Study: The effects of over-the-counter analgesics on orthodontic tooth movement

By Kristina Sakas, fourth-year dental student, Ostrow School of Dentistry

The most frequently asked question in every orthodontic office may be: “When are my braces coming off?” In the fast-paced, busy lives of patients, there is little time to spend on lengthy orthodontic therapy. In the ever-advancing field of orthodontics, many barriers have been overcome, leading to healthier results and more beautiful smiles. Now, the focus is on reducing treatment time (Profit, 2013). Faster care without sacrificing quality would be advantageous in (a) reducing hygiene problems, (b) increasing patient acceptance of treatment plans and (c) creating a higher level of overall treatment satisfaction. This new focus can be seen through the development of techniques such as the accelerated osteogenic orthodontics known as Wilckodontics and the micropulse technology seen in AcceleDent (Kau, 2011).

With the emphasis on shortening treatment time, it is critical that practitioners be aware of all medications.”

See ANALGESICS, page 4

Fig. 1: Alveolar bone from pressure zone of rat treated with ibuprofen/aspirin. Note small resorption areas (r), with few osteoblasts (ob), osteoclasts (oc), and osteocytes (os) in osseous matrix (m). Photos/Drs. Arias and Marquez-Orozco

Fig. 2: Alveolar bone from pressure zone of rat treated with acetaminophen/control. Note large resorption areas (r), many osteoblasts (ob), differentiated osteoclasts (oc) and osteocytes (os) on growth lines (c) in osseous matrix (m).

2013 MSO session set for Kansas City

By Sierra Rendon, Managing Editor

The 2013 Midwestern Society of Orthodontists Annual Session will take place Sept. 20–22 at the Sheraton Kansas City Hotel at Crown Center in Kansas City, Mo. This year’s session will be co-sponsored by the Missouri Society of Orthodontists and the South Dakota Society of Orthodontists.

The focus of this year’s meeting is “Orthodontics: A Palette of Progress.” The group aims for attendees to learn the latest research and esthetics from scientific lecturers including Drs. Mark Berkman, Aaron Molen, Chung Kau, Sebastian Baumgaertel and Abraham Lifshitz.

Marketing and management will be covered in a staff program featuring Amy Kirsch and Cathy Sundvall.

On Sunday, a doctor-staff lecture will focus on improving social media results with marketing and search engine optimization speaker Mary Kay Miller.

Attendees are also invited to tailgate with staff, family and colleagues in the MSO-private Budweiser Patio at the Saturday evening Royals vs. Rangers baseball game. Separate registration includes bus shuttle and complimentary buffet.

For more information on the annual meeting schedule and registration, visit www.msortho.org.
Hit the Mark with PROVEN Accuracy

Cutting-edge technology, delivering highly accurate digital impressions

PRECISE
3D-in-motion video technology creates a true replica of the oral anatomy

CONSISTENT
More accurate, and more consistently accurate, than other leading systems!

FLEXIBLE
Securely access open STL files that can be readily imported in a variety of digital workflows

COMFORTABLE
Small, lightweight and ergonomic wand

3M True Definition Scanner

Experience it live.
For dates, visit go.3M.com/TrueDefOTri

3M Unitek Orthodontic Products
© 2013 3M. All rights reserved. 1307

The new standard of care in orthodontics

Part 1

By Dennis J. Tartakow, DMD, MEd, EdD, PhD, Editor in Chief

Still in the early stages of the new millennium, we are in an era of dentistry and orthodontics where more accurate diagnoses are possible thanks to technological advances in imaging and scanning. We now have treatment capabilities that were not possible only a decade ago. Treatment outcomes have also improved with advances in periodontal treatment and operative dentistry. Diagnosis and treatment advances have improved the quality of dentistry and saved or prolonged permanent dentitions for millions of individuals. Such changes in the standards of care.

• See STANDARD, page 15
that patients are taking that could unknowingly slow down their orthodontic treatment. This must be accomplished by thorough evaluation of the patient’s medical history with close attention to medications, including over-the-counter (OTC) analgesics. Various analgesics taken by patients during orthodontic treatment, including traditional non-steroidal anti-inflammatory drugs, aspirin and acetaminophen, have been scientifically shown to decrease the rate of tooth movement (Tyrvola, 2001).

Mechanism of tooth movement

Orthodontic tooth movement is mediated by specific reactions at a cellular level that take place in the tissues surrounding the tooth. Cellular, chemical and mechanical reactions bring about the structural changes that prompt tooth movement. Bone is resorbed on the pressure side and deposited on the tension side of a tooth. An acute inflammatory response with periodontal vasodilatation occurs which increases intracellular levels of cyclic adenosine monophosphate (cAMP), calcium, collagenase and prostaglandins mediate tooth movement as a response to orthodontic force. Chemical mediators such as prostaglandins can pass through the bloodstream, reach the mechanically stressed tissues and interact with local cells. This can have an inhibitory effect on orthodontic tooth movement (D’avedamani, 2012).

