Gloucestershire Independent Dentists

Current controversies in patient management in oral surgery

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In order to prevent most operative complications we need to ask 4 simple questions
- Correct diagnosis?
- Correct treatment plan?
- Correct and informed patient?
- Correct Training?
Outline

- Bisphosphonate osteonecrosis of the jaws  BONJ
- CBCT
Phossy jaw
1940s
Watch factories
Fluorescent phosphononates
BONJ

- Bisphosphonates
  » Osteoclast inhibiting drugs
  » Inhibit intracellular vesicular transport
  » May inhibit angiogenesis
  » Cause osteosclerosis

- Types
  » IV
    » Amino  Pamidronate (Aredia)
              Zolendronic acid (Zometa)
    » Non amino  Alendronate (Fosamax)
  » Oral
    » Risendronate (Actonel)
    » Etidronate (Didronel)
    » Tiludronate (Skelide)
Relative Potency

- Not associated with BONJ
  - Etidronate (Didronel) 1
  - Tiludronate (Skelide) 10

- BONJ associated
  - Pamidronate (Aredia) 100
  - Alendronate (Fosamax) 1,000
  - Risedronate (Actonel) 10,000
  - Ibandronate (Boniva) 10,000
  - Zolendronic acid (Zometa) >100,000
Indications for bisphosphonates

- Bone pain disease progression
  - Metastatic bone disease (breast / prostatic)
  - Multiple myeloma
  - Hypercalcaemia of malignancy

- Skeletal disorders
  - Osteoporosis
  - Pagets disease
Risk factors BONJ

- 95% occurred in people being treated for cancer (increased intravenous BP doses)
- only 5% cases occurred in people treated for osteoporosis (lower oral doses).
- Dento-alveolar surgery-60% of cases due to removal of molars!
- Periodontitis / denture trauma
- Corticosteroids
- Smoking
- Age
- Immuno-compromised pts
BONJ

- Patients at risk
  - MH Metastatic bone malignancy / MM
  - 64% mandible
  - 73% extraction
  - Potent IV bisphosphonates >1 year
- Incidence of ON Weekly Alendronate
  - Osteoporosis 0.01-4% Extraction 0.09-0.34%
  - Pagets 0.26-1.8% 2.1-13.5%
  - Bone mets 0.88-1.15% 6.6-9.1%
Risk BONJ

- 62 yr old male
- Bone mets Prostatic Ca
- IV Alendronate 1 yr Jn 06-07
- XLA LL8 July 2006
- Present ‘dry socket’ Dec 06
- Reviewed Jan and April 07
BP’s Mechanism of action

1) Tissue level
   a. reduction of bone turnover

2) Cellular level
   a. inhibition of osteoclastic activity on the bone surface (Rodan et al., Strewler)
   b. inhibition of osteoclast recruitment on the bone surface (Rodan et al., Vitte et al.)
   c. osteoclast apoptosis (Hughes et al., Rogers et al.)
BP’s Mechanism of action

3) Molecular level

Interferes with osteoclast intercellular biochemical pathways

» Inhibition of farnesyl diphosphate synthase
» Metabolized to toxic analogue of ATP (non-nitrogen containing BP’s)

Bisphosphonates

- **Pharmacologic action:**
  - Inhibition of bone resorption

- **Pharmacokinetics:**
  - **Distribution:**
    - Rapid accumulation in sites of increased bone deposition/resorption,
    - Low plasma levels, $\frac{1}{2}$ life of “10 years +”
  - **Metabolism:**
    - Not metabolized (nitrogen containing)
  - **Excretion:** Renal
Staging

**Stage 1**

- Characterized by exposed bone that is asymptomatic with no evidence of significant soft tissue infection
**Staging**

**Stage 2**

- Exposed bone associated with pain, soft tissue and/or bone infection
Staging

**Stage 3**

- Pathologic fracture
- Exposed bone associated with soft tissue infection or pain that is not manageable with antibiotics due to the large volume of necrotic bone.
Suggested protocol for PREVENTION

- Oral hygiene preoperatively
- Regular dental check up
- Complete invasive procedures prior to IV bisphosphonates
  (? Short arch therapy)
- Avoid surgery during treatment
- ? Chlorhexidine mouth wash

- Preoperative CTX?

