Single dose oral tenoxicam for acute postoperative pain in adults (Review)

Moore OA, McIntyre M, Moore RA, Derry S, McQuay HJ


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Single dose oral tenoxicam for acute postoperative pain in adults

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ABSTRACT

Background

Tenoxicam is a non-steroidal anti-inflammatory drug (NSAID) licensed for use in rheumatic disease and other musculoskeletal disorders in the UK, and is widely available in other countries worldwide. This review sought to evaluate the efficacy and safety of oral tenoxicam in acute postoperative pain, using clinical studies of patients with established pain, and with outcomes measured primarily over 6 hours using standard methods. This type of study has been used for many decades to establish that drugs have analgesic properties.

Objectives

To assess the efficacy of single dose oral tenoxicam in acute postoperative pain, and any associated adverse events.

Search methods

We searched The Cochrane Library (Issue 1, 2009), MEDLINE (March 2009); EMBASE via Ovid (March 2009); the Oxford Pain Relief Database.

Selection criteria

Randomised, double-blind, placebo-controlled clinical trials of oral tenoxicam for relief of acute postoperative pain in adults.

Data collection and analysis

Two review authors independently assessed trial quality and extracted data. The area under the “pain relief versus time” curve was used to derive the proportion of participants with tenoxicam experiencing least 50% pain relief over 4 to 6 hours, using validated equations. The number needed to treat to benefit (NNT) was calculated using 95% confidence intervals (CI). The proportion of participants using rescue analgesia over a specified time period, and time to use of rescue analgesia, were sought as additional measures of efficacy. Information on adverse events and withdrawals was also collected.

Main results

Not one of sixteen studies identified by the searches and examined in detail studied oral tenoxicam in patients with established postoperative pain and therefore no results are available.
Authors’ conclusions

In the absence of evidence of efficacy for oral tenoxicam in acute postoperative pain, its use in this indication is not justified at present. Because trials clearly demonstrating analgesic efficacy in the most basic of acute pain studies is lacking, use in other indications should be evaluated carefully. Given the large number of available drugs of this and similar classes which are effective, there is no urgent research agenda for this particular drug.

PLAIN LANGUAGE SUMMARY

Single dose oral tenoxicam for acute postoperative pain in adults

Pain is commonly experienced after surgical procedures. Acute postoperative pain of moderate or severe intensity is often used (as a model) to test whether or not drugs are effective painkillers. In this case we could find no studies that tested oral tenoxicam against placebo. It is possible that the studies were done, but not reported, because they were used only to register tenoxicam with licensing authorities throughout the world. However, this leaves an important gap in our knowledge, and it means that we cannot be confident about using oral tenoxicam for acute painful conditions.

BACKGROUND

Acute pain occurs as a result of tissue damage either accidentally due to an injury or as a result of surgery. Acute postoperative pain is a manifestation of inflammation due to tissue injury. The management of postoperative pain and inflammation is a critical component of patient care.

This is one of a series of reviews whose aim is to present evidence for relative analgesic efficacy through indirect comparisons with placebo, in very similar trials performed in a standard manner, with very similar outcomes, and over the same duration. Such relative analgesic efficacy does not in itself determine choice of drug for any situation or patient, but guides policy-making at the local level. Recently published reviews include paracetamol (Toms 2008), celecoxib (Derry 2008), naproxen (Derry C 2009), diclofenac (Derry P 2009) and etoricoxib (Clarke 2009).

Acute pain trials

Single dose trials in acute pain are commonly short in duration, rarely lasting longer than 12 hours. The numbers of participants is small, allowing no reliable conclusions to be drawn about safety. To show that the analgesic is working it is necessary to use placebo (McQuay 2005). There are clear ethical considerations in doing this. These ethical considerations are answered by using acute pain situations where the pain is expected to go away, and by providing additional analgesia, commonly called rescue analgesia, if the pain has not diminished after about an hour. This is reasonable, because not all participants given an analgesic will have significant pain relief. Approximately 18% of participants given placebo will have significant pain relief (Moore 2006), and up to 50% may have inadequate analgesia with active medicines. The use of additional or rescue analgesia is hence important for all participants in the trials.

