

10 min on CNMP

Pharmacological Treatment



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Outline



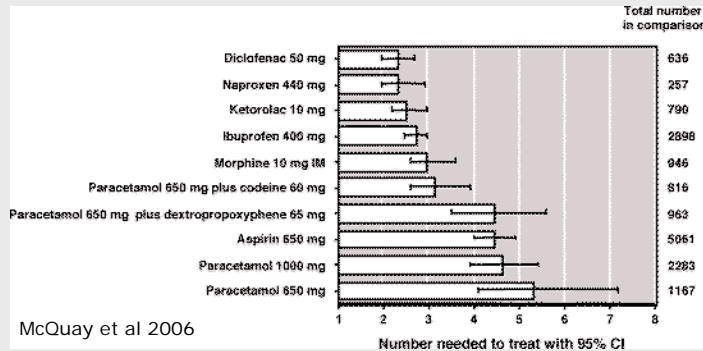
- Part A** the options we have
- Part B** specific indications
- Part C** supportive therapy/specials



Part A – the options we have NSAIDs



Oral NNT for >50% Pain Relief in Comparison to Morphine i.m.

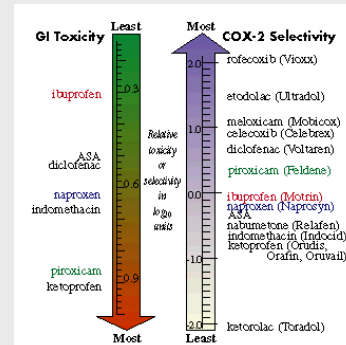


Part A – the options we have CV Risk, GI-Toxicity and NSAIDs

Cardiovascular RR (serious event) of Cox-2 selective and non-selective NSAIDs *

Drug	Studies	RR	95 % CI
Diclofenac	9	1.40	1.16-1.70
Rofecoxib	11	1.35	1.15-1.59
Meloxicam	3	1.25	1.00-1.55
Indomethacin	6	1.30	1.07-1.60
Ibuprofen	16	1.07	0.97-1.18
Celecoxib	11	1.06	0.90-1.23
Piroxicam	4	1.06	0.70-1.59
Naproxen	15	0.97	0.87-1.07

McGettigan P, Henry D. JAMA 2006 Sept; 296:1



Risk of
Risk of

CVD > Gastro →
Gastro > CVD →

Rather Naproxen+PPI
Rather Ibu+PPI/Coxib



Part A – the options we have

Opioids

Substance	Oral (mg)	s.c. (mg)	i.v. (mg)
Morphine	10	5	3
Codeine	100	x	x
Tramadol	50	33	x
Buprenorphine	rarely used	rarely used	x
Hydromorphone	2	1	0.7
Oxycodone	5-7.5	x	x
Fentanyl	rarely used	50 µg	30-50 µg
Methadone	1 (depends)	0.6	0.6



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usable in renal insufficiency



Part A – the options we have

Others

- In Germany: **Flupirtin** (Potassium-Channels/NMDA)
→ AE: Liver Failure
- in Germany: **Metamizol**
→ AE: Dizziness, Aplastic Anemia
- AD: TCA, SNRI (**Amitryptiline, Nortryptiline, Venlafaxine..**)
- Anticonvulsive Med. (**Gabapentine, Pregabaline, Lamotrigine, Carbamacepine,..**)
- Muscle-Relaxants (**Dantrolene, Baclofen, Pridinol**)
- Topical Drugs (**Capsaicin, Lidocain, NSAIDs**)
- Corticosteroids (**Dexamethason, ...**)



Part A – the options we have

Others – preferred / not preferred

- **Amitryptiline – Nortryptiline**
- **Venlafaxine/Duloxetine (SNRI) vs. SSRI**
- **Gabapentine vs. Pregabaline**
- **Muscle-Relaxants**
 - **Dantrolene** – no sedation
 - **Baclofen** – spasticity, experience
 - **Pridinol** – waiting for studies...
- **Topical Drugs (Capsaicin, Lidocain)**