Marks et al 2007

www.ada.org/prof/resources/topics/osteonecrosis.asp
Suggested protocol for MANAGEMENT

- Stop bisphosphonates if possible but stopping BPs is ineffective due to long T1/2 (>10 years)
- Remove dentures
- AVOID extractions RCT/extrusion orthodontics
- Debridement may worsen
- If surgery required (spreading infection, debilitating pain)
  - Antibiotics
    » Clindamycin and Metronidazole
    » Pentoxyfiline 400mg BD Vitamin E 1000IU
  - Antiseptic mouth wash Corsodyl 10 mls QDS
  - Analgesia paracetamol +/- opioid
  - Hyperbaric O2 ineffective? Hyperbaric O2 (1 study)
  - Ultrasound no evidence
    » Mehrotra & Ruggiero 2006
- www.ada.org/prof/resources/topics/osteonecrosis.asp
Recommendations

The Cancer Research UK website November 2005 Journal of Clinical Oncology
EB review Bandolier UK 2007
American Society for bone and mineral research Task Force ASBMR 2007
American Academy of Oral and Maxillofacial Surgeons AAOMS 2006
American College of Rheumatology ACR 2006
America Association of Endodontists AAE 2006
American Dental Association ADA 2006
Multidisciplinary Panel 2006

Good articles
Malden N, Beltes, Lopes V. Dental Extractions and Bisphosphonates: assessment, consent and management a proposed algorithm BDJ 2008
BPs and orthodontics

2 reported cases of orthodontic treatment post BP
Rinchuse D et al 2007 AAO

Case 1  35yr F Oral Fosamax > 1 year
30 months ortho RX Class II Div. Extraction spaces difficult to close in both maxilla and mandible

Case 2  78yr M close mandibular incisor spaces post XLA of LR2
IV Zoledronic acid monthly for 12 months Ortho RX took 13 month (ideal<6months)

Zahrowski recommendations AAO 2006
BPs and orthodontic extrusion

- Orthodontic extrusion of teeth to avoid ON
  - Eran Regev et al. Atraumatic Teeth Extraction in Bisphosphonate-Treated Patients J OMS 2008; 66;Issue 6

Table

- 1 6 mo Zoledronate Breast cancer F 47
- 2 2.5 yr Pamidronate Breast cancer F 55
- 3 10 yr Risedronate Osteoporosis F 70
- 4 22 mo Pamidronate Multiple myeloma M 47
- 5 N/A Zoledronate Multiple myeloma F 42
- 6 2 yr Zoledronate Breast cancer F 69
- 7 N/A Zoledronate Breast cancer F 67
- 8 9 mo Zoledronate Breast cancer F 57
- 9 2 yr Zoledronate Breast cancer F 72
- 10 10 yr Alendronate Osteoporosis F 73
BPs and implants

- 115 cases using 468 implants
- Retrospective study
- All oral BPs
- 2 implants failed
- No BONJ
- Avoid implants in pts on BPs > 3 years, concomitant corticosteroids

- Grant B et al JOMS 2008;66:223-230
Diagnosis and monitoring of osteomyelitis

- Leukocyte counts and
- C-reactive protein levels

Other Markers
- Hydroxylysylpyridinoline (HP)
- Lysylpyridinoline (LP)
Treatment of Osteomyelitis

- Diagnosis
- Patient /local factors
- Antibiotic
  - Metronidazole 200mg TDS
  - Penicillin V 250mg QDS (Clindamycin)
  - 6 weeks
- Surgical
  - Local debridement
- Review
Osteomyelitis

- New method for monitoring
  - Springer et al 2007
  - Urinary lysylpyridinolone (LP) and hydroxylysylpyridinolone (HP)
  - Useful tool @ $5 as marker of disease activity

- No evidence for hyperbaric oxygen therapy

- Limited evidence for Antibiotic protocols
  - Pentoxyfilline 400mg BD and vitamin E 1000IU

- UK survey of current practice

- Early surgical intervention
Recent cases Osteomyelitis

- Post extraction in mandible
- Healthy patients
- ‘recurrent’ dry sockets
- Repeated short AB therapy
- Persistent local mandibular pain
- +/- lymphadenopathy
- +/- IAN neuropathy
- BEWARE!
Osteoradionecrosis