Clinical trials measuring the efficacy of analgesics in acute pain have been standardised over many years. Trials have to be randomised and double blind. Typically, in the first few hours or days after an operation, patients develop pain that is moderate to severe in intensity, and will then be given the test analgesic or placebo. Pain is measured using standard pain intensity scales immediately before the intervention, and then using pain intensity and pain relief scales over the following 4 to 6 hours for shorter acting drugs, and up to 12 or 24 hours for longer acting drugs. Pain relief of half the maximum possible pain relief or better (at least 50% pain relief) is typically regarded as a clinically useful outcome. For patients given rescue medication it is usual for no additional pain measurements to be made, and for all subsequent measures to be recorded as initial pain intensity or baseline (zero) pain relief (baseline observation carried forward). This process ensures that analgesia from the rescue medication is not wrongly ascribed to the test intervention. In some trials the last observation is carried forward, which gives an inflated response for the test intervention compared to placebo, but the effect has been shown to be negligible over 4 to 6 hours (Moore 2005). Patients usually remain in the hospital or clinic for at least the first 6 hours following the intervention, with measurements supervised, although they may then be allowed home to make their own measurements in trials of longer duration.
Knowing the relative efficacy of different analgesic drugs at various doses can be helpful. An example is the relative efficacy in the third molar extraction pain model (Barden 2004).

**Tenoxicam**

This review looks at tenoxicam. Tenoxicam is widely available orally, as suppositories, and by injection in many European countries, as well as in some Asian and South and North American countries, including Japan and the USA. Tenoxicam is not much used in the UK, with only 12,000 prescriptions in England in 2007, but is more widely used in other countries in Europe.

Clinicians prescribe non-steroidal anti-inflammatory drugs (NSAIDs) on a routine basis for a range of mild-to-moderate pain. NSAIDs are the most commonly prescribed analgesic medications worldwide, and their efficacy for treating acute pain has been well demonstrated (Moore 2003). They reversibly inhibit cyclooxygenase (prostaglandin endoperoxide synthase), the enzyme mediating production of prostaglandins (PGs) and thromboxane A2 (Fitzgerald 2001). PGs mediate a variety of physiological functions such as maintenance of the gastric mucosal barrier, regulation of renal blood flow, and regulation of endothelial tone. They also play an important role in inflammatory and nociceptive processes. However, relatively little is known about the mechanism of action of this class of compounds aside from their ability to inhibit cyclooxygenase-dependent prostanoid formation (Hawkey 1999).

Tenoxicam (tradenames Apo-Tenoxicam, Mobiflex, Tilcotil, Tobitil) is one of the oxicam class of NSAIDs, acting in part through the non-selective inhibition of cyclo-oxygenase-1 and -2 to produce analgesic and antipyretic effects (Berg 1999). It is available in 20 mg oral tablets, 20 mg suppositories, and 20 or 40 mg powders for injection (intravenous or intra-muscular). Maximal plasma concentrations are reached after 1 to 2 hours for the standard oral preparations which have 100% bioavailability. Tenoxicam has a long half life of 67 hours (Nilsen 1994). Two main metabolites, the inactive 5’-hydroxy and 6-O-glucuronidated forms, are excreted in urine and bile, respectively (Nilsen 1994). Based on a limited systematic review tenoxicam may have somewhat reduced adverse events compared to piroxicam (Riedemann 1993).

**OBJECTIVES**

To assess the efficacy and adverse effects of single dose oral tenoxicam for acute postoperative pain using methods that permit comparison with other analgesics evaluated in standardised trials using almost identical methods and outcomes.

**METHODS**

**Criteria for considering studies for this review**

**Types of studies**

Studies would be included if they were double blind trials of single dose oral tenoxicam compared with placebo for the treatment of moderate to severe postoperative pain in adults with at least 10 participants randomly allocated to each treatment group. Multiple dose studies will be included if appropriate data from the first dose were available. Cross-over studies were included provided that data from the first arm were presented separately.

The following were excluded:

- review articles, case reports, and clinical observations;
- studies of experimental pain;
- studies where pain relief is assessed only by clinicians, nurses or carers (i.e., not patient-reported);
- studies of less than four hours duration or studies that fail to present data over four to six hours post-dose.

For postpartum pain, studies were included if the pain investigated was due to episiotomy or Caesarean section irrespective of the presence of uterine cramps; studies investigating pain due to uterine cramps alone were excluded.

**Types of participants**

Studies of adult participants (> 15 yrs) with established postoperative pain of moderate to severe intensity following day surgery or in-patient surgery were included. For studies using a visual analogue scale (VAS), pain of at least moderate intensity were equated to greater than 30 mm (Collins 1997).

**Types of interventions**

Tenoxicam or matched placebo administered as a single oral dose for postoperative pain.

