

# The Use of Amorphous Calcium Carbonate as a Supplement for Treating Equine Orthopedic Lesions: A Report on Eleven Cases

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## ABSTRACT

Calcium is an important mineral in the body and is critical for bone remodeling and healing processes. Superior bioavailability of amorphous calcium carbonate over crystalline calcium carbonate was recently confirmed in humans. Equine bone healing and fracture repair are challenging issues. A continuous pursuit to develop new therapeutic modalities, designed to improve fracture treatment and accelerate healing is ongoing. This case series aims to describe the clinical details, treatment and outcome of eleven cases presented with various orthopaedic pathologies, and treated with amorphous calcium carbonate supplement following surgical procedure. The majority of the cases had successful outcomes, with good functional and cosmetic results.

**Keywords:** Amorphous Calcium Carbonate; Orthopaedic; Equine.

## INTRODUCTION

Calcium is an important mineral in the body and is involved in many metabolic processes, such as bone turnover, exocytosis of neurotransmitters, muscular contraction, heart depolarizing mineral and participates in many other physiological functions (1).

Calcium from carbonate and citrate salts are the most commonly used forms of calcium supplements in humans (2). The relatively limited absorbability of calcium has resulted in an ongoing scientific debate as to the superior bioavailability of different calcium supplements.

Calcium carbonate has six known polymorphs, of which the most thermodynamically stable form is calcite. The least stable polymorph is the amorphous form, amorphous calcium carbonate (ACC) (3). The superior bioavailability of ACC over crystalline calcium carbonate was recently confirmed in humans, using a radioactive labeling rat model, where

increased bioavailability of up to 40% and 30% were seen in the serum and bone, respectively, while a 26% increase in retention levels was measured (4).

A study in rats, found superior effects of ACC-containing compounds over two of the most common calcium supplements in terms of bone loss prevention, and highlighted the advantage of synthetic ACC with respect to mechanical bone strength (5). Another study, has shown higher solubility and bioavailability of amorphous calcium carbonate versus commonly used crystalline calcium carbonate in rats (4).

Musculoskeletal conditions in equine patients are an important economic issue in the equine industry. Forces involved in equine fractures are generally much greater than those acting on bones in humans or smaller animal species. Bone remodeling and healing in equine patients is prolonged compared to other species (6) and complications such as delayed healing are occasionally encountered.

Additionally, equine orthopedic patients are prone to surgical site infections (SSI), which is a major concern for equine surgeons (7–9). Long bone open fractures are at a higher risk of developing SSI compared to closed fractures. As a result of the aforementioned, fracture repair of long bones in the horse is often challenging and associated with unsatisfactory outcomes, with a higher incidence of complications, such as fixation failure or delayed healing, compared to other species (6–11). Thus, a continuous pursuit to develop and evaluate new therapeutic modalities, designed to improve fracture treatment and accelerate healing is ongoing.

This case series aims to describe the clinical details, treatment and outcome of eleven cases presented with various orthopaedic pathologies, and treated with ACC supplement following surgical procedure.

## CASE SERIES

### History and clinical presentation

Medical records of equids that presented to the Koret School of Veterinary Medicine, The Hebrew University of Jerusalem, Israel, between 2021 and 2023 for orthopaedic conditions which were treated with ACC supplement were included in the study.

#### Case 1

A mature jenny, weighing 160 kg, found by animal shelter activists in the field, presented for right hind limb proximal fracture. The jenny was bright, alert and responsive; mucus membranes were pink and tacky, pulse was 60 bpm. The jenny was non-weight bearing on the right hind limb (5/5 lameness (AAEP)). Upon physical evaluation, distal open displaced tibial fracture was found. At the fractured site, two puncture wounds were found, medially and laterally. The wounds appeared chronic, presenting with granulation tissue and some chronic scarring.

Upon radiograph evaluation, a right distal diaphysis, oblique, displaced tibia fracture was demonstrated, with two large loose bone fragments (Figure 1). The jenny received initially IV fluid therapy with Lactated Ringer's solution. Analgesia was provided with phenylbutazone (Ve'toquinol, Lure, France), 4.4mg/kg bwt, i.v.) and antimicrobial treatment with benzyl penicillin sodium (Teva, Kundl, Austria), 22000 IU/kg bwt, i.v., q.i.d), gentamicin (Teva Pharmaceutical Industries, Petah Tikva, Israel), 6.6 mg/

kg bwt, i.v., s.i.d)) was initiated. The limb was bandaged and lateral and caudal splints were applied. The owners were advised that due to the severity and chronicity of the fracture, the prognosis for limb salvage was poor. The owners, nevertheless elected to pursue surgical intervention. Surgical open reduction and internal fixation (ORIF) was performed under general anesthesia. The fracture was amenable to reduction only following debridement of callus and fibrous tissue, suggestive of the chronic nature of the fracture. A 10 holes 4.5mm broad Locking Compression Plate (LCP) was applied craniolaterally and an 8 hole 4.5mm broad LCP was applied craniomedially. Cortical (5.5mm) screws and locking (5.0mm) screws were used for fixation. Tension relief sutures were made for closure. Post operatively, the jenny continued to receive antimicrobials and pain management for 10 days. In the immediate post-operative period the jenny was painful and non-weight bearing. Thus, additional analgesia, including morphine (Rafa Laboratories, Jerusalem, Israel) and xylazine (Ceva Animal Health, Glenorie, NSW, Australia), was administered via an epidural catheter. Improvement of lameness was noticed, however, position of the leg was nonetheless abnormal, and the jenny was still lame at walk. Ten days post operatively sutures were removed, the incision healed with no complications. Phenylbutazone was tapered and lameness deteriorated. One month after surgery the jenny was discharged home, severely lame at a walk and radiographs revealed no initial fracture healing process. At that stage, ACC (Amorphical, Industry region, Sapir, D.N, Arava, Israel ), 10 mg/kg/day, p.o.) was added to the treatment plan. Several (2-3) weeks following initial treatment with ACC there was a significant improvement in lameness and within 2 months, evidence of bone healing was identified on radiographs (Figure 2). Follow-up three years later, the jenny had no residual lameness, it ran free in a pasture with the rest of the herd.