- No evidence that antibiotics improve outcome
- Pentoxyfiline 400mg BD Vitamin E 1000IU
  Corsodyl 10 mls QDS
- Hyperbaric oxygen - no evidence base
- ?ultrasound therapy no evidence
- PREVENTION Short arch prior to radiotherapy
- Oral fluoride supplements before, during radiotherapy and afterwards
CBCT

- Be careful of artefacts!
Cone Beam CT

- Relative dose change due to tissue weighting (salivary gland tissue)
- Limitation with soft tissue – require medical CT for neoplasia
- Medicolegal issues
  - Health protection agency HPA
  - AAOMFR
    » Standards for training, machinery and criteria
## CBCT relative doses

<table>
<thead>
<tr>
<th>X-ray technique</th>
<th>Effective dose (µSv)</th>
<th>Risk of fatal cancer (per million)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intraoral radiograph (bitewing/periapical)</td>
<td>1 - 8.3</td>
<td>0.02 - 0.6</td>
</tr>
<tr>
<td>Anterior maxillary occlusal</td>
<td>8</td>
<td>0.4</td>
</tr>
<tr>
<td>Panoramic</td>
<td>3.85 - 30</td>
<td>0.21 - 1.9</td>
</tr>
<tr>
<td>Lateral cephalometric radiograph</td>
<td>2-3</td>
<td>0.34*</td>
</tr>
<tr>
<td>Cross-sectional tomography (single slice)</td>
<td>1 - 189</td>
<td>1 - 14</td>
</tr>
</tbody>
</table>

- Dental Panoramic Radiograph = approx 2-5 days background radiation
- 2 Bitewings = approx 16 hours background radiation
## Dose as Multiple of Panoramic Exposures

<table>
<thead>
<tr>
<th>Technique</th>
<th>Dose as multiple of Panoramic - ICRP&lt;sub&gt;1990&lt;/sub&gt;</th>
<th>Dose as multiple of Panoramic - ICRP&lt;sub&gt;2005&lt;/sub&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>NewTom3G - Full FOV</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td>Mercuray - Full FOV 10-100</td>
<td>77</td>
<td>43</td>
</tr>
<tr>
<td>Mercuray - Full FOV 15-120</td>
<td>138</td>
<td>80</td>
</tr>
<tr>
<td>Mercuray - 9&quot; FOV</td>
<td>44</td>
<td>32</td>
</tr>
<tr>
<td>Mercuray - 6&quot; FOV (maxillary)</td>
<td>26</td>
<td>21</td>
</tr>
<tr>
<td>I-CAT - Full FOV</td>
<td>11</td>
<td>8</td>
</tr>
<tr>
<td>Panoramic*</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>maxillo-mandibular CT scan†</td>
<td>333</td>
<td></td>
</tr>
<tr>
<td>maxillary CT scan†</td>
<td>222</td>
<td></td>
</tr>
</tbody>
</table>

Dosimetry of Cone Beam CT Limited Fields of View

<table>
<thead>
<tr>
<th>Technique</th>
<th>Effective Dose in $\mu$Sv - ICRP$_{1990}$ $W_t$</th>
<th>Effective Dose in $\mu$Sv – ICRP$_{2007}$ $W_t$</th>
<th>Approximate Dose as multiple of Panoramic - ICRP$_{2007}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full FOV</td>
<td>93</td>
<td>182</td>
<td>9</td>
</tr>
<tr>
<td>6 cm Mandible</td>
<td>24</td>
<td>75</td>
<td>4</td>
</tr>
<tr>
<td>6 cm Maxilla</td>
<td>10</td>
<td>37</td>
<td>2</td>
</tr>
<tr>
<td>6 cm Mandible (HR)</td>
<td>47</td>
<td>149</td>
<td>8</td>
</tr>
<tr>
<td>6 cm Maxilla (HR)</td>
<td>19</td>
<td>68</td>
<td>3.5</td>
</tr>
<tr>
<td>13 cm Man &amp; Max</td>
<td>40</td>
<td>111</td>
<td>6</td>
</tr>
</tbody>
</table>

