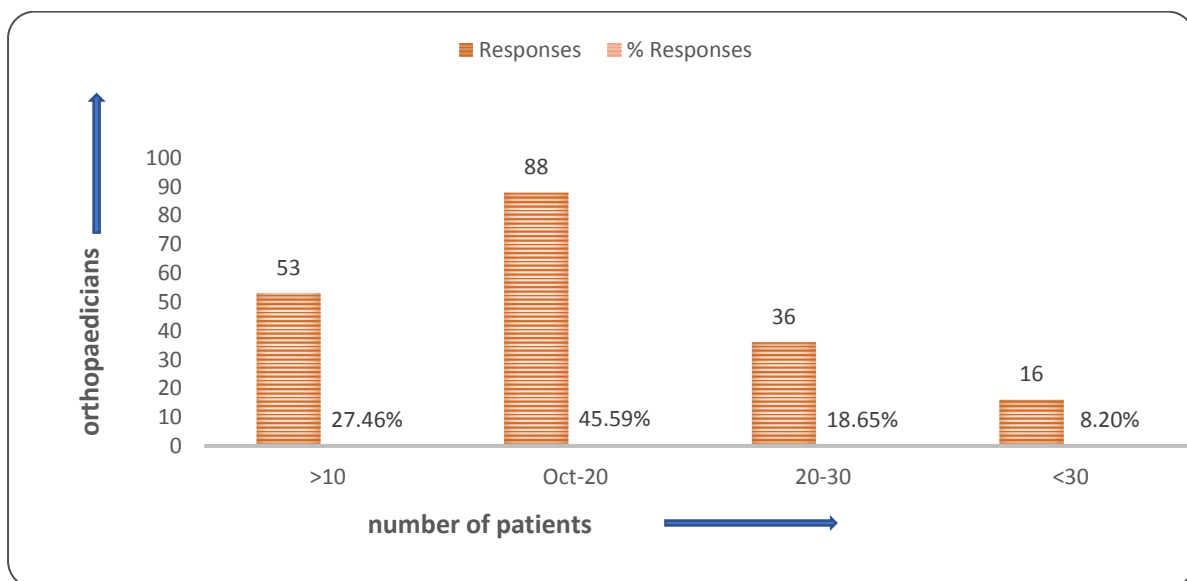


Figure 1: Percentage of Patients Examine in daily Clinical Practice

Inference: It was found that data taken from most of doctors have strong prescribing base with 10-20 patients / day.

II. What is Orthopaedicians first line therapy preferences for severe osteoarthritis?

Drugs	Response	% Response
Opioids Analgesic	19	9.84%
NSAIDS	150	77.72%
Viscosupplements	3	1.55%
Corticosteroids	10	5.18%
Both (Opioids and NSAIDS)	5	2.59%
Both (NSAIDS and Visco.)	2	1.03%
Both (NSAIDS and Cortico.)	4	2.07%

Table 2: First line treatment of Osteoarthritis.