Orthodontic patients often use over-the-counter analgesics to control the discomfort associated with tooth movement as well as to treat other ailments (Salmassian, Oesterle, Shellhart and Newman, 2009). Many of these pharmacological agents are known to systemically influence bone and the velocity of tooth movement by interfering with prostaglandin production and the inflammatory process. The pressure- and tension-side cellular responses to tooth movement occurring in three stages: “alterations in blood flow associated with pressure in the periodontal ligament (PDL), formation of several reactive chemical messengers and activation of cells” (Salmassian, et al., 2009). After force is applied, there is an increase of prostaglandin E and F levels in the PDL and gingival crevicular fluid. This is a critical step in increasing the number of osteoclasts, the rate of bone resorption and orthodontic tooth movement, and is the step that is affected by NSAID medication (Salmassian, et al.).

Process of orthodontic tooth movement

In order to appreciate how NSAIDs can affect the rate of orthodontic tooth movement, one must first understand the complex process. Tooth movement due to orthodontic forces is induced by prolonged application of mechanical forces, creating pressure and tension zones in the periodontal ligament and alveolar bone (Gameiro, Pereira-Neto, Magnani and Nauer, 2007). Bone is degraded on the pressure zone and resorbed by osteoclasts in Howship’s lacunae in the pressure zone (Knop, Shintovsck, Retamoso, Ribeiro and Turp, 2013). Remodeling occurs in dental and periodontal tissues, including dental pulp, periodontal ligament, alveolar bone and gingiva. These tissues, when exposed to mechanical loading, express significant macroscopic and microscopic changes. On a cellular level, orthodontic tooth movement is characterized by initial acute inflammation, followed by a chronic inflammatory process (Krishnan and Davidovich, 2006). The acute inflammatory process that characterizes the early stage of orthodontic movement consists of periodontal vasodilatation and migration of leukocytes. This inflammation is mainly exudative, indicating that the plasma and leukocytes are exiting the capillaries in areas of parodontal strain. These migratory cells produce a variety of cytokines that act as local inflammatory signals, interacting directly and indirectly with the population of resident parodontal cells.

Cytokines are responsible for evoking submucosal responses that are responsible for resorption of the periodontal tissues while facilitating tooth movement (Krishnan and Davidovich, 2006). Approximately two days following application of orthodontic force, the acute phase of inflammation subsides. It is replaced by a chronic, proliferative process involving fibroblasts, endothelial cells, osteoblasts and alveolar bone. This period will persist until the next orthodontic adjustment appointment when another period of acute inflammation will begin (Krishnan and Davidovich, 2006). It is during the acute inflammatory phase of orthodontic tooth movement that patients experience painful sensations and reduced chewing function. Ninety to 95 percent of orthodontic patients report experiencing this discomfort (Patel, et al., 2010). Indications of this phenomenon can be seen in the gingival crevicular fluid of teeth with significant elevations of inflammatory mediators such as cytokines and prostaglandins (Krishnan and Davidovich, 2006).

The discomfort associated with arch wire placement and subsequent tooth movement can be controlled by inhibiting the inflammatory response. This makes nonsteroidal anti-inflammatory drugs a logical choice for treating this type of pain. However, NSAIDs are also powerful inhibitors of prostaglandin synthesis, which recent studies have shown to be responsible for delaying or inhibiting orthodontic tooth movement. This area of research is critical to the field of orthodontics because it is important for orthodontists to be aware of it in order to find the analgesic of choice for treating patients experiencing discomfort that will not prolong the patient’s orthodontic treatment. The orthodontists can then educate his or her patients on proper pain management during treatment.