Roberts, Drage, Davies & Thomas, Cone Beam CT Dosimetry in Dentistry, BJR 2008 accepted for publication
Large volume Dental Cone Beam CT covers areas outside of the jaws including:
- posterior and middle cranial fossa
- orbits
- middle and inner ear
- upper and middle cervical vertebrae (cervical vertebrae)
- base of skull

Dentists have little/no training in interpretation of these areas

This imposes a duty upon those who interpret these images to evaluate and report any pathology within the imaged region and take appropriate action.
CBCT & Incidentalomas

- Arthritic changes to the cervical vertebrae
- High jugular bulbs
- Vascular, salivary and lymphatic calcifications
- Sinus pathology
CBCT & The Law

- The most effective way for dentists to minimize their liability is to use the smallest Field of View.
- Reduces the radiation dose to the patient.
- The established standard of care is to use the Field of View that adequately encompasses the area of interest.
CBCT canines

- 60-80% palatal
- 2x more common females
- CBCT better at observing resorption in adjacent teeth?
CBCT teeth proximal to IAN canal

- Tantanapornkul et al 2007 (161 teeth)
- Sensitivity    Specificity
- CBCT          93%       77%
- Panoramic     70%       63%
**CBCT teeth proximal to IAN canal**

- Tantapanomkul et al 2007 (161 teeth)
  - Sensitivity 93%  
  - Specificity 77%
- Panoramic 70% 63%

- Jhamb et al 2009
  - Spiral CT > panoramic but not sig (31)
  - 45% buccal, 39% in line, 10% lingual, 6.4% interradicular
  - 20% more than 6mm from nerve
  - 3% 0-1mm
  - 48% 0 mm with cortication
  - 29% 0 mm with cortical break

- No difference in specificity and sensitivity between panoramic and CBCT!

Radiographically localising IAN

- Localising IAN proximal to lower teeth
- Distant
Radiographically localising IAN

- Localising IAN proximal to lower teeth
- Proximal
CBCT

- May not be more useful than Panoramic radiographs for lower molars
Patient Collapse

» Diabetics
» Epileptics
» Steroids
» Pts at risk MI
» HIV
» Sedation
» Resus
Diabetics

- Type 1 insulin dependant
  - Record pts last meal
  - Glucometer >0.4mmol
  - If <0.4mmol glucose drink (50g)
  - If >10mmol carry in Rx but notify pt -GMP
Epileptics

- Unlikely to fit when stressed
  - Petit or grand mal?
- In general no contraindication to Rx
- Status epilepticus
  - >20mins persistent fits
    » 100% oxygen
    » IV access
    » 10mg diazepam/PR
Prevention MI

- Pt at risk
- Unstable angina
- MI last 6 months
- Preoperative GTN sublingual spray
HIV Infection

- Recent diagnosis
- Viral load HIV RNA 50k/ml high infectivity
- CD4 count
  - >200 cells/ml Rx as normal
  - If < 200 cells/ml Rx check blood profile
  - Neutropenia
  - Thrombocytopenia
  - Liver function
  - Coagulation screen
Contraindications to Sedation

PO2 <95%
- Liver function decreased
- Muscle weakness (myaesthenia gravis)
- Renal failure
- Drug alcohol abuse / dependancy?
- Pregnancy
- Sickle cell trait OK
- Sickle cell D
  » 100% O2 nasal canuli
  » Lidocaine 2%
  » Post op abs
  » Post op paracetamol (not NSAIDS)
  » Avoid Flumazenil
Steroid cover

- Normally 24-30mg Cortisol is released every day. In the stress this may increase to 300mg
  - Glucose metabolism
  - Fluid and electrolyte balance
  - Stress response
    » mobilisation of glucose and fat stores
    » Maintenance of BP
    » Permissive effects on pressor amines
Degree of suppression

- Dose of steroid
- Duration of treatment
- The response to stress does not seem to be significantly effected
- Steroid crisis
Steroid cover

- Previous recommendations
- Minimise risk of Hypotensive Collapse OR Hypoadrenal Crisis
- Daily dose of prednisolone
  - $\leq 15$mg medication taken no extra
  - $> 15$mg usual medication
  - +25mg hydrocortisone IV or IM at start of surgery
Steroid Crisis

- Stress of GA / surgery may induce a steroid crisis in patients not able to respond in normal manner
- Only two cases reported in Maxillofacial literature both under GA
- No reported cases under LA
Steroid cover