Part B – specific indications

Neuropathic pain^{1,2,3}

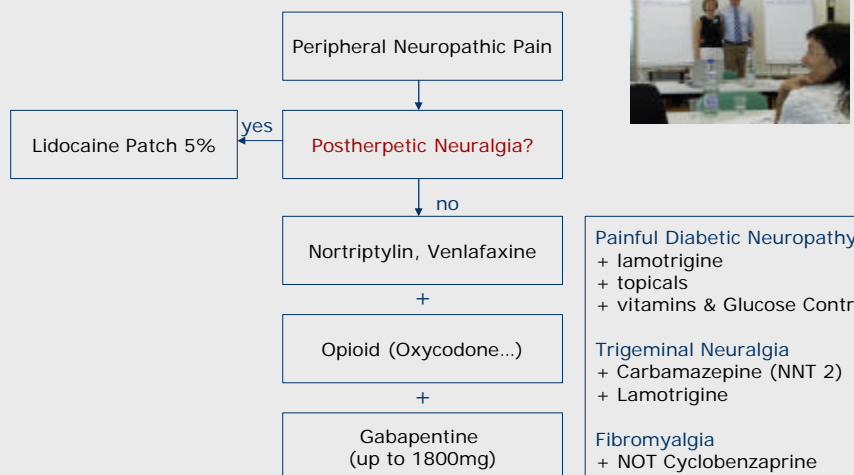
Substance	NNT	NNH Major	NNH Minor
Amitriptylin	3.6	>20(y);3-11(o)	6
Nortriptylin	3-4	less/similar?	less ¹
Venlafaxine	3-5	16	9
Gabapentine 1800mg	2-3	11	?
Pregabalin 300mg	3-4	16	?
Tramadol	4	?	?
Oxycodone (ret)	3	38	?

1-Neurology. 1998 Oct;51(4):1166-71, 2-Cochrane DB of Syst. Reviews 2005/2007
3-MedGenMed. 2007; 9(2): 36.



Part B – specific indications

Neuropathic pain³



according to Finnerup et al, MedGenMed. 2007; 9(2): 36. - largely modified for Geriatric purpose



Part B – specific indications

Osteoarthritis and Musculoskeletal Pain^{1,2}

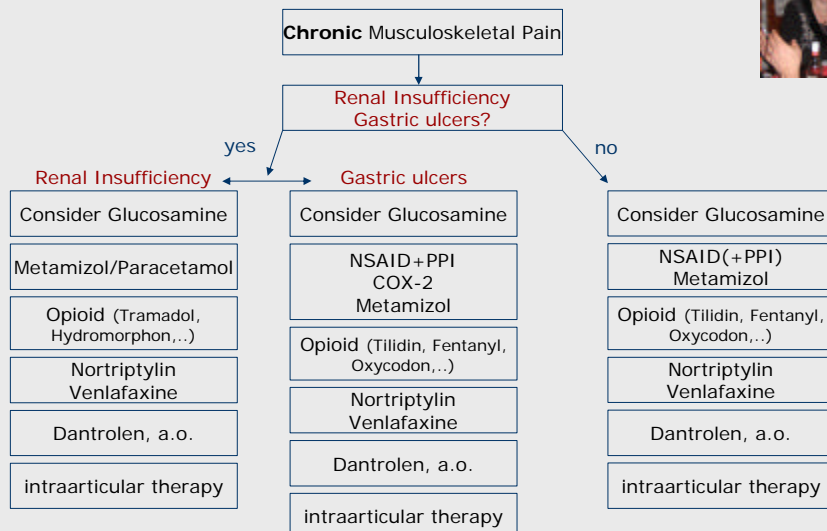
- if chronic mostly with neuropathic components
→ similar approaches
- intra-articular therapy with **corticosteroids** and **viscosupplementation** have short term benefits
- **NSAIDs** probably more useful in acute pain
 - Avocado/Soyabean in combination with NSAID more effective?
- **Acetaminophen** effective if 3-4g/daily (NNT >3) but risk of liver failure increased¹
- **Glucosamine** probably effective short term, conflicting results, no side effects

1-Watkins et al Aminotransferase elevations in healthy adults receiving 4 grams of acetaminophen daily: RCT. JAMA. 2006 Jul 5;296(1):87-93. 2-www.RX-Files.ca