**Types of outcome measures**

Data was collected on the following outcomes:

- participant characteristics;
- patient reported pain at baseline (physician, nurse or carer reported pain will not be included in the analysis);
- patient reported pain relief expressed at least hourly over four to six hours using validated pain scales (pain intensity and pain relief in the form of VAS or categorical scales, or both);
- patient global assessment of efficacy (PGE), using a standard categorical scale;
- time to use of rescue medication;
- number of participants using rescue medication;
- number of participants with one or more adverse events;
- number of participants with serious adverse events;
- number of withdrawals (all cause, adverse event).
Search methods for identification of studies

To identify studies for inclusion in this review, the following electronic databases were searched:
- Cochrane CENTRAL (Issue 1, 2009),
- MEDLINE via Ovid (March 2009),
- EMBASE via Ovid (March 2009),
- Oxford Pain Relief Database (Jadad 1996a).

Please see Appendix 1 for the MEDLINE search strategy, Appendix 2 for the EMBASE search strategy and Appendix 3 for the Cochrane CENTRAL search strategy. Additional studies were sought from the reference lists of retrieved articles and reviews.

Language

No language restriction was applied.

Unpublished studies

No manufacturing or distributing pharmaceutical company was contacted for unpublished trial data.

Data collection and analysis

Selection of studies

Two review authors independently assessed and agreed the search results for studies that might be included in the review.

Quality assessment

Two review authors independently assessed the included studies for quality using a five-point scale (Jadad 1996b) that considers randomisation, blinding, and study withdrawals and dropouts.

Data management

Data were extracted by two review authors and recorded on a standard data extraction form. Data suitable for pooling were entered into RevMan 5.0.17.

Data analysis

For each study, the mean TOTPAR, SPID, VAS TOTPAR or VAS SPID (Appendix 4) values for active and placebo were converted to %maxTOTPAR or %maxSPID by division into the calculated maximum value (Cooper 1991). The proportion of participants in each treatment group who achieved at least 50%maxTOTPAR was calculated using verified equations (Moore 1996; Moore 1997b). These proportions were converted into the number of participants achieving at least 50%maxTOTPAR by multiplying by the total number of participants in the treatment group. Information on the number of participants with at least 50%maxTOTPAR for active and placebo was used to calculate relative benefit/relative risk (RR), and number-needed-to-treat-to-benefit (NNT).

Pain measures accepted for the calculation of TOTPAR or SPID were:
- five-point categorical pain relief (PR) scales with comparable wording to "none, slight, moderate, good or complete";
- four-point categorical pain intensity (PI) scales with comparable wording to "none, mild, moderate, severe";
- VAS for pain relief;
- VAS for pain intensity.

If none of these measures was available, the number of participants reporting "very good or excellent" on a five-point categorical global scale with the wording "poor, fair, good, very good, excellent" were used for the number of participants achieving at least 50% pain relief (Collins 2001).

The number of participants reporting treatment-emergent adverse effects was extracted for each treatment group. RR estimates were calculated with 95% confidence intervals (CI) using a fixed-effect model (Morris 1995). NNT/Number-needed-to-treat-to-harm (NNH) and 95% CIs were calculated using the pooled number of events using the method devised by Cook and Sackett (Cook 1995). A statistically significant difference from control was assumed when the 95% CI of the RR did not include the number one. Homogeneity was examined visually using L’Abbé plots (L’Abbé 1987).

Sub-group analyses were planned to determine the effect of dose, presenting condition (pain model), and high versus low (two or fewer versus three or more) quality trials. A minimum of two studies and 200 participants must be available in any sensitivity analysis (Moore 1998).

RESULTS

Description of studies

Results of the search

Sixteen studies were examined in detail by reading abstracts and the full paper obtained in electronic or paper format.
Included studies
No studies were found matching the inclusion criteria.

Excluded studies
All the sixteen studies examined were excluded. Four studies were excluded because they were studies of preemptive analgesia in which tenoxicam was administered before participants had established pain (Blake 1997; Colbert 1998; Moiniche 1995; Roelofse 1996a). Two studies had no extractable data for the first 6 hours that could be used (Callesen 1999; Eggers 1999). Three studies had no placebo arm (Cassaro 1990; Cheung 1992; Scaglione 1993). Six studies used intravenous tenoxicam only, sometimes without placebo and sometimes with a preemptive design (Hsu 2003; Kumara 1998; Merry 1998; Merry 2002; Salman 2000; Windsor 1996). One study used rectal administration (Roelofse 1996b).

Risk of bias in included studies
There were no included studies, so bias could not be evaluated.

