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Research Paper
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Effect of unilateral mandibular distraction osteogenesis on mandibular morphology in rabbits with antigen-induced temporomandibular joint arthritis

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Abstract. Aim was to evaluate effect of unilateral distraction osteogenesis (DO) on mandibular morphology in rabbits with antigen-induced arthritis in the temporomandibular joint (TMJ). Forty 8-week-old rabbits were divided into four groups. In groups A,C, arthritis was induced in the right TMJ. Groups A,B underwent DO. Group D served as control group. Cephalometric analysis of mandibular angle, mandibular ramus height, mandibular collum height, and total posterior mandibular height was done on CT-scans preoperatively (T0), after distraction (T1), and at euthanasia (T2). Two-factor ANOVA evaluated the effect of DO and antigen-induced arthritis. No effect of DO or arthritis was observed on mandibular angle or mandibular collum height. For T0–T1, DO increased mandibular ramus height 12.3% (95% CI 5.2–19.4%) in group B ($P = 0.001$) and total posterior mandibular height 6.2% (95% CI 0.3–12.1%) in group A ($P = 0.04$) and 10.0% (95% CI 4.3–15.7%) in group B ($P = 0.001$). For T1–T2, no significant changes occurred in arthritic rabbits (group A). In conclusion, DO increased total posterior mandibular height in rabbits with arthritis. Postoperatively, no significant effect of DO was observed in rabbits with arthritis. Mandibular DO could be a viable treatment modality in patients with TMJ-arthritis.

Key words: distraction osteogenesis; temporomandibular joint; juvenile arthritis; animal experimental study; rabbits.

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Juvenile idiopathic arthritis (JIA) is a chronic condition characterized by inflammation of the synovial tissue, with onset before the age of 16 years and a persistence of more than 6 weeks.[1] The incidence of JIA varies between 7 and 23/100,000 children per year in the Scandinavian countries.[2] Arthritis of the temporomandibular joint (TMJ) in JIA affects the mandibular intracapsular growth zones, thereby inducing unilateral or bilateral degenerative changes of the mandibular morphology.[3–6] Diagnostic imaging has revealed morphological changes of the mandibular condyle in 62–87% of patients with JIA.[3,4] TMJ arthritis causes growth disturbances of the entire craniomandibular complex with high variation in severity depending on the time of TMJ arthritis onset and overall craniofacial growth pattern.[5,8,9] Cephalometric studies have shown a high prevalence of mandibular retrognathism, asymmetry, a clockwise rotational skeletal growth pattern with increased anterior lower face height, reduced posterior lower face height, and open bite.[5,9–11]

Growth disturbances may be reduced by early interceptive treatment, which promotes normal growth, reduces orofacial symptoms, and normalizes facial proportions.[12–15] However, severe growth disturbances may necessitate surgical procedures, e.g. conventional orthognathic surgery, alloplastic joint prostheses, and costochondral grafts to normalize occlusion, facial proportions, and jaw relations.[16–18] Distraction osteogenesis (DO) is a gradual elongation of segmented bone by the use of an external force and the creation of new bone in the distraction gap.[19] Studies have shown consistent results following mandibular DO (MDO), which has been advocated as a predictable treatment modality with few complications.[20–24]

Several authors have argued that MDO is a viable treatment modality in patients with JIA.[25–28] A low rate of degenerative changes in the TMJ of JIA patients following MDO has been reported in two studies,[21–23] and only minor subjective complaints and limited objective changes in various functional parameters following MDO in patients with JIA have been reported.[25] In finite element analyses of MDO, it has been reported that DO changes the stress distribution in the TMJ, but that the induced stress is low and probably results in only insignificant changes in the morphology of the condyle and TMJ.[29,30] In experimental studies involving healthy animals, it has been indicated that the direction of the vector may influence the effect of DO on the TMJ.[31] Furthermore, adaptive changes in the TMJ following MDO at physiological levels have been documented in healthy animals.[32] Studies assessing the effect of MDO in animals with pathological conditions in the TMJ are currently not available; therefore the purpose of the present study was to evaluate the effect of unilateral MDO on mandibular morphology in rabbits with antigen-induced TMJ arthritis.