- No evidence for cover for routine dental procedures or minor oral surgery.
- Patients should take their normal dose
- Cover may be required for surgery under taken under GA or if patient has missed their routine steroid dose
Treatment of anticoagulated patients
Anti-platelet drugs

- Commonly used to prevent morbidity from arterio-vascular disease IHD, PVD and CVA
- Aspirin (75mg-300mg)
- Diprymidole
- Clopidogril 75mg
- SSRIs also impair platelet aggregation
- Sodium valproate, an anticonvulsant used in patients with bipolar disorders - high incidence of thrombocytopenia
Bleeding - anticoagulants

- Coagulation clinic card
- INR normally maintained between 2-3
- Check on day of surgery
- If =<4 routine extractions OK
- If >4 no extraction
- If extensive extractions required =<2
- If urgent + >4 need Haematologist referral
Aspirin

- Irreversible inhibition of cyclooxygenase at 80mg
- Prevents formation of Thromboxane A2
- Action within 1 hour of ingestion
- Nine days duration for one dose
- No evidence of significant increased bleeding after oral surgery
- Do not stop aspirin pre surgery
Other anti-platelet agents

- Do not alter any anti-platelet drug pre surgery
Anticoagulants

- Warfarin / Coumadin commonest anticoagulant worldwide
- Vitamin K antagonist reducing the synthesis of factors II VII IX and X of the coagulation cascade
Warfarin / Coumadin

- 48 hours to take effect
- 98% protein bound in plasma
  - Metronidazole, erythromycin, miconazole all potentiate
- Monitored by INR
- Target range of INR depend on disease
- Anticoagulation record book
Target international normalised ratios

- Prevention of thromboembolic disease
- Indication: Target INR range
  - DVT: 2-3
  - PE: 2-3
  - AF: 1.5-2.5
  - Prosthetic heart valve: 2.5-4

- None above INR of 4 if > 4 refer back to haematologist
Complications of Coumarins

- INR >1-4 increased risk of minor bleeding after surgery
- Risk of alteration of the INR (clotting) outweighs the risk of bleeding
- INR should be checked within 72 hours of the procedure
Warfarin does not need to be stopped before primary care dental surgical procedures

- The consensus from reviews on the management of dental patients taking warfarin is that patients requiring dental surgical procedures in primary care and who have an International Normalised Ratio (INR) below 4.0 should continue warfarin therapy without dose adjustment.

- Continuing warfarin during dental surgical procedures may increase the risk of postoperative bleeding requiring intervention.

- Most cases of postoperative bleeding are easily treated with local measures such as packing with a haemostatic dressing, suturing and pressure.

- Stopping warfarin increases the risk of thromboembolic events; the risk of thromboembolism after withdrawal of warfarin therapy outweighs the risk of oral bleeding as bleeding complications, while inconvenient, do not carry the same risks as thromboembolic complications.

- Stopping warfarin is no guarantee that the risk of postoperative bleeding requiring intervention will be eliminated as serious bleeding can occur in non-anticoagulated patients.
Local measures

- INR<4 continue routine minor oral surgery
- Adrenaline containing local analgesia
- Infiltration preferred to ID block
- Pack with Haemacel / surgical
- Suture sockets
- Check for haemostasis
- Postoperative advice
Tranexamic acid mouthwash should not be used routinely in primary dental care

- Tranexamic acid mouthwash in primary dental practice is expensive, difficult to obtain and of no more benefit than other local haemostatic measures.

- When used alone with no local haemostatic dressing, tranexamic acid mouthwash reduces postoperative bleeding compared to placebo mouthwash.

- When used in combination with local haemostatic measures and suturing, tranexamic acid mouthwash provides little additional reduction in postoperative bleeding.
General measures

- Treat Monday morning
- Stage multiple extractions
- Avoid ID blocks
- Caution on patients with fluctuating INR
- Do not prescribe NSAIDS
New NICE algorythm

Management of dental patients on warfarin undergoing surgical procedures in primary care

Does the patient have one of the following medical problems:
- Fever/infection
- Liver impairment and/or alcoholism
- Renal failure
- Thrombocytopenia, haemophilia, or other disorder of haemostasis

OR
- Is currently receiving a course of cytotoxic medication?