Clinical studies on effects of various analgesics on orthodontic tooth movement

Nonsteroidal anti-inflammatory analgesics such as aspirin, ibuprofen and naproxen have been found to reduce the rate of orthodontic tooth movement. Research shows these effects result from diminishing the number of osteoclasts through inhibition of biosynthesis of prostaglandins when they act over the cyclooxygenase-mediated catalysis of arachidonic acid (Arias and Marquez-Orozco, 2006). When the number of osteoclasts is diminished, there is a decrease in bone resorption and, therefore, a reduction in the rate of tooth movement. Histological studies were performed comparing bone in the pressure zone from rats, that had been administered these drugs, with bone from rats that received acetaminophen or a control, while undergoing orthodontic tooth movement (Arias and Marquez-Orozco, 2006). Acetaminophen, being inactive as a central nervous system level without inhibiting peripheral prostaglandin secretion and maintaining the normal gastric mucosa, COX-2 on the other hand, is regulated by inflammatory mediators and creates prostaglandins that play a role in pathophysiological and inflammatory processes, including pain. Studies have also found that these prostaglandins not only mediate inflammation but also participate in bone formation and induction of bone resorption through activation of osteoclastic cells (Sari, et al., 2004). Specifically, it is believed that they are responsible for remodeling the number of osteoclasts through enhancement of their ability to form a ruffled border, thus effecting bone resorption (Krishnan and Davidovich, 2006). Prostaglandins and NSAIDs regulate osteoclasts, reduced Howship lacunae (Knop, et al., 2011), and no observed growth lines (Arias and Marquez-Orozco, 2006). The control and acetaminophen group (Fig. 2) showed abundant remodeled areas, few and smaller osteoblasts, indistinguishable osteoclasts in the pressure region, abundant parallel lamellar osteocytes, reduced Howship lacunae (Knop, et al., 2011), and no observed growth lines (Arias and Marquez-Orozco, 2006). Acetaminophen as the drug of choice

Acetaminophen is a nonopioid analgesic in the family of paramphenolones. The exact mechanism of action of acetaminophen has not been determined. Acetaminophen differs from other nonsteroidal anti-inflammatory drugs and prostaglandin inhibitors because although it has similar antiinflammatory and analgesic properties, it exhibits little effect on the central nervous system. According to Anderson (2008), the analgesic effect is produced at the central nervous system level without inhibiting peripheral prostaglandin secretion via cell membranes as typical NSAIDs do. Acetaminophen, being inactive as an anti-inflammatory agent in peripheral tissues, does not inhibit prostaglandin synthesis (Arias and Marquez-Orozco, 2006). Beyond the fact that it is not detrimental to orthodontic tooth movement, acetaminophen is a readily available, over-the-counter, inexpensive analgesic that has been found to equally effective

‘Tooth movement due to orthodontic forces is induced by prolonged application of mechanical forces, creating pressure and tension zones in the periodontal ligament and alveolar bone.’

See ANALGESICS, page 6

Ortho Tribune U.S. Edition | FALL 2013
Not only can you choose where to have your server, but the next version of topsOrtho will give you even more to love:

• **High-def reporting.** This focus on patient statuses and appointment dispositions allows for closer patient tracking by using a different way of entering, gathering, and monitoring patient statistics.

• **topsChecklist.** With this iPad application, you can create checklists for any task. For example, you can collect patient medical histories by handing a patient or accountholder an iPad, which they can use to fill out and sign the forms.

• **Enhanced treatment notes.** The Treatment Notes section now includes a new treatment status column, next appointment, and disposition. It also allows you to approve notes, indicate treatment method, self-grade treatment timing, and use a checkbox to mark appointments as starting or ending treatment.

• **Automatic backup.** Your practice data will be backed up automatically to an off-site location.

Contact us for a sneak peak at how our next release will help your practice!

- **Phone:** +1 (770) 627-2527
- **E-mail:** sales@topsOrtho.com

(Ask us about the secret weapon that will revolutionize your ability to see what’s happening in your practice.)
ANALGESICS, Page 4

‘With acetaminophen being the most commonly used OTC medication in the United States, it is important that patients are informed about guidelines for its usage. Overdose of acetaminophen is the most common cause of acute liver failure.

As ibuprofen and a placebo in controlling discomfort after archwire placement (Salmassian, Oesterle, Shellhart and Newman, 2009). Therefore, acetaminophen might be the drug of choice in treating mild to moderate discomfort associated with orthodontic treatment.

NSAID use and the orthodontic practitioner

Clinicians are responsible for comprehensive evaluation of a patient’s medical history and for its use as an integral part of the patient’s diagnosis. This includes an understanding of how a patient’s medication — prescription or over-the-counter — will affect his or her treatment.

Given the frequency of NSAID use in this country, clinicians in the dental field are likely to encounter patients who are using these drugs regularly. Furthermore, the use of NSAIDs in the United States is likely to hold tremendous growth because of the aging population that is facing conditions such as arthritis, for which the medication using NSAID medications to allow for increasingly active lifestyles. Given that more orthodontic practices are focusing on oral health of all ages, this issue of increased NSAID use is more prevalent than ever (Turpin, 2009).