#### Case 2

A five years old Arabian show horse mare presented with a chief complaint of left mandibular tooth root infection. The mare had several months' history of left mandibular swelling with recent pus discharge from a small central sinus tract over the swelling. The referring veterinarian diagnosed an oro-cutaneous fistula over 306-tooth root.

Upon clinical examination, the mare presented with



**Figure 1:** Lateral radiograph of the right hind limb of a mature jenny (Case 1) showing open, distal diaphysis, oblique/transverse, severely displaced, comminuted tibial fracture, with several large loose bone fragments.

dysphagia and a left ventral mandibular hard swelling over 306-tooth root with central 0.5cm diameter pus secreting wound. On radiographs, osteolysis of the left mandible body over 306 apical aspect, with pathological fracture was demonstrated (Figure 3). The mare was treated with similar pre-surgical treatment as Case 1, and since 306 was found unstable, oral extraction of 306 tooth was performed, under general anaesthesia. The mare recovered uneventfully, and was discharged two days following surgery, with normal mastication. At two months follow up, the mare presented normal mastication, however a bony proliferation, about three cm diameter developed over the previous fistula area, at the ventral left mandible

On radiographs there was evidence of the bone loss area at the pathological fracture line, with some callus formation around and soft tissue swelling but no healthy bony healing (Figure 4). Upon follow up 4 months following extraction, there was evidence of initial fracture line healing process, but it was preliminary only, and the bony callus appeared enlarged. At that stage the mare started a 2 months course of ACC (5mg/kg/day, p.o.). Three years later, the mare pre-



**Figure 2:** Lateral radiograph of the right hind limb of a mature jenny (Case 1), 3 months post fracture repair, two months following initiation of ACC treatment, showing satisfying fracture healing process.

sented again to the hospital for colic, and underwent colic surgery. There was no evidence of the bony proliferation of the mandible at clinical examination.

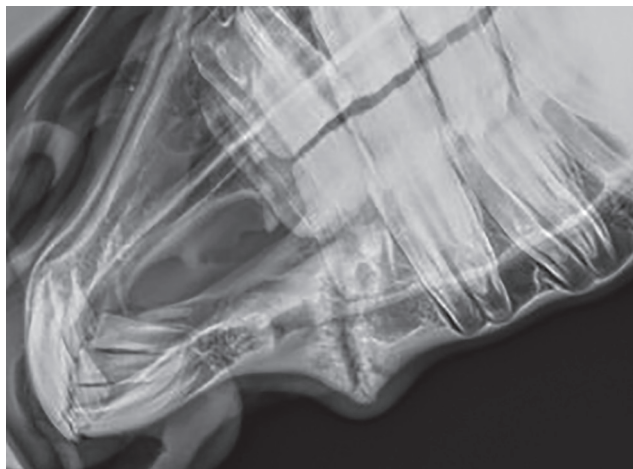
### Case 3

A yearling donkey, weighing 130 kg, found in the field by animal shelter activists, presented with severe right front (RF) limb lameness at a walk. Upon presentation, the right proximal radius region was hot, painful, swollen and unstable and a radial fracture was suspected. Radiographs confirmed right, closed, proximal, oblique, distally displaced, radial fracture (Figure 5). The donkey received similar





**Figure 3:** Left dorsal-right ventral oblique radiograph of a five years old Arabian mare (Case 2), showing osteolysis of the left mandible body over 306 apical tooth root with pathological fracture.



**Figure 4:** Left dorsal-right ventral oblique radiograph of a five years old Arabian mare (Case 2), two months following 306 extraction, showing marked bone loss and lack of healing at the pathological fracture line, with some ventral irregular callus formation around the fracture line and soft tissue swelling.

medications as previously described cases, and was submitted for ORIF surgery under general anesthesia. The fracture was repaired with two 12 holes, 4.5mm broad LCPs, placed laterally and cranially. Reduction was imperfect, but was satisfactory for this case. Intraoperative bleeding was significant, and thus blood transfusion was administered. Immediately following surgery, the donkey was severely lame. Methadone (Ceva Animal Health, Glenorie, NSW, Australia), and dexamethasone (Omega, Montreal, Canada) were added to the treatment, and palmar splint was placed



**Figure 5:** Dorso-palmar right front limb radiograph of a yearling donkey (Case 3) showing a proximal, oblique, distally displaced, mildly comminuted, radial fracture.

up to the olecranon edge. No improvement was noticed, thus the methadone was replaced with buprenorphine (Richter Pharma, Wels, Australia), with significant improvement noticed. The incision healed well and the donkey was walking well following splint removal. The donkey was discharged home 10 days after surgery, with tapered oral phenylbutazone (Logifarm, Modiin, Israel) plan and 2 months of ACC (20mg/kg/day, p.o.) Four months later, the donkey had fully recovered and was free in the paddock with the herd.

#### Case 4

An 8 years old pleasure riding Single foot mare, weighing 490 kg, presented with a chief complaint of chronic, right hind (RH) limb lameness.