Materials and methods

Animals

The study was conducted in accordance with national guidelines for the care and use of animals in research. The research protocol was approved by the Animal Experiments Inspectorate in Denmark. Forty 8-week-old New Zealand white rabbits were used (*Oryctolagus cuniculus*; KB Lidköpings Kaninfarm, Sweden). Before commencing the study, the rabbits were allowed to acclimatize for 14 days. All rabbits were housed in pairs in approved caging with slotted floors in a temperature and humidity-controlled room on a standardized light–dark routine. A laboratory rabbit diet supplemented with fresh hay and tap water was provided ad libitum throughout the study. Environmental enrichment consisted of a variety of daily fresh vegetables.

The rabbits were randomized into four groups by block randomization (groups A, B, C, and D) (Fig. 1). Arthritis was induced in the right TMJ of the animals in groups A and C by the method introduced by Kapila et al.[33] DO of the right ramus was performed in groups A and B. Group D served as a healthy, non-operated TMJ control group.

Antigen-induced arthritis

At the age of 10 weeks, the rabbits in groups A and C were pre-sensitized to ovalbumin[33] using 1 ml of ovalbumin (1 mg/ml; Sigma Chemicals, Germany) dissolved in physiological saline and Freund's complete adjuvant (Sigma Chemicals). Two weeks later, the procedure was repeated using 1 ml of ovalbumin dissolved in physiological saline and Freund's incomplete adjuvant. After a further 1 week, the rabbits in groups A and C were tested for sensitivity to ovalbumin by subcutaneous injection of 1 ml (1 mg/ml) ovalbumin on a shaved spot (3 cm × 3 cm) on the back. Twelve hours later, the shaved spot was inspected to detect clinical signs of inflammation. Redness (more than 1 cm × 1 cm) or swelling (more than 0.5 cm × 0.5 cm) was an indication of successful sensitization. One week after sensitization and every 3 weeks during the remaining study period, arthritis was induced in the right TMJ by injection of sterile, filtered 0.1 ml ovalbumin dissolved in physiological saline (10 mg/ml). The rabbits were sedated (Rompun Vet; Bayer Animal Health GmbH, Germany) to allow manipulation of the mandible and palpation of the condylar head before any intra-articular injection was performed. At the times corresponding to intra-articular injections of ovalbumin in groups A and C, the rabbits in groups B and D were sham-treated with intra-articular injections of 0.1 ml sterile and physiological saline in the right TMJ.

Distraction osteogenesis

At the age of 15 weeks, a surgical procedure was performed in groups A and B to allow MDO of the right mandibular ramus. After general anaesthesia (Rompun Vet), the skin lateral to the right mandibular ramus was shaved, and through a submandibular incision followed by sub-periosteal dissection, the lateral part of the mandible was exposed. The vector of the distraction device (Alveolar Ridge Distractor; Synthes, USA) was determined and placed at a 90° angle to the occlusal plane. After adjusting and determining the final position of the distraction device relative to the lateral surface of the ramus, the central part of the horizontal ramus osteotomy corresponding to the location of the distraction device was performed using piezoelectric surgery (Piezosurgery; Mectron s.p.a., Carasco, Italy). Next, the distraction device was fixed with six 4-mm-long 1.3-mm-diameter self-tapping screws (Synthes), and the osteotomy was completed to the posterior and anterior borders of the ramus (Fig. 2). The functioning of the distraction device and the absence of bony resistance were tested prior to layered suturing of the skin (Vicryl 4–0, Ethicon, USA and Monosof 3–0, Covidien Medical Supplies, USA). The activating arm (10 mm) of the distraction device penetrated the skin near the mandibular angle allowing good access for activation. After a latency period of 5 days, the distraction phase was initiated with activation of the distraction device by 1.3 mm every second day until a total of approximately 7 mm of distraction was achieved. During activation, the rabbits were sedated (Rompun Vet) to allow safe activation of the device and reduce the stress levels of the animals.

Euthanasia

At the age of 25 weeks and after 8 weeks of consolidation, the rabbits were sedated