Part B – specific indications

Musculoskeletal Pain



Source: own literature review, expert consultation
27.06.2008

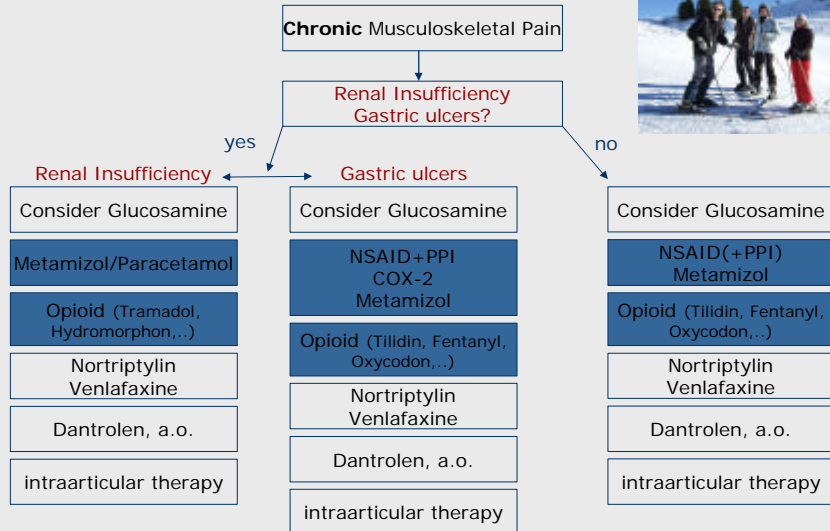


Part B – specific indications

Musculoskeletal Pain



Bethesda Geriatric Clinic – Ulm - Germany



Source: own literature review, expert consultation
27.06.2008

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Part C – supportive therapy

for adverse effects of most popular pain-meds



Bethesda Geriatric Clinic – Ulm - Germany

- OPIOIDS
 - → Always consider opioid rotation
 - Vomiting → MCP, Haloperidole, Dimenhydrinate
 - Dizziness → explain that it may resolve, switch opioid
 - Constipation → Macrogol, Lactulose...
 - Delirium → low, slow; switch opioid; Antipsychotics; DD: pain!
 - Itching → explain; switch; topical; anti-histamin med.; TCAs...
- NSAIDs
 - Edema → reduce dose; withdraw; use stockings;
 - Delirium → withdraw
 - Gastrointestinal Complications → PPI, Misoprostol, H2-Blocker, Withdraw/switch

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Part C – special facts (Geriatric-relevant)



- Combination Therapy can lower doses BUT
- Compliance Problem more prominent (use fixed comb.)
- Favor central acting meds towards bedtime
- substandard doses often beneficial because older Persons can have lower
 - renal function: careful with NSAIDs+Cox-II , rather Acetaminop.?
careful with opioids, prefer Tilidin, Hydromorphon
 - sodium excretion: NSAIDs → higher rate of edema → increase of diuretic use! Think of OTC drugs!
 - liver function: careful with Acetaminophen (>3g/daily or less)
careful with sutained release formulas
 - cognitive function: Opioids can cause Delirium-like effects, dizziness
 - CV function: remember slide [4?](#)



BENEFIT vs. RISK



Thank you!

SOME LINKS/LITERATURE

http://painmed.org/pdf/medical_treatment_utilization_schul_e_guidelines.pdf

<http://www.jr2.ox.ac.uk/bandolier/booth/painpag/Acutrev/Analgesics/Leagtab.html>

Saarto, T; Wiffen, PJ (2005/2007) Antidepressants for neuropathic Pain; Cochrane DB for Systematic Reviews, Issue: Volume (1), 2008

McGettigan P, Henry D. Cardiovascular risk and inhibition of cyclooxygenase. A systematic review of the observational studies of selective and nonselective inhibitors of cyclooxygenase 2. *JAMA*. 2006; 296

Larson AM et al. Acetaminophen-induced acute liver failure: results of a United States multicenter, prospective study. *Hepatology*. 2005 Dec; 42(6):1364-72.

Finnerup NB, Otto M, Jensen TS, Sindrup SH. An evidence-based algorithm for the treatment of neuropathic pain, *MedGenMed*. 2007 May 15; 9(2):36. Review.

Kurth T et al. Inhibition of clinical benefits of aspirin on first myocardial infarction by nonsteroidal anti-inflammatory drugs. *Circulation*. 2003; 108:1191-1195.

Martell et al, Systematic Review: Opioid treatment in chronic in back pain, *Ann Intern Med*. 2007 Jan 16; 146(2):116-27.