The mare suffered from 12 months RH limb lameness, diagnosed as osteoarthritis (OA) of the distal tarsal joints by radiographs of the referring veterinarian. The mare was treated with steroids and hyaluronic acid (Dechra, North Yorkshire, United Kingdom) injections to the right tarsometatarsal (TMT) joint, with marked improvement, however



**Figure 6:** Dorso-plantar right hind radiography of an 8years old single foot mare (Case 4), showing severe osteolytic and osteogenesis changes of the RH distal intertarsal (DIT) and Tarsometatarsal joints, with multiple osteophytes, more pronounced medially.

with the intervals between injections decreasing and the response waned. The horse was referred to the hospital for surgical distal tarsal arthrodesis.

Upon clinical examination, severe distal tarsal bony proliferation and fibrosis, severest on the medial aspect were noted. The mare was mildly lame at a walk and severely lame at a trot. Radiographs revealed severe osteolytic and proliferative bony changes of the RH distal intertarsal (DIT) and TMT joints, with multiple osteophytes, more pronounced medially (Figure 6). Diagnosis of severe OA (bone spavin) was confirmed. Upon radiographic evaluation, mild OA changes were found on left hind TMT and DIT joints.

The mare received similar pre-operative treatment as in the previously described cases, including epidural treatment, and fluoroscope guided distal tarsal joints arthrodesis was performed. DIT and TMT cartilage was removed by drilling in a fan shape. A dorso-medial LCP T-plate was placed, from central tarsal bone to the third metatarsal, with locking



**Figure 7:** Post-operative dorso-lateral-plantaro-medial oblique (DLPMO) radiograph of the right hind of an 8years old single foot mare (Case 4), showing distal tarsal joints arthrodesis using T-LCP and transarticular screws.

screws and 5.5mm cortical screws. Two trans-articular abaxial 5.5mm cortical screws were placed in lag fashion from distal to proximal (Figure 7).

Post-operative hind limb weakness and lameness was noted, severest on RH. Significant improvement was noted after 48h. The mare was discharged home with omeprazole (Ceva Animal Health, Glenorie, NSW, Australia ) 4mg/kg bwt, p.o, s.i.d), antibiotics and non-steroidal anti-inflammatory drugs, similar to the previously described case. Two months after surgery, the mare developed severe non-weight bearing lameness on the RH. Severe incisional sensitivity was noted, despite satisfactory healing of the soft tissues. Radiographs revealed small tarsal bones osteolysis with no evidence of bony fusion within the joints (Figure 8). The mare was discharged home with ACC (10 mg/kg/day, p.o.) for 2 months. Two months follow-up showed marked improvement in lameness, with full weight bearing. Radiographic examination, at that stage, demonstrated significant dorso-medial osteogenesis

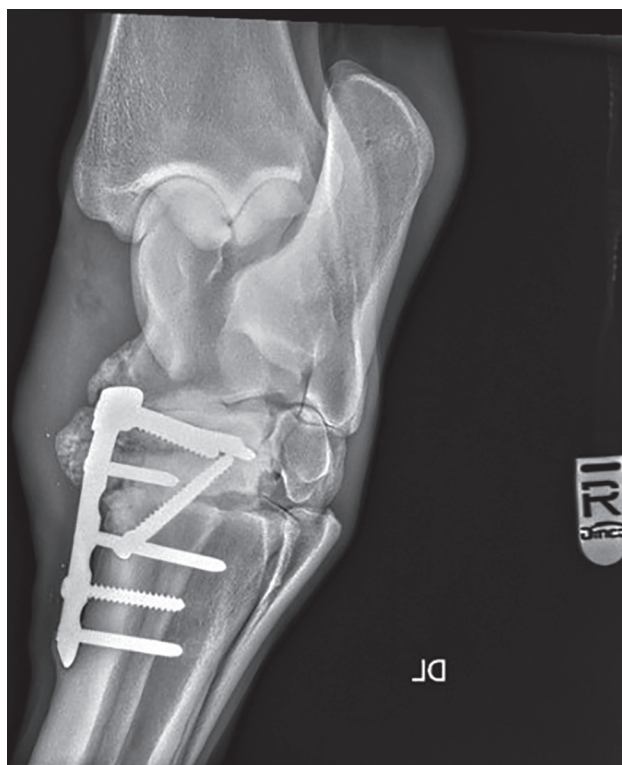


**Figure 8:** DLPMO right hind radiography of an 8 years old single foot mare (Case 4), showing significant small tarsal bones osteolysis with no radiographic evidence of healing.

over the proximal intertarsal joint (PIT), and initial signs of radiographic arthrodesis of the distal tarsal joints were noted. The ACC supplementation was continued for additional 2 months. Follow-up radiographs showed improved distal tarsal joints fusion, but also dorso-medial excessive bony proliferation over the PIT and the distal talus (Figure 9). Over the following 2 months the lameness diminished, bony fusion progressed radiographically, and the mare returned to light work. During the following year the mare had an episode of acute tarsocrural effusion that was treated with intraarticular hyaluronic acid and steroids injection, with the episode resolving. At the time of writing, the mare was being ridden extensively; sound for her owner; with complete, stable radiographic fusion of the TMT and DIT joints.

### Case 5

A 3-month-old Arabian filly, weighing 110kg, was referred to the hospital due to RF P1 fracture. The filly was found with acute non-weight bearing right front limb lameness.



**Figure 9:** DLPMO of the RH limb of an 8 years old single foot mare (Case 4), 4 months following initiating ACC treatment. Significant dorso-medial osteogenesis over the proximal intertarsal joint (PIT), and radiographic evidence of fusion of the distal tarsal joints.