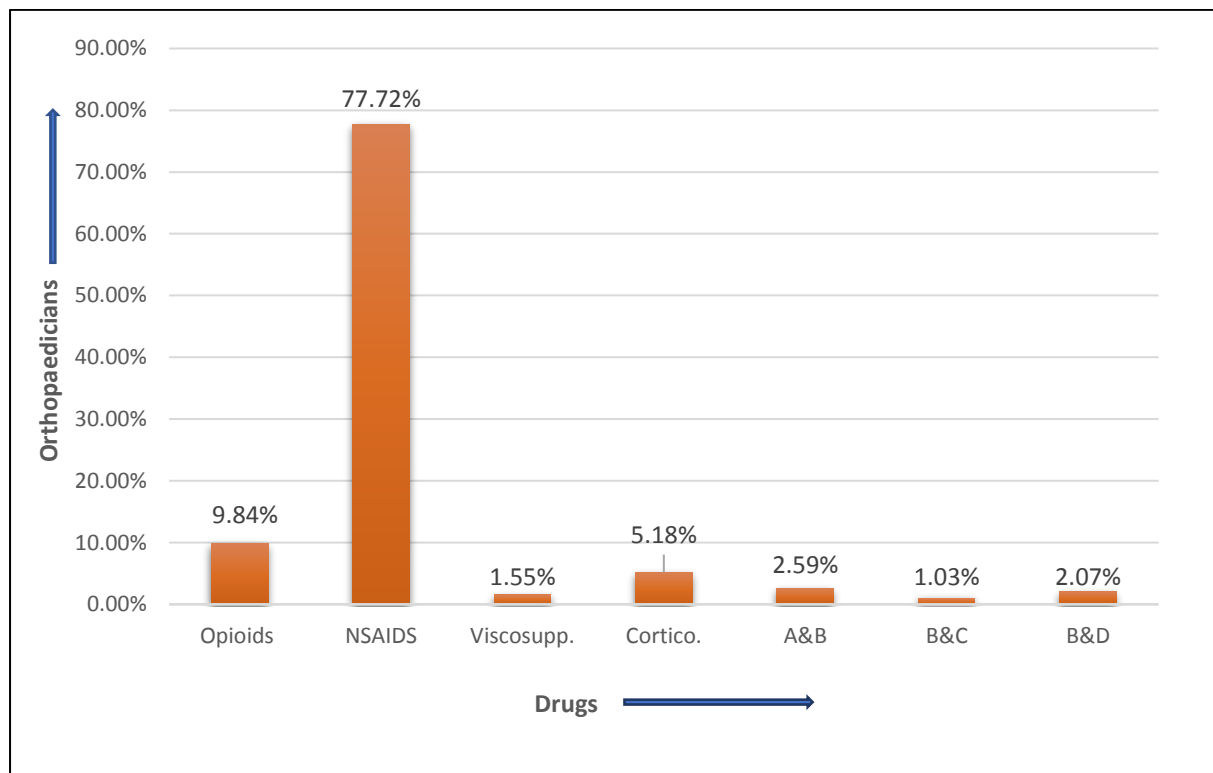


Figure 2: First line treatment of osteoarthritis

Inference- It was found that most of surgeons preferred NSAIDS as first line treatment of osteoarthritis. Opioids preferred less because of side effects and addictions as compared to NSAIDS because they are having supportive treatment and it fits with pocket of OA patients.