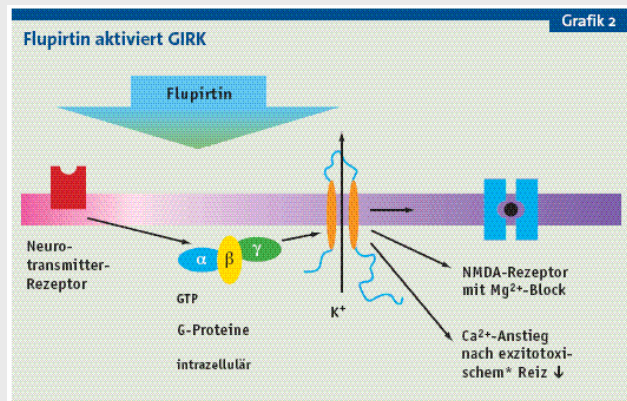


NNT Neuropathic Pain

Drug	Central Pain	Peripheral Pain*	PNP	Post-herpetic Neuralgia	Peripheral Nerve Injury	Trig. Neur.	HIV NP	Mixed Neur.Pain
TCA	4.0 (2.6-8.5)	2.3 (2.1-2.7)	2.1 (1.9-2.6)	2.8 (2.2-3.8)	2.5 (1.4-11)	ND	ns	NA
SNRI	ND	5.1 (3.9-7.4)	5.1 (3.9-7.4)	ND	NA	ND	ND	ND
Gabapent./Prega.	NA	4.0 (3.6-5.4)	3.9 (3.3-4.7)	4.6 (4.3-5.4)	NA	ND	ND	8.0 (5.9-32)
Opioids	ND	2.7 (2.1-3.6)	2.6 (1.7-6.0)	2.6 (2.0-3.8)	3.0 (1.5-74)	ND	ND	2.1 (1.5-3.3)
Tramadol	ND	3.9 (2.7-6.7)	3.5 (2.4-6.4)	4.8 (2.6-27)	ND	ND	ND	ND
NMDA antag.	ND	5.5 (3.4-14)	2.9 (1.8-6.6)	ns	Ns	ND	ND	ns
Topical lidocaine	ND	4.4 (2.5-17)	ND	NA	ND	ND	NA	4.4 (2.5-17)
Cannabinoids	6.0 (3.0-718)	ND	ND	ND	ND	ND	ND	ns
Capsaicin	ND	6.7 (4.6-12)	11 (5.5-317)	3.2 (2.2-5.9)	6.5 (3.4-69)	ND	NA	NA



Flupirtin



Does haloperidole make my penis small??!

- Enter your search terms Submit search form Webyouqa.com
- **Question:**
- I have studies that haloperidole and other dopamin blockers increase prolactin hormone which is anti 5-hydroxy testosterone. I am 23 years old with 16 cm penis. I'm taking just 0.5 mg haloperidole per day as anti anxiess which is effective for me. does it make my penis smaller if I take it in a short period of 2-3 months??!

Answer:

It doesn't make it any smaller just keeps it the same size so if you are getting older and bigger it looks like it's getting smaller.

Opioids available in US

Table 1
Opioids Available in the U.S.

Mu-Receptor Agonists	
Affentanil	Morphine
Codeine	Opium
Fentanyl	Oxycodone
Hydrocodone	Oxymorphone
Hydromorphone	Propoxyphene
Levorphanol	Remifentanyl
Meperidine	Sufentanil
Methadone	Tramadol
Kappa-Receptor Agonists/Mu-Receptor Antagonists	
Buprenorphine	Nalbuphine
Butorphanol	Pentazocine
Mu-Receptor Antagonists	
Nalmefene	Naltrexone
Naloxone	



glucosamine

- The review included 2592 adults in 20 RCTs. The mean age of participants was generally 50–70 years. RCT duration was 3 weeks to 3 years
- Participants received glucosamine or placebo/active control. In all but one trial, glucosamine sulfate (as opposed to glucosamine hydrochloride) was used
- The results were mixed
- Glucosamine outperformed NSAIDs ibuprofen and piroxicam for pain in three trials, including one top quality trial that followed 319 participants for 20 weeks
- Overall, glucosamine helped pain more than placebo. However, concealment allocation was adequate in only eight of the 15 relevant trials, and seven out of these 8 trials found no difference between glucosamine and placebo
- It was unclear whether glucosamine improved function more than placebo
- Glucosamine was as safe as placebo
- After the Cochrane review was completed, a large RCT found glucosamine hydrochloride and chondroitin in combination but not individually to be effective for moderate to severe knee pain and to have no effect on mild pain. In half of patients on this combination, significant improvement occurred at 4 weeks. A further 15% of patients had improved significantly at 24 weeks¹⁷
- A subsequent large RCT found 4–24 weeks of glucosamine sulphate 1500 mg/day was highly effective for relieving pain and improving function in knee OA¹⁸

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Plain language summary glucosamine for osteoarthritis

Does glucosamine work for treating osteoarthritis?

This Cochrane review looked at the best studies done to date on glucosamine. Twenty studies tested over 2500 people with osteoarthritis of the knee or hip. Most of the studies were 2 to 3 months long. To test how well glucosamine works, researchers compared people who had either glucosamine (as a pill or an injection), fake pills or injections, or a non-steroidal anti-inflammatory drug (NSAID).

How well does glucosamine work?