The referring veterinarian diagnosed a comminuted RF P1 fracture on radiographs, and referred the filly to the hospital after external coaptation using a bandage and a splint. Upon arrival, the filly was non-weight bearing on her RF. The fracture was closed and no wound was present in the region. Radiographic evaluation revealed a comminuted proximo-lateral to disto-medial oblique, displaced P1 fracture. Neither pastern joint nor physis involvement were noted. The filly was treated with preoperative Flunixin meglumine (Ceva, Animal Health, Glenorie, NSW, Australia) 1mg/kg, i.v, b.i.d), and a prophylactic regional limb perfusion (RLP) was performed with benzyl penicillin and Amikacin. The filly was then submitted for fracture fixation under general anesthesia. Fracture configuration, prevented direct lag screw repair due to lack of longitudinal bony strut. Thus, using a narrow 4 hole, 4.5mm LCP the fracture was repaired and a temporary pastern arthrodesis in conjunction with transfixation pin cast, using three 4.8mm positive threaded pins (Figure 10). Immediately post-operatively, the filly was full weight bearing





**Figure 10:** Intraoperative latero-medial radiograph of a 3-month-old Arabian filly (Case 5), showing fracture fixation of P1 comminuted proximo-lateral to disto-medial oblique, displaced fracture, using LCP and pin cast. The procedure is performing temporary proximal interphalangeal joint arthrodesis.

and continued with the pre-operative treatment. The filly was discharged home 10 days following surgery and returned for check-up one month after surgery. The filly was walking well on the casted limb, but severe osteopenia of distal third metacarpal, P1 and P2 was noted upon radiography. The pin cast was removed and the incisions healed well. A half limb cast was applied and the filly was discharged home two days later with ACC supplementation (10mg/kg/day) and NSAID's. Two months later the filly presented with severe lameness. On radiographs, bony proliferation was noted over P2 with increased bone density and bone lysis around the plate



**Figure 11:** Intraoperative dorso-palmar radiograph of a 3 month old Arabian filly (Case 5), 2 months following initial surgery, showing facilitated ankyloses of the PIP joint under general anesthesia.

screws. These signs raised the suspicious of implant infection. The filly was subjected for implant removal, following cast removal necrotic skin was found. Amikacin and Cefazolin (Pfizer, East New York, NY, USA) impregnated plaster of paris (POP) beads (Kerrier, Palm Beach Gardens, Florida, USA) were implanted; and the filly was discharged with chloramphenicol (Pharma Tamar, Thikala, Greece, 50mg/kg bwt, p.o, t.i.d) and continued ACC for an additional month. As lameness did not improve, the filly was re-admitted to the hospital, and underwent facilitated ankyloses under general anesthesia. The pastern articular cartilage was debrided and cancellous bone graft was implanted (Figure 11), followed by half limb cast. Lameness did not improve the following 2 weeks, and the cast was removed. On radiographs, there was initiation of fracture healing but distal P1 lysis and severe



**Figure 12:** LH latero-medial radiographs of a 7-month-old Arabian filly (Case 6) showing bilateral hind limbs PIP subluxation and severe OA changes.

P2 lysis, around the previously placed screw, were noted. The antibiotics were changed to doxycycline (Dexcel Pharma, Or Akiva, Israel, 10mg/kg bwt, p.o, t.i.d), and a bandage split cast applied. Two weeks later the lameness improved, but severe fetlock laxity developed. On radiographs there was increased bone density on both P1 and P2. Fracture healing had progressed. After corrective shoeing, the filly improved further, and at the time of writing, 26 months after initial surgery, the filly was sound at light exercise and was turned out to paddock.

### Case 6

A 7-month-old Arabian filly, weighing 145kg, was referred to the VTH due to chronic, bilateral hind limbs, proximal interphalangeal joint (PIPJ) subluxation.

The filly suffered from the condition for several months, which led to severe bilateral PIPJ OA and difficulty in standing up from recumbency. Following telephonic consultation, the filly was referred to the VTH for bilateral PIPJ arthrodesis.



**Figure 13:** Ten weeks follow-up LH latero-medial radiograph of a 7-month-old Arabian filly (Case 6) showing progressive fusion of the proximal interphalangeal joint.

Upon presentation, noticeable bilateral hind limb lameness was noted at a walk and severe bilateral hind limbs dorsal PIPJ bony proliferation was palpated. Radiographs confirmed the diagnosis of bilateral hind limbs PIPJ severe proliferative OA and subluxation (Figure 12).

The filly was treated pre-operatively with phenylbutazone, and RLP with amikacin and benzyl penicillin; and was submitted for bilateral hind limbs PIPJ arthrodesis under general anesthesia.

Upon surgery bony proliferation removal, cartilage removal and osteostixis were performed as previously described (12). Three holes narrow 4.5mm PIP-LCP plate was placed with abaxial transarticular 5.5mm lag screws (Figure 13). Bilateral half limb casts were placed. Postoperatively the filly was treated with phenylbutazone and antibiotics (benzyl penicillin sodium, gentamicin) for 6 days. Lameness improved significantly, the filly was discharged home with tapered phenylbutazone treatment and one month of ACC (10mg/kg/day).

Three weeks later the casts were removed and mild heel bulb cast sores were seen, incisions started to heal, but the left hind limb incision did not completely close. The right hind limb showed flexor tendons laxity.

On radiographs, no abnormalities were noted. One week later, there appeared to be good granulation tissue over the left hind incision, but the filly developed bilateral severe hind limbs metacarpophalangeal laxity. Heel extensions were fit and the filly was discharged home with phenylbutazone and



additional 2 months of ACC therapy. Upon 10 weeks follow-up, the filly was walking well, laxity significantly improved and satisfactory radiographic PIPJ fusion process was seen (Figure 14). At the 2-year follow-up the filly was sound and ridden with no apparent lameness.