Effects of interventions
There were no included studies, so effects could not be evaluated.

DISCUSSION
Tenoxicam is a widely available NSAID, in many parts of the world, and is available by oral, rectal, and intravenous or intramuscular injection. It is disappointing that no classical analgesic studies of efficacy of oral tenoxicam compared with placebo in patients with established pain have been published.

It is almost certain that such studies have been performed, as they would have been required for registration purposes. Previously, large numbers of unpublished trials of this design have been included in systematic reviews of tramadol (Moore 1997c), and large numbers of analgesic trials of many designs with dexketoprofen (Moore 2008). Obtaining unpublished clinical trial data is, however, a long and complicated process, made more difficult by drugs being older, and with original trial data hard to find.

There is a literature showing that tenoxicam has analgesic properties in acute pain, but most of those were studies of intravenous use perioperatively in patients without established pain. While in general these studies showed some efficacy of tenoxicam, the disparate nature of designs, doses, and conditions, predominantly without any placebo comparator, means that there is little in the way of conventional evidence of efficacy for oral tenoxicam in postoperative pain.

Some studies were large, and may have utility in assessing adverse events. For instance, one study examined perioperative intravenous plus postoperative oral tenoxicam (80 mg perioperatively and 40 mg orally for each over four days) (Merry 1998). Surgical site bleeding was somewhat higher with tenoxicam, and in up to 10% of participants in otorhinolaryngology surgery.

AUTHORS’ CONCLUSIONS
Implications for practice
In the absence of evidence of efficacy for oral tenoxicam in acute postoperative pain, its use in this indication is not justified. Because trials clearly demonstrating analgesic efficacy in the most basic of acute pain studies is lacking, use in other indications should be evaluated carefully.

Implications for research
Given the large number of available drugs of this and similar classes to treat postoperative pain, there is no urgent research agenda.

ACKNOWLEDGEMENTS
We wish to thank Caroline Struthers at the PaPaS Cochrane Review Group for help with searching.
References to studies excluded from this review

Blake 1997 [published data only]

Callesen 1999 [published data only]

Cassaro 1990 [published data only]

Cheung 1992 [published data only]

Colbert 1998 [published data only]

Eggers 1999 [published data only]

Hsu 2003 [published data only]

Kumara 1998 [published data only]

Merry 1998 [published data only]

Merry 2002 [published data only]

Moiniche 1995 [published data only]

Roelofse 1996a [published data only]

Roelofse 1996b [published data only]

Salman 2000 [published data only]

Scaglione 1993 [published data only]

Windsor 1996 [published data only]

Additional references

Barden 2004

Berg 1999
Berg J, Fellier H, Christoph T, Grarup J, Stimmeleder D. The analgesic NSAID lornoxicam inhibits cyclooxygenase (COX)-1/-2, inducible nitric oxide synthase (iNOS), and the formation of interleukin (IL)-6 in vitro. Inflammation Research 1999;48:369–79.

Clarke 2009

Collins 1997

Collins 2001
Cook 1995

Cooper 1991

Derry 2008

Derry C 2009

FitzGerald 2001

Hawkey 1999

Jadad 1996a

Jadad 1996b

L'Abbé 1987

McQuay 2005

Moore 1996

Moore 1997a

Moore 1997b

Moore 1997c

Moore 1998

Moore 2003

Moore 2005

Moore 2006

Moore 2008

Morris 1995

Nilsen 1994
## Characteristics of Studies

**Characteristics of excluded studies  [ordered by study ID]**

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<td>Blake 1997</td>
<td>Analgesic administration is pre-emptive to surgical intervention. Study is focused on pharmacokinetics rather than analgesic response</td>
</tr>
<tr>
<td>Callesen 1999</td>
<td>No 6 hour pain data.</td>
</tr>
<tr>
<td>Cassaro 1990</td>
<td>No placebo arm. Pain outcomes used were not single dose.</td>
</tr>
<tr>
<td>Cheung 1992</td>
<td>No placebo arm.</td>
</tr>
<tr>
<td>Colbert 1998</td>
<td>Analgesic administration is pre-emptive to surgical intervention</td>
</tr>
<tr>
<td>Eggers 1999</td>
<td>No 6 hour pain data.</td>
</tr>
<tr>
<td>Hsu 2003</td>
<td>Intravenous administration. No oral route.</td>
</tr>
<tr>
<td>Merry 1998</td>
<td>Intravenous administration. No oral route.</td>
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<tr>
<td>Merry 2002</td>
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<td>Moiniche 1995</td>
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<td>Roelofse 1996a</td>
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<td>Roelofse 1996b</td>
<td>Rectal administration of analgesia.</td>
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<td>Scaglione 1993</td>
<td>Study is focused on pharmacokinetics rather than analgesic response. No placebo arm</td>
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<tr>
<td>Windsor 1996</td>
<td>Intravenous administration. No oral route. Analgesic administration is pre-emptive to surgical intervention</td>
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APPENDICES