III. Do Orthopaedicians prefer hyaluronic acid?

Hyaluronic Acid	Response	%Response
Yes	162	84%
No	31	16%

Table 3: Preferring Hyaluronic Acid

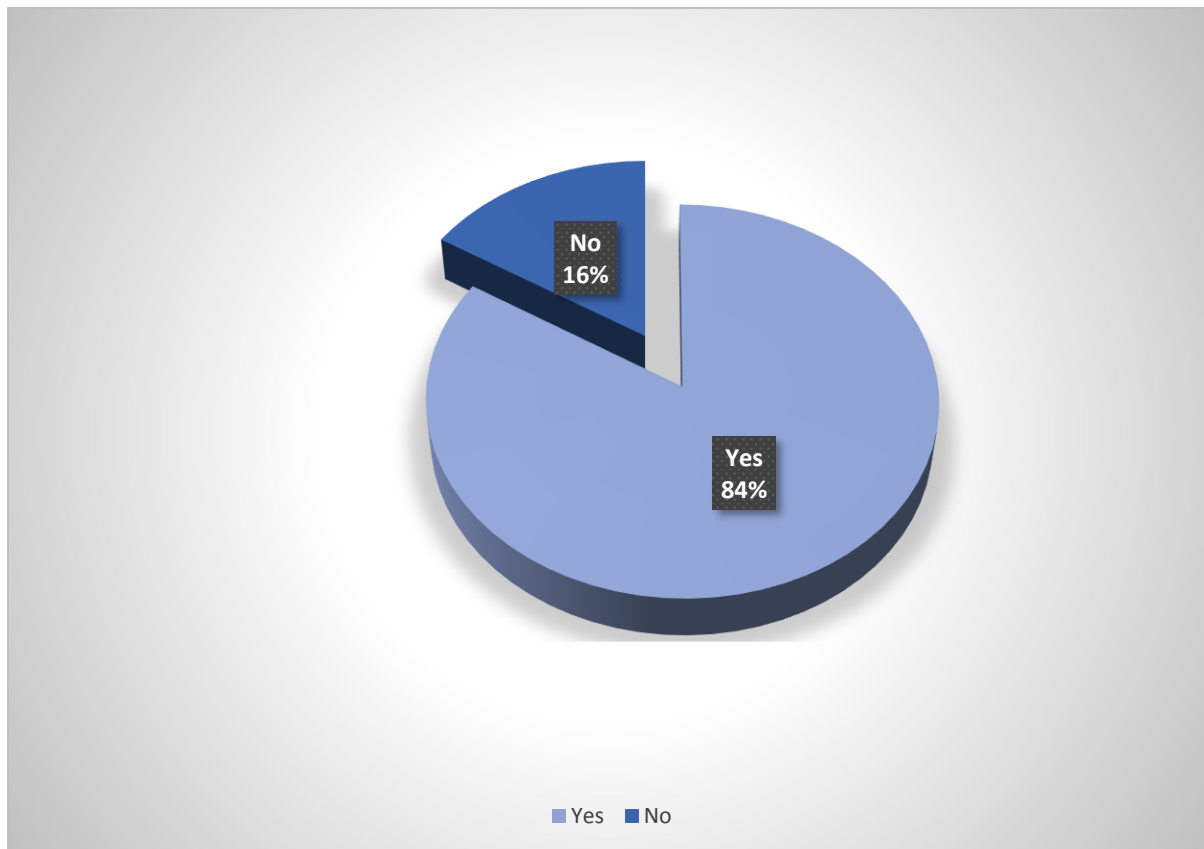


Figure 3: Preferring Hyaluronic Acid

Inference: It was found that Hyaluronic Acid is Preferred by most of the Doctors because it Decreases cushioning of Knees and provide lubrication.

IV. How do you use Hyaluronic acid?

Hyaluronic Acid	Response	Response%
Alone	57	35%
With steroids	106	65%

Table 4: Hyaluronic Acid use

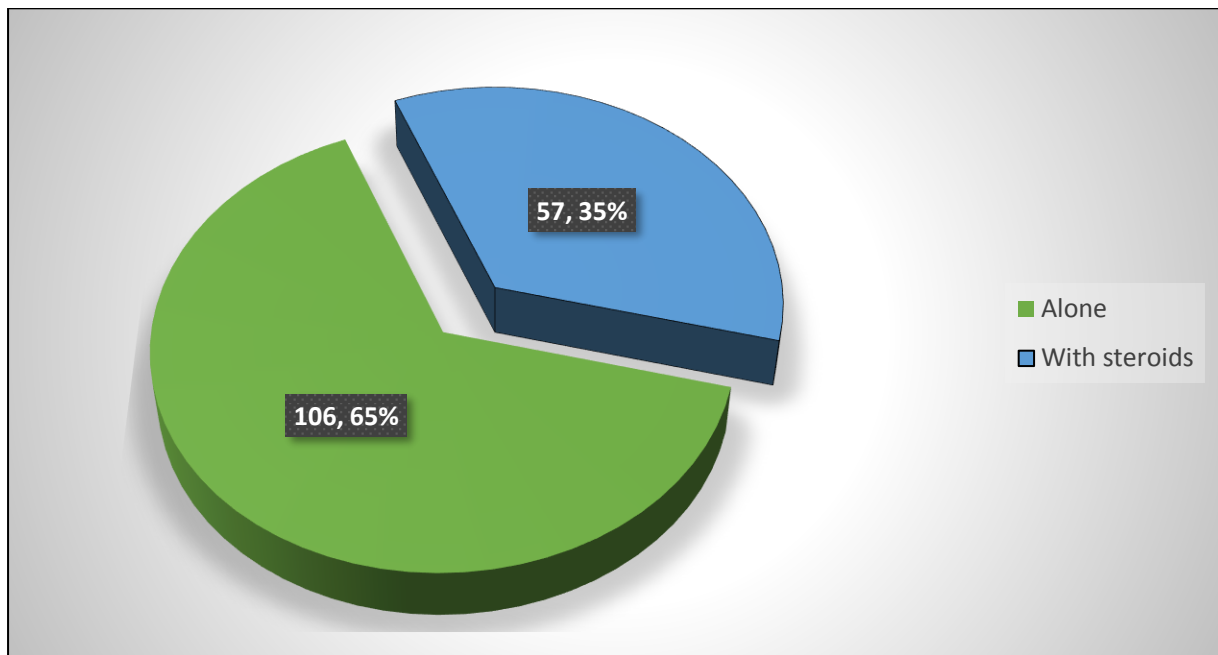


Figure 4: Hyaluronic Acid use

Inference:It was found that most of the Orthopaedicians use Hyaluronic acid alone as compared to given along with steroids. Hyaluronic acid plays vital role in OA for maintain the function and elasticity of the synovial fluid. It binds well with water, forming highly viscous polymers that increase the ability of the synovial fluid to cushion the joint and absorb shocks, providing pain relief that lasts longer.