### Case 7

A 7 years old warmblood gelding, weighing 470kg, was referred to the VTH due to chronic, severe RH limb lameness. The horse suffered from RH limb lameness of several months duration, intermittently non-weight bearing that was localized by the referring veterinarian to the distal tarsal joints. The horse was treated with steroids injections to the tarso-crural and TMT joints with intermittent improvement. The horse was referred to the hospital for radiographs and further evaluation. Upon arrival, the horse presented severe RH lameness that became non-weight bearing lameness, following manual pressure over the distal tarsal joints. Severe distal tarsal bony and fibrotic swelling was noted, more pronounced on the medial aspect, with sensitivity on palpation of the lateral aspect of the distal tarsal joints. Moderate tarso-crural effusion was also present.

Severe osteolytic and osteogenesis changes of the RH distal inter-tarsal (DIT) with mild dorsal TMT osteophytes were seen on radiographs. Contrast radiography and diagnostic analgesia and steroids injection to the DIT yielded no significant improvement initially, with a non-uniform contrast spread. Two days following injection marked improvement in lameness was seen, but the horse was still lame at a walk.

Diagnosis of severe calcitrant right hind DIT and TMT osteoarthritis was established, and distal tarsal arthrodesis was recommended. Pre-operative treatment was similar to Case 4, and the horse underwent RH distal tarsal arthrodesis, similar to the surgical technique was performed as in case 4. Post-operative treatment was similar, and ACC was administered (initially 10mg/kg/day followed by 15mg/kg/day). Immediately post operatively the horse was walking well.

Following hospital discharge, the horse suffered from incisional edema and minor drainage; that were successfully treated with antibiotics. Three months following surgery, the horse suffered from mild intermittent lameness at walk. Bony proliferation and fibrotic swelling over the distal tarsal joints, mainly over the medial aspect were noted. Radiographs revealed some abnormal osteolysis and osteogenesis of the small tarsal bones, and distal tarsal joints, consistent with

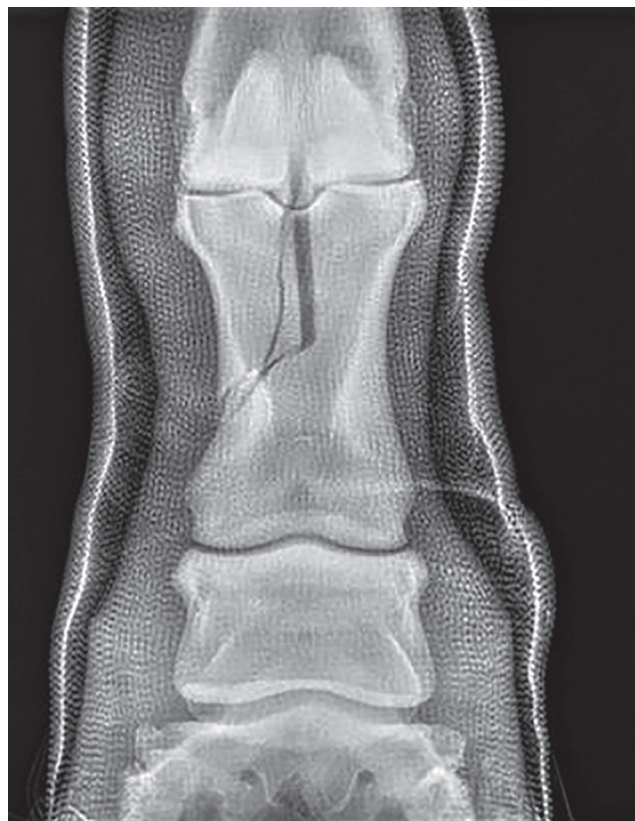
initiation of bony fusion. The horse continued to improve clinically and radiographically over the following months but did not become sound enough for athletic activity.

### Case 8

An 8 years old Arabian stallion racehorse, weighing 450 kg, was referred to the VTH due to RF P1 fracture.

One day prior to arrival, the horse showed an acute non-weight bearing RF limb lameness during training. Phenylbutazone was given by the owners with no improvement. Referring veterinarian radiographs on admission day, demonstrated a RF P1 axial, non-displaced fracture. The horse was treated with Flunixin meglumine and Penicillin, the leg was stabilized with bandage and fiberglass cast and was referred to the hospital for further treatment.

Upon arrival, the horse presented with severe RF lameness at a walk. On radiographs, RF P1 axial, minimally displaced P1 fracture, with minimal distal dorso-medial obliquity, and metacarpophalangeal joint involvement was diagnosed (Figure 14). The horse was subjected to arthroscopic guided lag screw fracture repair. Pre-operative treatment was similar to previously described, including RLP administration. The fracture was reduced arthroscopically guided and three 4.5mm and one 5.5mm cortical screws were placed in lag fashion (Figure 15). A half limb cast was placed at the end of surgery. Post-operative treatment was similar to previously described cases. Several days after surgery the horse was bearing full weight comfortably and 6 days following surgery the horse was discharged home with phenylbutazone tapered over 1 week and ACC for 2 months (15mg/kg/day). Three weeks following surgery, the horses presented for pus discharges proximal to the cast. The horse walked well on the leg. Following cast removal, superficial heel bulb and proximal-palmar third metacarpal pressure sores were found. The incisions healed well. Sutures were removed, and the leg was triple bandaged. Upon radiography, good joint congruity and fracture healing processes were noted. The horse was treated at home with Inter-leukin-1- receptor antagonist (IRAP) (Orthogen, Dusseldorf, Germany) injections to the metacarpophalangeal joint and continued treatment with ACC. The horse was walking well, with no obvious lameness. On recheck one month later, the cast wounds had healed well. Upon radiography, progressive healing of the axial aspect of the fracture line was evident, with



**Figure 14:** Dorso-palmar RF radiography of an 8 years old Arabian stallion (Case 8) at presentation, showing minimally displaced, axial, P1 fracture, with minimal distal dorso-medial obliquity, and metacarpophalangeal joint involvement.

clear radiolucent fracture line at the oblique distal aspect, as no compression was accomplished there. On long-term follow-up, the horse was sound and back to its previous level of racing.