YES
- REFER to a dental hospital or hospital-based oral/maxillofacial surgeon.

NO
- Obtain an INR measured ideally within 24 hours but not more than 72 hours before the procedure.

NO
- Reschedule the procedure for when the INR is <4.0. Consider referral to a dental hospital or hospital-based oral or maxillofacial surgeon if the INR is maintained <4.0 or criteria is erratic.

YES
- Does the patient have a stable INR of 4.0 or below?

YES
- Follow current guidelines for endocarditis prophylaxis (interactions see page 11).

NO
- Does the patient need prophylactic antibiotics (i.e. are they at risk of endocarditis)?

NO
- Consider the timing of the procedure
  - In the morning – immediate re-bleeding problems can be managed during the working day.
  - At the beginning of the week – delayed re-bleeding problems can be managed during the working week.

- Use a local anaesthetic containing a vasoconstrictor.
- Give local anaesthetics by infiltration or intraligamentary injection wherever practical. Avoid regional nerve blocks where possible. However, if there is no alternative administer cautiously using an aspirating syringe.
- Gently pack the socket with an absorbable haemostatic dressing (e.g. Surgicel®, Haemostat®, Spongostan®).
- Carefully suture the socket.

There is no indication for routinely prescribing antibiotics following minor dental surgical procedures in this group of patients (interactions see page 11).

Does the patient require postoperative analgesia?

YES
- Paracetamol is the analgesic of choice.
  - AVOID non-steroidal anti-inflammatory drugs (NSAIDs) e.g. ibuprofen, aspirin, diclofenac (interactions see page 11). Dihydrocodeine is available on NHS prescription.

NO
- Patients should be given clear instructions on the management of the clot in the postoperative period (see page 10).
FDA offers warfarin guidelines

- By Associated Press | August 17, 2007
- WASHINGTON -- Federal health officials are stopping short of recommending genetic tests for patients on the blood-thinner warfarin, even though they have said such screenings could prevent thousands of complications each year.
- Genetic testing can reveal which patients may require less of the drug and lead doctors to recommend doses closer to the lower end of the scale.
Endocarditis Prophylaxis Guidelines

- NICE draft 2007
- British Society for antimicrobial Chemotherapy (BSAC 2006)
- European Cardiac Society
- American Heart Society (1997)
What is endocarditis?

- Usually bacterial infection
- 50% of cases are due to streptococcus viridans
- Lesions consist of clumps of organisms, fibrin and platelets
- Causing local damage, embolic phenomena and immune complex damage
Endocarditis facts

- Incidence: 10 per 100,000
- Mortality: 20%
- Incidence after dental Rx: 20/million
- Incidence PenV anaphylaxis: 20/million
Symptoms

- Flu like symptoms
  - Cough
  - Difficulty breathing
  - Headache
  - Arthralgia
  - Osler's nodes
  - Petechial haemorrhage
  - Splinter haemorrhage
  - Finger clubbing
Dental relevance

- IE occurs despite prophylaxis
- More likely due to low grade chronic bacteraemia as a result of possessing teeth
- Bacteraemia during eating and brushing teeth
- Antibiotic prophylaxis does not eliminate bacteraemia
- More pts die from anaphylaxis to AB cover than IE (risk PenV anaphylaxis 20/million)
- No proven link to dental Rx
Current Guidelines NICE

- AB cover for dental treatment not recommended
- Patients at risk of IE should maintain high standard of oral health
- Chlorhexidine mouth wash is not recommended
- Dentists must warn patients re IE symptoms
- No AB cover for ENT or O&G
Prevention of patient collapse

- Cardiopulmonary resuscitation
  - UK 30:2
  - Belgium 15:2
  - USA continuous chest compressions
  - France?
Most efficient?

- Get the defibrillator there ASAP!
- Every minute delay = increase 7% mortality
Know your boundaries
Thank you
References

- RCS and RCA working party 1990
- First 5 years in Dentistry GDC publication 2000
- Tordoff et al Anaesthesia 1995;51;585-7
- J One day surgery 1997
- Vyryan et al Anaesthesia 1995;50:983-984
- Seymour Brit J OMFS 1985;23:410-418
- Cochrane systematic review of ibuprofen for third molar surgical pain 2002
Le fornet avalanche

- When you don’t stand a chance