V. Which is your preferred IA steroid when given along with HA?

Steroids	Response	Response%
Triamcilonone	20	35%
Dexamethasone	18	32%
Methylprednisolone	19	33%
Betamethasone	0	0

Table 5: Hyaluronic acid with steroids

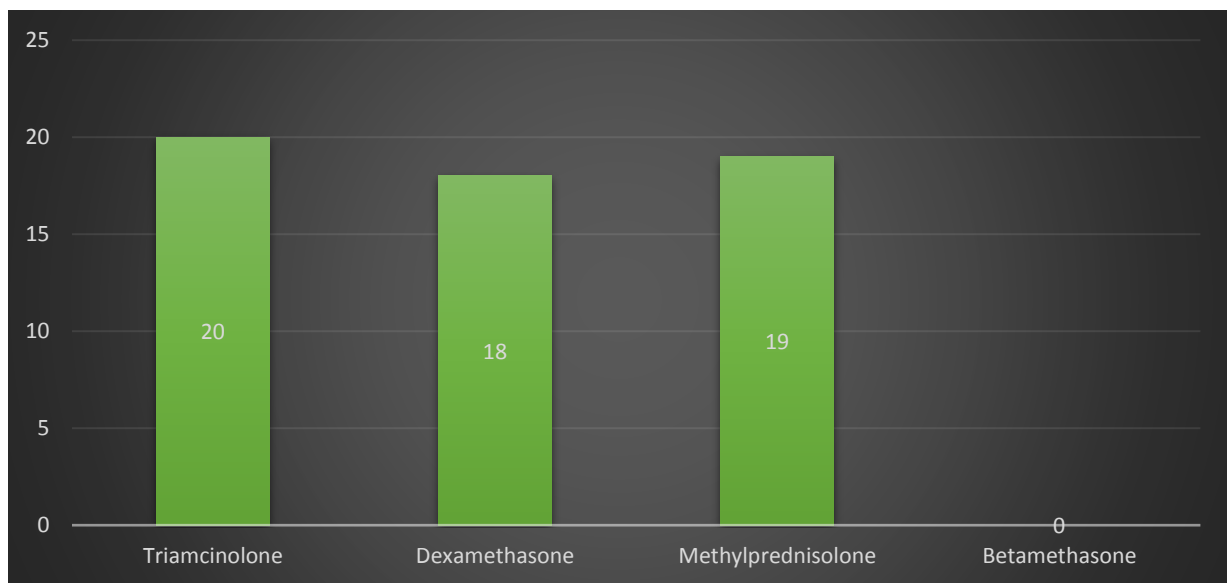


Figure 5: Hyaluronic Acid with steroids

Inference:It was found that Triamcinolone, Methylprednisolone and Dexamethasone is equally preferred by Orthopaedist and surgeons. It is due to HA is vital for maintain the function and elasticity of the synovial fluid. Hyaluronic acid with Steroid is designed to supplement the reduced amount of natural hyaluronic acid found in synovial fluid in OA joints, while the steroid component treats inflammation and provides fast relief withindays of injection.