### Case 9

A 15 years old Arabian mare, weighing 400kg, was admitted to the VTH with left front (LF) PIPJ luxation.

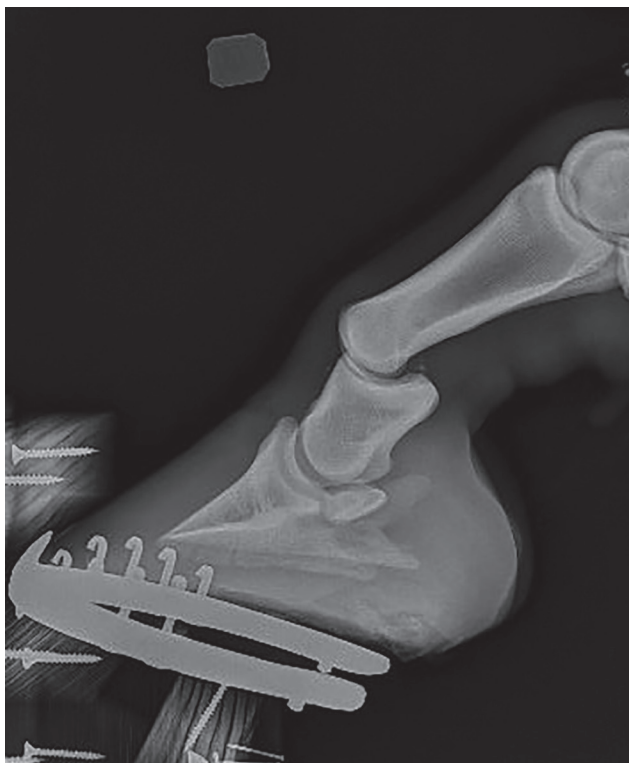
The mare was displayed acute non-weight bearing LF limb lameness one day prior to admission, and was diagnosed with LF PIPJ luxation via radiography (Figure 16). The mare was treated with Phenylbutazone and Marbofloxacin, the leg was temporarily stabilized with Kimzey Leg Saver splint and the mare was referred for definitive treatment. Upon arrival, the mare was minimally weight bearing on the splint. The mare received pre-operative treatment and underwent LF PIPJ arthrodesis as previously described in case 6. Recovery was uneventful



**Figure 15:** Intra-operative dorso-palmar RF radiography of an 8 years old Arabian stallion (Case 8) showing three 4.5mm and one 5.5mm cortical screws, placed in lag fashion.

and the mare continued post-operative treatment similar to previously described, including 6 days of RLP and ACC (15mg/kg/day). The mare was discharged home walking well on the cast, with systemic antibiotic therapy with Marbofloxacin in addition to ACC and phenylbutazone. Three days following discharge acute LF limb lameness appeared. Despite recommendation for immediate evaluation at the hospital, the mare arrived 7 days later, with severe LF limb lameness. Cast removal revealed palmar proximal sesamoids deep pressure sores, with superficial sores on the proximal dorsal third metacarpus, with discharge of pus.

Incision line healed well. Following cast removal, RF limb lameness was observed: "Egg shell" walk and the mare



**Figure 16:** Latero-medial LF radiography of a 15 years old Arabian mare (Case 9), showing LF proximal interphalangeal joint luxation.

was clinically assessed to suffer from contralateral limb laminitis. Upon radiography, there were no significant findings of both front limbs. The mare was discharged home with Modified Ultimate shoes (Nanric, Lawrenceburg, KY, USA) in addition to the previously described treatment. Despite recommendations for laminitis treatment by the referring veterinarian, the mare was only partially treated, with no corrective shoeing. Twenty-four months following surgery, the mare has severe RF limb lameness, with chronic laminitis, evident radiographically. Complete radiographic PIPJ fusion was evident (Figure 17).

### Case 10

A 17 years old miniature horse mare, weighing 90 kg, was referred to the VTH for chronic deteriorating RF limb lameness.

The mare lived in a zoo, as a pet and had few months' history of unwillingness to lift RF limb, with no improvement under treatment with NSAIDs, but some improvement with glucosamines. Muscle atrophy on the LF shoulder and LH pelvis was present upon clinical examination, with cuboidal



**Figure 17:** Latero-medial LF radiography of a 15 years old Arabian mare (Case 9), 24 months following surgery, showing complete radiographic fusion of the proximal interphalangeal joint.