Appendix 1. Search strategy for MEDLINE (via Ovid)

1. tenoxicam.sh
2. tenoxicam.ti,ab,kw.
3. OR/1-2
4. pain, postoperative.sh.
5. ((postoperative adj4 pain$) or (post-operative adj4 pain$) or post-operative-pain$ or (post$ NEAR pain$) or (postoperative adj4 analgesi$) or (post-operative adj4 analgesi$) or ("post-operative analgesi$"))).ti,ab,kw.
6. ((post-surgical adj4 pain$) or ("post surgical" adj4 pain$) or (post-surgery adj4 pain$)).ti,ab,kw.
7. (("pain-relief after surg$") or ("pain following surg$") or ("pain control after").ti,ab,kw.
8. (("post surg$" or post-surg$) AND (pain$ or discomfort)).ti,ab,kw.
9. ((pain$ adj4 "after surg$") or (pain$ adj4 "after operat$") or (pain$ adj4 "follow$ operat$") or (pain$ adj4 "follow$ surg$"))).ti,ab,kw.
10. ((analgesi$ adj4 "after surg$") or (analgesi$ adj4 "after operat$") or (analgesi$ adj4 "follow$ operat$") or (analgesi$ adj4 "follow$ surg$"))).ti,ab,kw.
11. OR/4-10
12. randomized controlled trial.pt.
13. controlled clinical trial.pt.
14. randomized.ab.
15. placebo.ab.
16. drug therapy.fs.
17. randomly.ab.
18. trial.ab.
19. groups.ab.
20. OR/12-19
21. 3 AND 11 AND 20

Appendix 2. Search strategy for EMBASE (via Ovid)

1. tenoxicam.sh
2. tenoxicam.ti,ab,kw.
3. OR/1-2
4. postoperative pain.sh.
5. ((postoperative adj4 pain$) or (post-operative adj4 pain$) or post-operative-pain$ or (post$ NEAR pain$) or (postoperative adj4 analgesi$) or (post-operative adj4 analgesi$) or ("post-operative analgesi$"))).ti,ab,kw.
6. ((post-surgical adj4 pain$) or ("post surgical" adj4 pain$) or (post-surgery adj4 pain$)).ti,ab,kw.
7. (("pain-relief after surg$") or ("pain following surg$") or ("pain control after").ti,ab,kw.
8. (("post surg$" or post-surg$) AND (pain$ or discomfort)).ti,ab,kw.
9. ((pain$ adj4 "after surg$") or (pain$ adj4 "after operat$") or (pain$ adj4 "follow$ operat$") or (pain$ adj4 "follow$ surg$"))).ti,ab,kw.
10. ((analgesi$ adj4 "after surg$") or (analgesi$ adj4 "after operat$") or (analgesi$ adj4 "follow$ operat$") or (analgesi$ adj4 "follow$ surg$"))).ti,ab,kw.
11. OR/4-10
12. clinical trials.sh.
13. controlled clinical trials.sh.
14. randomized controlled trial.sh.
15. double-blind procedure.sh.
17. ((doub$ or trebl$ or tripl$) adj25 (blind$ or mask$)).ab.
18. placebo.$ab.
19. random.$ab.
Appendix 3. Search strategy for Cochrane CENTRAL