VI. What is the percentage of the patient getting relief, when treated with IA hyaluronic acid alone?

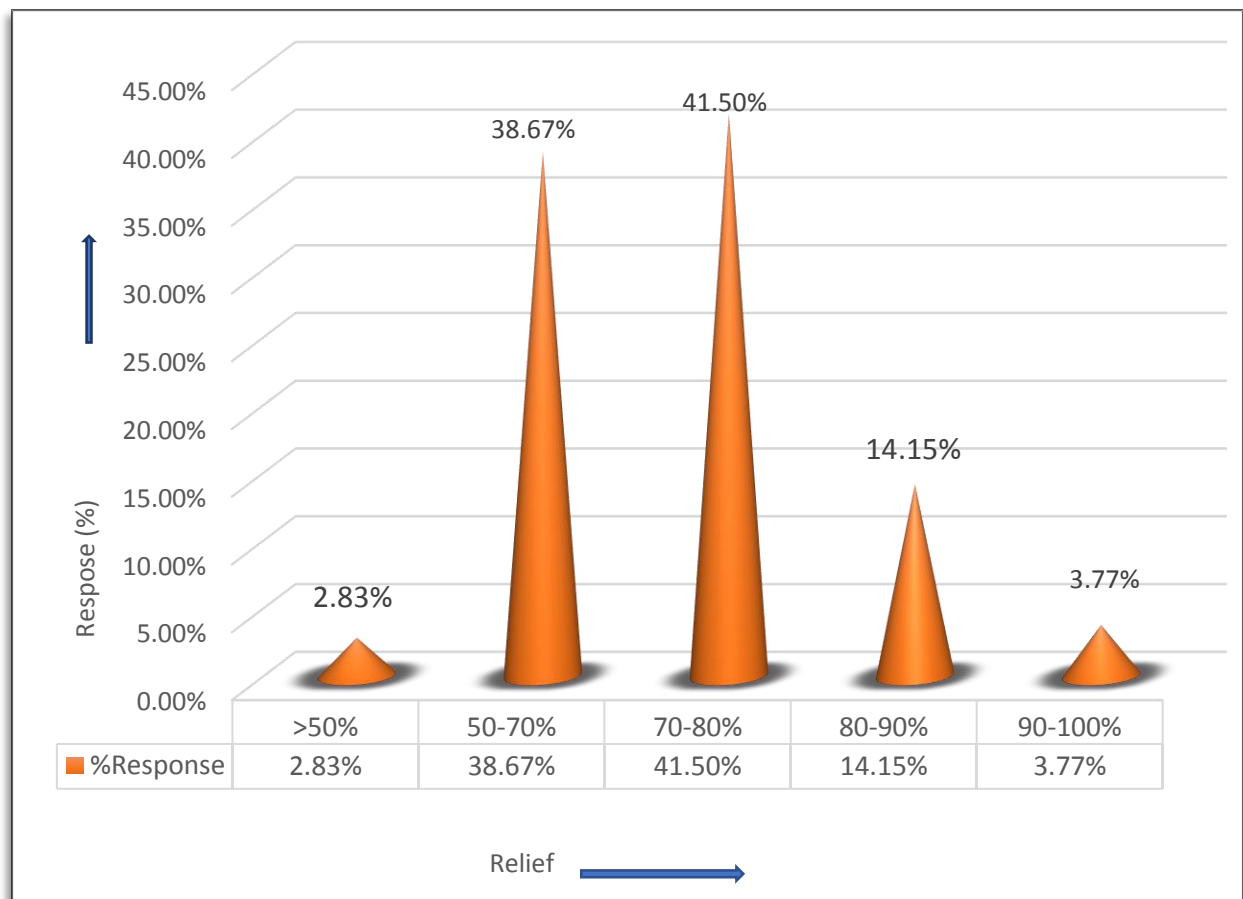


Figure 6: Response of patients getting relief

Inference: It was found that 70-80% Therapeutic effect shows by Hyaluronic acid using Alone. It increases elasticity and lubrication of joints take place.