Common analgesics prescribed

Prescription and over-the-counter use of analgesics among adults in the United States is extremely high. Most of the OTC medications are anti-inflammatory drugs that have analgesic, antipyretic and anti-inflammatory action. They are used in treating headaches, arthritis, sports injuries, menstrual cramps and other illnesses. Aspirin, a drug considered to be in the NSAID category but distinguished from it by its irreversible inhibition of COX enzymes (Grosser, 2011), is the only anti-inflammatory drug that has a stronger effect, although it has similar analgesic and antipyretic effects.

It is important to note that cold and allergy medications often contain these analgesics as well. In a survey of American adults, OTC analgesics were shown to be the most frequently used of all medications and are taken by 20 percent of the adult population in a given week (OTC Medications, n.d.). The non-prescription analgesics acetaminophen, aspirin and ibuprofen are the most frequently used drugs in the United States (Borne Survey, 2009). In any given week, 23 percent of adults in the United States report use of acetaminophen, aspirin or ibuprofen. The most frequently used NSAIDs are ibuprofen, 17 percent used aspirin and 3.5 percent use naproxen (NSAIDs, n.d.).

Over-the-counter analgesics are also regularly used by children. Of all prescription and OTC drugs taken by children in the United States, ibuprofen and acetaminophen are the two most frequently used (OTC Medications, n.d.). NSAIDs are mainly used in children in treating inflammatory pain, including chronic conditions such as juvenile idiopathic arthritis (JIA). They are used for both its anti-inflammatory and analgesic properties.

NSAIDs are also used in children to treat mild to moderate acute pain where inflammation is the source (Garanian and Graudins, 2006). Acetaminophen is the first drug of choice for analgesia and treatment of febrile illness in single-dose therapy for children because its analgesic and antipyretic effects are equivalent to NSAIDs but with less adverse effects.

The effects of aspirin and NSAIDs are not unique to children. Of all pre-schoolers in the United States, ibuprofen is the most frequently used of all medications and analgesics were shown to be the most important (Graziano and Graudins, 2006).

Adverse side effects of commonly used analgesics

In spite of the therapeutic efficacy and widespread usage of aspirin and NSAIDs, there are unwanted and serious side effects that occur in children and adults. It is doubtful that if these drugs were developed in the century that they would have been regulatory approved because of the many and serious adverse effects (Jones, 2008).

The most common side effects that occur with aspirin and NSAID use are gastrointestinal (GI) (Grosser and Smyth, 2011), but other organ systems are also affected (Jones, 2008). GI symptoms occur in approximately 60 percent of users of these drugs (Jones, 2008). They are potentially serious and include dyspepsia, reduced appetite, abdominal pain and diarrhea. These effects may be due to the creation of gastric or intestinal ulcers that occur in 15 percent of regular users of aspirin and NSAIDs (Grosser and Smyth, 2011). Blood loss from ulcers may be slow, leading to anemia, or become acute and life threatening.

Risk is increased by consumption of alcohol, use of glucocorticoids, helicobacter pylori infection and other factors that injure the mucosa (Grosser and Smyth, 2011). The vast majority of deaths related to NSAID and aspirin use are because of gastrointestinal bleeding (NSAIDs, n.d.). GI effects can occur, especially in patients who have heart, liver or kidney disease (Grosser and Smyth, 2011). Hypersensitivity to aspirin and NSAIDs is also seen in some individuals. NSAIDs are contraindicated late in pregnancy because of an increased risk of postpartum hemorrhage and potential fetal death (Grosser and Smyth, 2011).

Acetaminophen, which is used for its antipyretic and analgesic actions, has other adverse effects that contribute to its potential misuse and toxicity.

At anti-inflammatory doses, aspirin and other salicylates stimulate respiration by increasing oxygen consumption and production of carbon dioxide, and also by direct stimulation of the respiratory center in the medulla Salicylates at high doses, can cause injury to the liver.

Use is contraindicated in patients younger than age 20 with viral illness associated with fever because of its correlation with a severe hepatic injury and encephalopathy seen in Reye’s syndrome. Aspirin ingestion prolongs bleeding time and impairs platelet function. A 325 mg dose of aspirin can double a person’s bleeding time for four to seven days. This calls for usage to be stopped at least one week prior to surgery and for caution or avoidance in patients with hepatic damage, hyperprothrombocytopenia, vitamin K deficiency, hemophilia or who are undergoing long-term treatment with oral anti-coagulants.

Long-term use also increases thyroidal uptake and iodine clearance, and at high doses, hearing impairment and tinnitus commonly occur (Grosser and Smyth, 2011).

