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Bisphosphonates effects in surgery sites

Submission date 29/11/2024	**Recruitment status** No longer recruiting	[ ] Prospectively registered [ ] Protocol
Registration date 03/12/2024	**Overall study status** Completed	[ ] Statistical analysis plan [ ] Results
Last Edited 03/12/2024	**Condition category** Oral Health	[ ] Individual participant data [ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Postoperative symptoms following the surgical extraction of mandibular third molars, such as pain, are among the most frequent challenges faced by practitioners. The application of materials directly into the socket immediately after extraction may reduce the severity of these complications. This study aims to evaluate the efficacy of bisphosphonates loaded onto gelatin sponges compared to gelatin sponges alone in reducing pain following surgical extraction of mandibular third molars.

Who can participate?
Patients aged 18 - 30 years old with thin upper lip

What does the study involve?
20 Participants with 40 bilateral impaction third mandibular molars, one surgical site will receive a gelatin sponge, while the site will receive bisphosphonates loaded onto gelatin sponges

What are the possible benefits and risks of participating?
The anticipated benefit of the study is the resolution of complications associated with the impaction of mandibular third molars. The potential risks include varying degrees of pain and edema, which are naturally associated with the surgical extraction process itself.

Where is the study run from?
Damascus University (Syria)

When is the study starting and how long is it expected to run for?
October 2020 to November 2024

Who is funding the study?
Damascus University (Syria)

Who is the main contact?
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Contact information

Type(s)
Public, Scientific, Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Protocol serial number
UDDS-591/14122020/SRC-717

Study information

Scientific Title
The efficacy of bisphosphonates following surgical extraction of mandibular third molars: a randomized controlled trial

Study objectives
This study was designed to test the hypothesis that bisphosphonates loaded onto a gelatin sponge can improve the clinical and radiographical outcomes following a surgical extraction of impacted third mandibular molars

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 14/12/2020, Damascus University (Almazzeh St, Damascus, 20872, Syria; +96390404840; dl.srd@damascusuniversity.edu.sy), ref: 591

Study design
Split-mouth randomized controlled trial

Primary study design
Interventional

Study type(s)

Treatment, Efficacy

Health condition(s) or problem(s) studied
Bilateral impaction of mandibular third molars

Interventions
Randomization:
The two mandibular surgical sites were randomly assigned to one of two materials for application within the socket: Group A (left side: gelatin sponge, right side: bisphosphonates-loaded gelatin sponge) or Group B (left side: bisphosphonates-loaded gelatin sponge, right side: gelatin sponge). The allocation sequence was generated using a computer-based random number generator with a 1:1 allocation ratio. The allocation sequence was concealed in opaque, sealed envelopes labeled with the patient's initials to ensure blinding. These envelopes were opened immediately before surgery.

Surgical Phase:
The oral cavity was disinfected with 0.12% chlorhexidine. Local anesthesia was administered using a syringe with a long 27-gauge needle. Inferior alveolar nerve block anesthesia (targeting the inferior alveolar and lingual nerves) was performed, along with supplementary infiltration anesthesia (targeting the buccal nerve in the depth of the vestibular sulcus). Lidocaine 2% with epinephrine 1:80,000 was used as the anesthetic agent. A surgical incision was made extending from the retromolar area to the distal buccal side of the second molar, followed by a sulcular incision around the adjacent molars and, in some cases, a vertical release incision. A full-thickness mucoperiosteal flap was elevated. Buccal and occlusal bone was removed using a surgical handpiece with copious irrigation to prevent heat-induced bone damage. The third molar was luxated and extracted using elevators, and sectioned if necessary.

Application of Materials and Closure:
Control group A: Gelatin sponge placed in the socket.
Experimental group B: Gelatin sponge soaked in bisphosphonate (CIPLA, India) solution (0.24 mg) was applied to the socket.
In both groups, the flap was repositioned and sutured using 3-0 silk sutures in an interrupted pattern. It is worth noting that the time interval between the procedures on the right and left sides was two weeks, starting first with the patient's right side while adhering to the randomization protocol assigned to each patient.

Postoperative Phase:
Patients were instructed to use cold compresses, avoid heat exposure, refrain from rinsing or spitting for 24 hours, and start mouth rinses with 0.12% chlorhexidine the next day.
Post-operative medications included Augmentin 1000 mg administered every 12 hours for five days, Ibuprofen 400 mg taken every 8 hours after meals for five days, and Chlorhexidine 0.12% mouth rinse used twice daily for two weeks. Sutures were removed one week post-surgery.