VII. What is the percentage of patient getting relief, when it treated with IA hyaluronic acid with steroids?

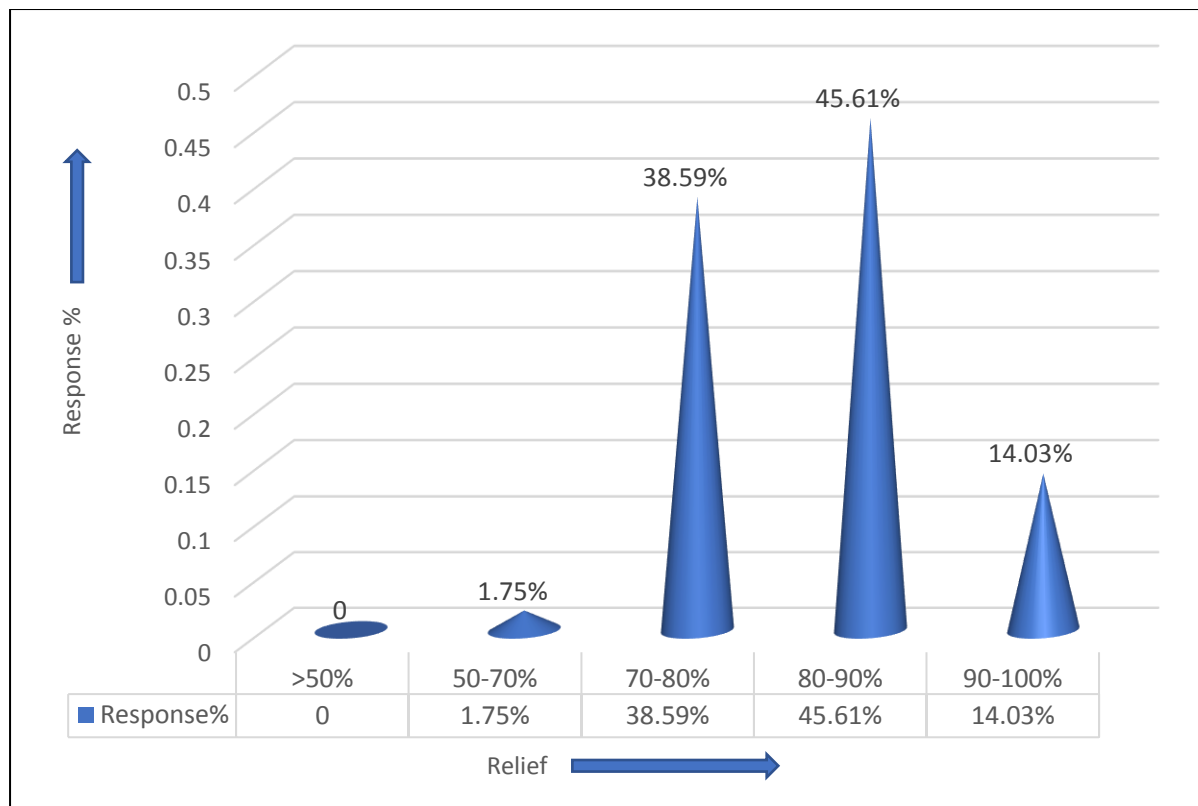


Figure 7: Response of patient getting relief

Inference:It was found that 80-90% response is shown by hyaluronic acid with steroids. The high concentration and total delivered dose of hyaluronic acid combined with steroids creates a fast-acting high viscosity solution that helps provide cushioning from normal physical activities like walking and biking.

Limitation of study:

- Due to personal attitudes, individual values and organizational policies, practioners' in the medical profession keep most of their understanding secret.
- The researcher received minimal cooperation from some respondents. The unavailability of target respondents due to their busy schedules was a major challenge. Therefore, accessibility of records was limited hence limiting the availability of more information that would have permit elaborate research.
- Resources constrains also posed a great limitation with constrained finances and very busy schedules therefore the researcher having limited to carry out the research.

Conclusion:

Osteoarthritis, though one of the most common diseases with patient frequencyto patient daily, mostly affecting both elderly men and woman, is also one of the neglected diseases. Lack of overt symptom in the initial stages of the diseases and unavailability of economical diagnostics tools to aid in early diagnosis, on common treatment regime, makes the situation grim.

As more Anti- osteoarthritis molecules become widely available in India, it is imperative for surgeons to select appropriate therapy for their patients.

- ✚ In the present study, orthopaedic surgeons mostly prescribe NSAIDS or opioids analgesic like (Acetaminophen, Tramadol, celecoxib and morphine) in Ahmedabad, Surat and Jaipur. Orthopaedic surgeons preferred economical condition and safety compliances of patient to prescribe the osteoarthritis drug. Viscosuppliment (Hyaluronic acid) prescribed very less because of its costly medication.
- ✚ Treatment of osteoarthritis with viscosuppliment is costly but more effective in case severe osteoarthritis. Some doctors said that it shows better results. For the use of viscosuppliment the factors like cost of treatment might have long term implication in the treatment of osteoarthritis and thus need to be addressed.
- ✚ Viscosuppliment (Hyaluronic acid) used in treatment of Osteoarthritis to improve properties of synovial fluid, provide increased mobility and enhanced joint protection and protect the surface of articular cartilage.
- ✚ Viscosuppliment with steroids having better therapeutically outcomes as compared with prescribing Hyaluronic acid alone. It proves clinically that hyaluronic acid with steroids provides fast short- term pain relief within days of injection and strong safety profile in both an initial injection as well as repeat injection.

Suggestions:

- NSAIDS are more economical as compared to viscosupplements but they are having more lifelong durability and changes life modification of OA patients.
- Hyaluronic acid used along with steroids having more therapeutic efficacy as compared with using alone because:
 - HA provides Lubrication, elasticity and cushioning of joints
 - treats inflammation and provides fast relief and cushion



The high conc. and total delivered dose of hyaluronic acid combined with steroids creates fast acting high viscosity solution that helps provide cushioning from normal physical activities like walking and biking.

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