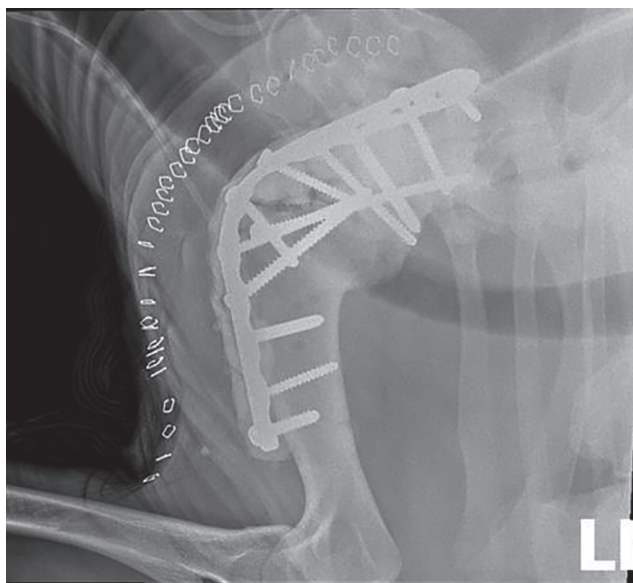
LF hoof. Pain on LF shoulder extension and LH upward fixation of the patella. Severe lameness was noted on LF trot. Significant, though incomplete, improvement with scapulo-humeral joint block was demonstrated. Upon radiography LF scapulo-humeral joint osteoarthritis was diagnosed (Figure 18). Scapulo-humeral injection with steroids and hyaluronic acid was performed, lameness improved significantly, but several months later deteriorated again and a second injection yielded partial and temporary improvement. Thus, scapulo-humeral arthrodesis was recommended and performed a year later when zoo consent was received. Pre-operative radiography revealed significant deterioration in the degree of OA (Figure 19).

Preoperative systemic antibiotics and Phenylbutazone were applied similar to previously described and the mare underwent shoulder arthrodesis under general anesthesia. Following cartilage curettage and removal, the intermediate humeral tubercle was removed using an oscillating saw. Arthrodesis was performed using cranio-lateral 4.5mm 11 holes, narrow LCP and trans-articular lag screws. Plate luting was performed, using PMMA. Amikacin and meropenem impregnated POP beads and medical grade honey was applied near the implants. A stent bandage was sutured on the incision.

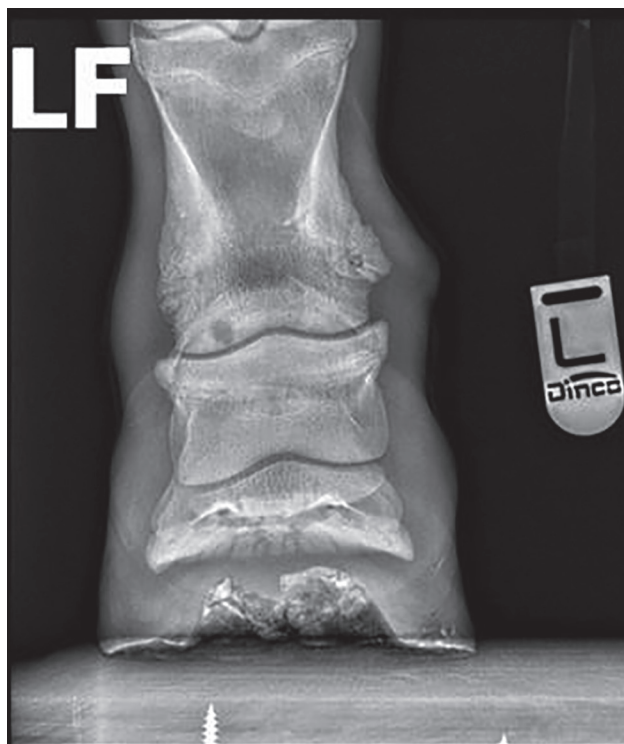




**Figure 18:** Medio-lateral pre-operative LF radiography of a 17 years old miniature horse mare (Case 10), showing scapulohumeral joint OA, with joint space loss, flattening of the glenoid cavity with excessive osteophytes on the caudal and cranial aspects of the humeral head.



**Figure 19:** Medio-lateral post-operative LF radiography of a 17 years old miniature horse mare (Case 10), arthrodesis was performed using cranio-lateral 4.5mm LCP and trans-articular lag screws



**Figure 20:** LH dorso-plantar radiograph of a 5m old Arabian foal (Case 11) showing distal P1 periosteal reaction, sequestrum of P1 mid shaft and a 5mm diameter subchondral bone cyst on medial P1 condyle.

Systemic antibiotics, phenylbutazone and methadone were administered. The mare was discharged 6 days after surgery with marbofloxacin, tapering phenylbutazone, and ACC for 2 months (15 mg/kg/ day).

Incisional infection appeared few days following discharge, the infection was superficial, and it was treated by cleansing and healed uneventfully.

Long-term follow-up revealed delayed scapulohumeral joint bony union, and continued lameness at a walk despite improvement.

### Case 11

A 5 month old Arabian foal was presented to the VTH for 2 months duration LH limb lameness.

Two months prior to presentation, the foal suffered a traumatic injury to the LH fetlock and pastern area. Two weeks later lameness had deteriorated. Referring veterinarian radiographs revealed periosteal reaction on distal P1 and proximal P2, with P1 sequestrum.

The foal presented with non-weight bearing LH limb lameness. A chronic wound on the lateral aspect of the pas-

tern was noted. The pastern was swollen, but not warm or sensitive on palpation.

Radiographs showed PIPJ OA, assumed septic in origin, secondary to traumatic injury, and medial P1 condyle subchondral bone cyst (Figure 20).

Proximal inter-phalangeal joint arthrodesis was recommended, but due to radiographic and clinical improvement 4 weeks later, the foal was elected for cyst drilling and injection. Preoperative treatment with Flunixin meglumine (1mg/kg) and penicillin and Amikacin through RLP as previously described were administered. The subchondral bone cyst was drilled, debrided and steroids and antibiotics (Amikacin) were injected. The foal was discharged with Flunixin Meglumine (0.5mg/kg BID for 3 days) and ACC (15mg/kg) for 2 months. On long-term follow-up, the cyst was radiographically filled and the foal was clinically sound.