1. MESH descriptor Tenoxicam
2. tenoxicam:ti.ab.kw.
3. OR/1-2
4. MESH descriptor Pain, Postoperative
5. ((postoperative adj4 pain$) or (post-operative adj4 pain$) or post-operative-pain$ or (post$ NEAR pain$) or (postoperative adj4 analgesi$) or (post-operative adj4 analgesi$)) or (“post-operative analgesi$”):ti,ab,kw.
6. ((post-surgical adj4 pain$) or (“post surgical” adj4 pain$) or (post-surgery adj4 pain$)):ti,ab,kw.
7. (“pain-relief after surg$”) or (“pain following surg$”) or (“pain control after”):ti,ab,kw.
8. (“post surg$” or post-surg$) AND (pain$ or discomfort):ti,ab,kw.
9. ((pain$ adj4 “after surg$”) or (pain$ adj4 “after operat$”) or (pain$ adj4 “follow$ operat$”) or (pain$ adj4 “follow$ surg$”)):ti,ab,kw.
10. ((analgesi$ adj4 “after surg$”) or (analgesi$ adj4 “after operat$”) or (analgesi$ adj4 “follow$ operat$”) or (analgesi$ adj4 “follow$ surg$”)):ti,ab,kw.
11. OR/4-10
13. Controlled Clinical Trial:pt.
15. MeSH descriptor Double-Blind Method
17. ((doubl$ or trebl$ or tripl$) adj25 (blind$ or mask$)):ti,ab,kw.
18. placebo$:ti,ab,kw.
19. random$:ti,ab,kw.
20. OR/12-19
21. 3 AND 11 AND 20

Appendix 4. Glossary

Categorical rating scale:
The commonest is the five category scale (none, slight, moderate, good or lots, and complete). For analysis numbers are given to the verbal categories (for pain intensity, none=0, mild=1, moderate=2 and severe=3, and for relief none=0, slight=1, moderate=2, good or lots=3 and complete=4). Data from different subjects is then combined to produce means (rarely medians) and measures of dispersion (usually standard errors of means). The validity of converting categories into numerical scores was checked by comparison with concurrent visual analogue scale measurements. Good correlation was found, especially between pain relief scales using cross-modality matching techniques. Results are usually reported as continuous data, mean or median pain relief or intensity. Few studies present results as discrete data, giving the number of participants who report a certain level of pain intensity or relief at any given assessment point. The main advantages of the categorical scales are that they are quick and simple. The small number of descriptors may force the scorer to choose a particular category when none describes the pain satisfactorily.

VAS:
Visual analogue scale: lines with left end labelled “no relief of pain” and right end labelled “complete relief of pain”, seem to overcome this limitation. Patients mark the line at the point which corresponds to their pain. The scores are obtained by measuring the distance between the no relief end and the patient’s mark, usually in millimetres. The main advantages of VAS are that they are simple and quick to score, avoid imprecise descriptive terms and provide many points from which to choose. More concentration and coordination are needed, which can be difficult post-operatively or with neurological disorders.
TOTPAR:
Total pain relief (TOTPAR) is calculated as the sum of pain relief scores over a period of time. If a patient had complete pain relief immediately after taking an analgesic, and maintained that level of pain relief for six hours, they would have a six-hour TOTPAR of the maximum of 24. Differences between pain relief values at the start and end of a measurement period are dealt with by the trapezoidal rule. This is a simple method that approximately calculates the definite integral of the area under the pain relief curve by calculating the sum of the areas of several trapezoids that together closely approximate to the area under the curve.

SPID:
Summed pain intensity difference (SPID) is calculated as the sum of the differences between the pain scores over a period of time. Differences between pain intensity values at the start and end of a measurement period are dealt with by the trapezoidal rule. VAS TOTPAR and VAS SPID are visual analogue versions of TOTPAR and SPID. See “Measuring pain” in Bandolier's Little Book of Pain, Oxford University Press, Oxford, 2003; pp 7-13 (Moore 2003).

WHAT’S NEW

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HISTORY
Protocol first published: Issue 1, 2009
Review first published: Issue 3, 2009

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CONTRIBUTIONS OF AUTHORS
OM, MM, and SD performed searching, data extraction, and analysis, including assessment of study quality. RAM helped with analysis and acted as arbitrator. All review authors contributed to the writing of the review. SD will be the contact for any updates of this work.
DECLARATIONS OF INTEREST

SD, RAM & HJM have received research support from charities, government and industry sources at various times. RAM and HJM have consulted for various pharmaceutical companies. RAM, and HJM have received lecture fees from pharmaceutical companies related to analgesics and other healthcare interventions. Support for this review came from Oxford Pain Research, the NHS Cochrane Collaboration Programme Grant Scheme, and NIHR Biomedical Research Centre Programme.

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

There are no differences between the protocol and the review.

NOTES

The authors declare that there is unlikely to be any further studies to be included in this review and so it should be published as a 'stable review'.

INDEX TERMS

Medical Subject Headings (MeSH)

Acute Disease; Administration, Oral; Anti-Inflammatory Agents, Non-Steroidal [*administration & dosage]; Pain, Postoperative [*drug therapy]; Piroxicam [administration & dosage; *analogs & derivatives]

MeSH check words

Adult; Humans