Acetaminophen, which is used for its analgesic and antipyretic effects, is a drug that is generally well-tolerated at therapeutic doses, showing low incidence of GI side effects and no cardiovascular or respiratory side effects. Acetaminophen overdose, however, can cause liver damage (Grosser and Smyth, 2011). With acetaminophen being the most commonly used OTC medication in the United States, it is important that patients are informed about guidelines for its usage. Overdose of acetaminophen is the most common cause of acute liver failure (Wolf, et al., 2012).

Poor product labeling has been identified as a factor that has contributed to overdose of acetaminophen. A study published in the Journal of General Internal Medicine by Wolf, et al. (2012) that surveyed 500 adult patients taking acetaminophen showed that 3.8 percent of participants would take more than the recommended maximum daily 4 gram dose of acetaminophen per day and 5.2 percent would have taken a dangerously high dose (more than 6 grams per day). In another part of this study, 45.6 percent of patients would have exceeded maximum recommended doses by taking two products that contain acetaminophen.

Consumers do not adhere closely to labeled instructions and also do not recognize active ingredients in OTC pain medications (Wolf, et al., 2012). Because of these studies, in July 2011, Johnson & Johnson McNeil division lowered the maximum dose for Tylenol from 4,000 mg (eight extra strength Tylenol pills) to 3,000 mg (six extra strength Tylenol pills) to reduce the risk of accidental acetaminophen overdose and possible liver failure and death (Mitri, 2011).

With acetaminophen included in more than 600 OTC medications, as well as certain prescription analogues, people can unknowingly ingest too much acetaminophen. Patients with liver disease or who drink alcohol heavily should avoid acetaminophen to decrease the risk of liver disease (Wolf, et al., 2012).

In children, it is uncommon to have serious toxicity associated with NSAID use; however, similar effects that occur in adults can occur in children but with some variation. Although serious GI effects are uncommon in children,
Are In-House Payment Plans Too Much To Handle?

OrthoBanc Can Help!

Visit us at these meetings to learn how . . .

OrthoVoice, Las Vegas, NV, September 20-21
RMSO, Colorado Springs, CO, September 27-29
SAO, Hilton Head, SC, October 3-5
SWSO, Dallas, TX, October 11-12
PCSO, San Diego, CA, October 18-19
NESO, Rio Grande, Puerto Rico, November 15-17

Fall 2013

Call 888-758-0585 today or visit www.orthobanc.com.
Ortho Tribune U.S. Edition | FALL 2013

**ANALGESICS, Page 6**

NSAIDs should be given with food to diminish mild gastrointestinal symptoms that can occur. Hepatitis is another side effect that can occur in children during NSAID treatment, but is most common with ibuprofen.

Therefore, liver function in children should be monitored in those receiving long-term NSAID treatment. Incidence of renal toxicity in pediatric patients is low, with 0.2-0.4 percent prevalence in children with juvenile idiopathic arthritis (Gazarian and Graudins, 2006). CNS effects, including headache, skin reactions and bronchospasm, can also occur in children using NSAIDs. Long-term NSAID use in children can also prolong bleeding time through inhibition of platelet aggregation (Gazarian and Graudins, 2006).

**Discussion**

Knowledge of the effects of NSAIDs on orthodontic tooth movement must encourage dental professionals to take a step back and focus on the foundation of patient care, starting with the medical history. Consideration of medications taken by patients that can interfere with tooth movement is important in order to reduce negative effects of prolonging orthodontic treatment.

Many studies on NSAIDs, such as those by Knop, Shintcovsk, Retamoso, Ribeiro and Tanaka, as well as Arias and Marquez-Orozco, have been conclusive in showing that NSAIDs slow down tooth movement by blocking the inflammatory response through inhibition of prostaglandins.

In spite of the fact that these studies are scientific and well-designed, there is some uncertainty when extrapolating data and applying it to humans in a clinical scenario. Weaknesses include animal subjects, variability in experimental design, drug administration technique and force characteristics (Bartzela, Turp, Motschall, E., et al., 2006). Medication effects on the rate of orthodontic tooth movement: A systematic literature review. American Journal of Orthodontics and Dentofacial Orthopedics, 131(5), pages 364-370.


‘Acetaminophen should, therefore, be considered the analgesic drug of choice for patients undergoing orthodontics, unless contraindicated by the patient’s medical history or physician.’

**About the author**

**KRISTINA SAKAS** graduated in 2010 from Indy University with a bachelor of arts degree in biology and a minor in chemistry. With a love for dentistry, she continued her education at the Ostrow School of Dentistry at USC as a candidate for doctor of dental surgery. Kristina is currently a fourth-year dental student. In the future, she hopes to pursue a career as an educator in the field of orthodontics. For any additional information regarding this article, please contact sakas@usc.edu.