Pain: The high quality studies showed that pain improved about the same whether people took glucosamine or fake pills. If all of the studies are examined (including low quality and old studies), then glucosamine improved pain more than fake pills. Pain may improve by 13 more points on a scale of 0 to 100 with glucosamine than with fake pills.

Studies testing only the Rotta brand of glucosamine (including low quality and old studies) showed that glucosamine improved pain more than fake pills.

Function: The high quality studies show that glucosamine improved pain more than fake pills when measured by one type of scale, but improved the same amount as fake pills when measured by another scale. This result is the same whether all of the studies (including low quality and old studies) or whether studies using the Rotta brand of glucosamine are analysed.

How safe is it?

The number of people taking glucosamine who had side effects was about the same as the number who took fake pills. Side effects mainly included stomach upset and other joint pain.

What is the bottom line?

It was shown in a previous Cochrane review that glucosamine taken for 6 weeks decreases pain and improves function (physical ability) in people with osteoarthritis.

When compared to the previous review, this review which analyzes newer studies and more high quality studies, shows there is "platinum" level evidence that pain does not improve as much when taking glucosamine for 2 to 3 months.

Depending on the scale used to measure function (physical ability), function may not improve at all or as much. Glucosamine seems to be safe.

Authors' conclusions

This update includes 20 studies with 2570 patients. Pooled results from studies using a non-Rotta preparation or adequate allocation concealment failed to show benefit in pain and WOMAC function while those studies evaluating the Rotta preparation show that glucosamine was superior to placebo in the treatment of pain and functional impairment resulting from symptomatic OA. WOMAC outcomes of pain, stiffness and function did not show a superiority of glucosamine over placebo for both Rotta and non-Rotta preparations of glucosamine. Glucosamine was as safe as placebo.



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opoids in back pain

Cochrane Database Syst Rev. 2007 Jul 18; (3):CD004959_...

Links



chronic low-back pain.

A. Furlan A, Mailis-Gagnon A, Atlas S, Turk D.

University Health Network, TWH-Comprehensive Pain Unit, 399 Bathurst St, 4th Floor, Toronto, Ontario, Canada, M5T 2S8. adeshp@uhnres.utoronto.ca

BACKGROUND: The use of opioids in the long-term management of chronic low-back pain (LBP) appears to be increasing. Despite this trend, the benefits and risks of these medications remain unclear. **OBJECTIVES:** To determine the efficacy of opioids in adults with chronic LBP. **SEARCH STRATEGY:** We electronically searched CENTRAL, CINAHL and PsycINFO to May 2006; MEDLINE and EMBASE to May 2007. We supplemented our search by reviewing references in relevant systematic reviews and identified trials. **SELECTION CRITERIA:** We included randomized or quasi-randomized controlled trials assessing the use of opioids (as monotherapy or in combination with other therapies) for longer than four weeks, in adults with chronic LBP. Studies were included if they compared non-injectable opioids to other treatments. Comparisons between opioids were excluded. **DATA COLLECTION AND ANALYSIS:** Two authors independently assessed methodological quality and extracted data onto a pre-designed form. Results were statistically pooled using RevMan 4.2. We reported on pain and function using standardized mean difference (SMD) with 95% confidence interval (95% CI) and on side effects using absolute risk difference (RD) with 95% CI. **MAIN RESULTS:** We included four trials. Three compared tramadol to placebo. Pooled results revealed that tramadol was more effective than placebo for pain relief, SMD 0.71 (95% CI 0.39 to 1.02), and improving function, SMD 0.17 (95% CI 0.04 to 0.30). The two most common side effects of tramadol were headaches, RD 9% (95% CI 6% to 12%) and nausea, RD 3% (95% CI 0% to 6%). One trial comparing opioids to another analgesic (naproxen) found opioids were statistically significant for relieving pain but not improving function. When re-calculated, the results were not statistically significant for either pain relief (SMD -0.58; 95% CI -1.42 to 0.26) or improving function (SMD -0.06; 95% CI -0.88 to 0.76). **AUTHORS' CONCLUSIONS:** Despite concerns surrounding the use of opioids for long-term management of chronic LBP, there remain few high-quality trials assessing their efficacy. The trials in this review, although achieving high internal validity scores, were characterized by a lack of generalizability, inadequate description of study populations, poor intention-to-treat analysis, and limited interpretation of functional improvement. Based on our results, the benefits of opioids in clinical practice for the long-term management of chronic LBP remains questionable. Therefore, further high-quality studies that more closely simulate clinical practice are needed to assess the usefulness, and potential risks, of opioids for individuals with chronic LBP.



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