## DISCUSSION

Several studies demonstrated a significantly higher bioavailability of ACC, compared to other formulations, with higher fractional calcium absorption values in both human patients and rats (2,4,13). The effectiveness of calcium supplements with or without vitamin-D in reducing bone loss and preventing fractures has been the focus of many clinical trials and several meta-analyses (14-16). According to a meta-analysis, calcium combined with vitamin-D was associated with a 12% reduction of fracture risk (14). Some of these studies reported significant effect of calcium supplementation in reducing bone loss (14-16). The effectiveness of calcium supplementation on the prevention of fractures on the other hand was less conclusive (17,18) most likely due to the fact that it is a modest effect, significance is not easily found in studies.

The effects of ACC supplementation on bone turnover and fracture healing has not yet being described in equine patients. Orthopedic conditions in equine patients are an important economic issue in the equine industry. Long bone fracture repair in the horse is often challenging and associated with a higher incidence of complications than other species including fixation failure, delayed healing and surgical site infection (6-9,11). Based on studies conducted in other species, a hypothesis that supplementation to equine orthopedic patients with ACC could promote

bone healing and shorten recovery time was grounded (2,5,5,14,16,17). The current study is a clinical case series, aimed to describe the clinical details, treatment and outcome of eleven cases presented with various orthopaedic complaints, and treated with ACC supplement following surgical procedure.

The study design, being retrospective and lacking of a control group, are the main limitations of the study. Thus, a firm conclusion regarding the efficacy of ACC on fracture healing and bone turnover on equine orthopedic patients cannot be drawn from the current study. Additional limiting factors, relating to the nature of the study, is the fact that each case had a different orthopedic pathology, some of the cases presented in an emergency situation, requiring urgent treatment, while others were presented as chronic surgical cases. In addition, the severity of the lesion, and patient systemic condition differed significantly between cases. Nevertheless, most cases in this study showed satisfactory recoveries and relatively good bone healing progress. In some cases, the results appear to be better than expected, relative to the severity of the lesion and current knowledge regarding convalescence period for the specific orthopedic pathologies.

For example, Case 1, the jenny suffering from chronic non-healing tibial fracture, was severely lame with minimal bony healing for months after surgery however, after ACC therapy, showed good fracture healing and excellent outcome. This positive outcome was remarkable; compared to the current knowledge regarding tibial fracture repair in equids (9). Similarly, Case 3 showed good outcome and satisfying fracture healing following radial fracture, despite carrying a poor prognosis (9,11). Donkeys appeared to be more resilient than horses, however studies show that fracture healing can be problematic and delayed in donkeys, similar to horses (19,20). In one reported case, it seemed that PRP (Platelet Rich Plasma) encouraged and speeded bony healing after fracture repair (19). While in Case 1, there appeared to be a direct temporal relation, between marked lameness improvement conjoined with commencing of bony healing, and ACC therapy initiation.

Case 2, with chronic pathologic mandibular fracture, had a prolonged convalescence period. However, in this case as well, the ACC therapy appeared to have a positive effect. The pathological mandibular fracture did not heal for months after the tooth was extracted. Following initiation of ACC

administration, fracture healing progressed and excessive bone callus was resorbed and remodeled.

Case 6 had a good recovery progression for bilateral PIPJ arthrodesis, with good owner satisfaction. Cases 4 and 7, both had distal tarsal arthrodesis due to chronic distal tarsal joints osteoarthritis. In both cases satisfactory bony healing and joint fusion was achieved and Case 4 returned to full athletic activity. Case 8, had an excellent outcome with complete owner satisfaction and return to flat racing. Recovery process and bone healing were satisfying and relatively fast.

Obviously, not all cases had rapid and satisfactory outcome. Case 10, suffered delayed healing process and remained lame at a walk. Case 9, experienced post-operative contralateral limb laminitis that caused it to be consistently lame at a walk. This post-operative complication is common in equine orthopedic patients, and presents a great challenge for equine practitioners (9). Limited owner compliance has led delayed evaluation and suboptimal treatment resulting in unsatisfactory results.

Case 11, showed good and rapid healing, with excellent owner satisfaction.

All cases were treated with various non-steroidal anti-inflammatory drugs, as well as local and/or systemic antibiotics treatment as part of the standard of care for equine clinical cases. Thus, the effect of ACC on orthopedic cases healing, and surgical site infection incidence cannot be isolated. Healing process was most likely influenced in all cases by additional factors, such as additional treatments given. Other factors that may influence healing process such as patient signalment (age, sex, etc.), season, type of orthopedic condition and surgery, open/closed fracture, chronicity of the orthopedic condition and more, which had not been counterbalanced due to the nature of the study. These factors should be examined in future studies, and their influence on the variables of interest should be researched.

As there are no published data regarding the use of ACC in equine patients, the dosage given was not uniform, and was changed during the study period according to the manufacturer's recommendation. In order to establish effective dosage, additional clinical and experimental studies are required.

Although this study has not yet drawn firm scientific evidence for the efficacy of ACC usage in equine patients,

this study does present the first ACC usage in a clinical case series. The results of most of the presented cases are excellent, and constitute the corner stone for further figuring the benefits of ACC supplement in equine patients. Additionally, no side effects, such as colic signs, were recorded in any of the presented cases following ACC supplementation. Future studies are necessary to establish the experimental and clinical benefits, as well as the recommended dosage of ACC in equids.

#### DECLARATIONS

The authors declare no conflicts of interest related to this report. The amorphous calcium carbonate supplement (Densypet) was produced and supplied by Amorphical, Industry region, Sapir, D.N, Arava.

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