Outcome measurements:
Pain Index:
The Visual Analog Scale (VAS) was employed to compare pain intensity between the two sides and across follow-up days for each side. This scale is represented as a graded continuum from 0 to 10 where the patient specifies the corresponding number. Pain intensity was assessed on the first, third, and seventh days post-surgery for each side individually and recorded on the patient' s chart.

Edema Index (EI):
Postoperative facial edema following the surgical extraction of mandibular third molars was evaluated using the Tape Method, as described by Gabka and Matsumura. This method involves three millimetric measurements between five reference points:
Measurement S1: From the lateral canthus of the eye to the angle of the mandible.
Measurement S2: From the tragus of the ear to the corner of the mouth.
Measurement S3: From the tragus of the ear to the chin apex.
The average facial edema was calculated by summing the values of these three measurements on the second (T2) and fifth (T5) days post-surgery. These results were compared with the baseline measurements taken preoperatively (T0) for both sides.
Radiographic Healing and Bone Density Assessment on 3D Imaging:

Cone-beam computed tomography (CBCT) scans were performed for each surgical extraction site at two time points:

T0: Immediately after the surgical extraction.
T1: Two months post-surgery.
To minimize errors caused by patient head movement during imaging or variations in measurement locations, the sagittal, coronal, and axial planes were standardized. This ensured consistent section alignment across all radiographic studies conducted at different time intervals.

Healing Index (HI):
The degree of clinical healing was monitored on the third and seventh days following surgical extraction for both sides, using the Landry Healing Index as the assessment tool which consist of 5 levels:
Score 1, very poor (with presence of 2 or more signs) >50% of red gingiva, presence of granulation tissue, bleeding on palpation and suppuration, and incision margins not epithelialized, with loss of epithelium beyond incision margin.
Score 2: poor healing with >50% of red gingiva, presence 2 signs, and incision margins not epithelialized, with exposed connective tissue.
Score 3: Good healing with 25–50% red gingiva, absence of signs and incision margin does not expose connective tissue.
Score 4: Very good healing with <25% of red gingiva, absence of signs and incision margin does not expose connective tissue
Score 5: Excellent healing with all pink tissue color, absence of signs and incision margin does not expose connective tissue

Intervention Type
Procedure/Surgery

Primary outcome(s)
1. Pain intensity measured using the Visual Analog Scale (VAS) on days 1, 3, and 7 post-surgery
2. Facial edema measured using the Tape Method on baseline and days 2 and 5 post-surgery
3. Radiographic healing and bone density assessment measured using cone-beam computed tomography (CBCT) scans immediately after the surgical extraction and 2 months post-surgery

Key secondary outcome(s))
The degree of clinical healing measured using the Landry Healing Index on days 3 and 7 post-surgery

Completion date
15/11/2024

Eligibility

Key inclusion criteria
1. Patients aged between 18 and 30 years
2. Symmetrically positioned, non-impacted mandibular third molars requiring surgical extraction in the same patient
3. Medically healthy patients with no systemic diseases
4. Patients who have provided informed consent to participate in the study

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
30 years

Sex
All

Total final enrolment
20

Key exclusion criteria
1. Patients with syndromic conditions
2. Allergy to any of the medications used in the study
3. Presence of localized lesions or acute infections in the third molar region
4. Patients with a history of radiotherapy for tumors in the head and neck region
5. Patients taking medications that affect bone metabolism
6. Presence of temporomandibular joint (TMJ) disorders, such as condylar dislocation or displacement
7. Patients with poor oral hygiene
8. Pregnant or breastfeeding women
9. Smokers and alcohol consumers
10. Non-cooperative patients
11. A time discrepancy exceeding 10 minutes between extractions on both sides

Date of first enrolment
15/01/2021

Date of final enrolment
15/09/2024

Locations

Countries of recruitment
Syria

Study participating centre
Damascus University, Faculty of Dentistry, Department of Oral and Maxillofacial Surgery
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Sponsor information

Organisation
Damascus University

ROR
https://ror.org/03m098d13

Funder(s)

Funder type
University/education

Funder Name
Damascus University

Alternative Name(s)
University of Damascus, , DU

Funding Body Type
Government organisation

Funding Body Subtype
Universities (academic only)

Location
Syria

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are/will be available upon request from Mustafa Jaweesh, jaweeshmustafa1@gmail.com, and Dr Yasser Alsayed Tolibah, yasser94.tolibah@damascusuniversity.edu.sy or Yasseralsayedtolibah@gmail.com

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes