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ACUTE PAIN

Introduction

In many ways the subject of acute pain and its treatment encapsulates a whole range of issues that affect delivery of healthcare. Audits persist in telling us that acute pain is poorly treated, and that we must do better. We have at our disposal a range of techniques to use, their appropriateness depending on circumstances; for many we now have evidence of their effectiveness. The wider problem is that for many patients with or likely to suffer acute pain, different techniques need to be used at different times. What is lacking is coordination, management, or both, that allows effective techniques to be delivered effectively. And, if they are delivered effectively, we have little or no idea whether doing so costs more or less, and whether better delivery is efficient in healthcare economic terms (if not in human or moral terms). There is also a side issue, that all of the foregoing refers primarily to acute pain in hospitals, and that dealing with acute pain in the community opens up a whole series of new problems that are not dealt with here.

This essay on acute pain will therefore be entirely conventional in its structure. It will first discuss the evidence that acute pain is, in general, not handled well. It will examine a patient "journey", and set the scene for what interventions are most appropriate at particular parts of that journey. It will describe how clinical trials in acute pain are often done, and in the thinking behind different outcomes. It will examine the evidence we have for particular interventions, both those that work, and some that do not. It will peruse the evidence, such as it is, that methods of management can make a big contribution to reducing acute pain (better described as "doing the simple things well"). Finally, it will make a nodding acquaintance with some thinking behind health economics.

It will not be possible here to describe in detail all of the very many technical methods of pain relief and what is involved in them, so we will concentrate on those most commonly used.

How well is acute pain treated?

A large survey of over 3000 recently discharged patients from 36 NHS hospitals [1] showed that many patients (medical and surgical) had moderate or severe pain in hospital (Table 1). Other surveys show much the same thing. In adults, a detailed survey with structured interviews of 200 patients up to 72 hours after elective surgical procedures showed that moderate to severe pain was common, especially on movement [2].

The situation is no better for children. A questionnaire survey for the whole of Sweden was conducted in 1996. All anaesthesia, ENT, surgery, paediatric surgery, orthopaedic, general paediatric and plastic surgery departments were sent questionnaires to sample both nurse and physician perspectives of acute pain in children [3]. The response rate was 75% and indicated that 6,344 children had undergone surgery in the previous month (out of the 2.02 million aged 18 years and under). Of these, 73% were estimated to have had some pain, and 23% of those with pain (17% of the total) had moderate to severe pain.

In individual hospital departments, the percentage of children with moderate to severe pain despite treatment varied from 0% to 100%. The number of children treated in the month was a major determinant of pain (Table 2). There were also 766 cases of non-postoperative acute pain, and in this case 31% had moderate to severe pain despite treatment.

Table 1: Pain in hospital from a survey of 36 NHS hospitals

Problem	Number/total	Percent
Pain was present all or most of the time	1042/3162	33
Pain was severe or moderate	2755/3157	87
Pain was worse than expected	182/1051	17
Had to ask for drugs	1085/2589	42
Drugs did not arrive immediately	455/1085	41

Table 2: Moderate or severe pain in children in hospital in Sweden

Children treated in previous month	Range (%) with moderate or severe pain
More than 200	0-10
100-200	0-35
50-100	0-50
Less than 50	0-100

Nor is there much evidence that particular techniques can deliver significantly better results. An extensive review of postoperative pain and pain relief after major surgery indicated that about 1 in 5 patients experiences severe pain, or poor or fair pain relief [4]. Moderate or severe pain at rest or on movement was also common.

The review [4] sought studies that characterised the incidence of moderate to severe and severe pain after major surgery with three analgesic techniques - intramuscular analgesia, patient controlled analgesia (PCA) and epidural analgesia. Studies of any architecture were looked for using MEDLINE, reference lists, and hand searching four major journals; unpublished audit data were also included.

Studies had to have pain or pain relief as an outcome, and be in abdominal, major gynaecological, orthopaedic or thoracic surgery. Pain had to be assessed using visual analogue scales or verbal rating scales, and give proportions of patients with pain or pain relief of particular intensity. The outcome sought was the incidence of analgesic failure, and is reported in various ways. For pain intensity it was moderate or severe, or severe pain. For pain relief it was poor, or poor to fair pain relief. For epidural studies, premature catheter dislodgement was also used as a marker of analgesic failure.

The shortest period of observation was 24 hours. Paediatric, day stay, and minor surgery, and where observations were for less than 24 hours were excluded. Intrathecal opioids were also excluded, as were combined spinal and epidural analgesia or regional blocks.

Pain intensity results were obtained from 123 papers with 19,909 patients, pain relief results from 53 papers with 9,068 patients and epidural catheter displacement from 32 papers with 13,629 patients. Most studies were published since 1985. The surgical disciplines were mixed, with different anaesthetic techniques; for instance, epidural analgesia was more often used with thoracic surgery.

Moderate to severe pain at rest was reported by two thirds of patients receiving intramuscular analgesia (Figure 1), 36% with patient controlled analgesia and 21% of those with epidural analgesia. Moderate to severe pain on movement was reported by 78% of patients receiving intramuscular analgesia (Figure 2), 25% with patient controlled analgesia and 38% of those with epidural analgesia. Poor pain relief was reported by 2-5% of patients, and poor or fair pain relief by 17-21% of patients (Figure 3).

Figure 1: Moderate to severe pain at rest

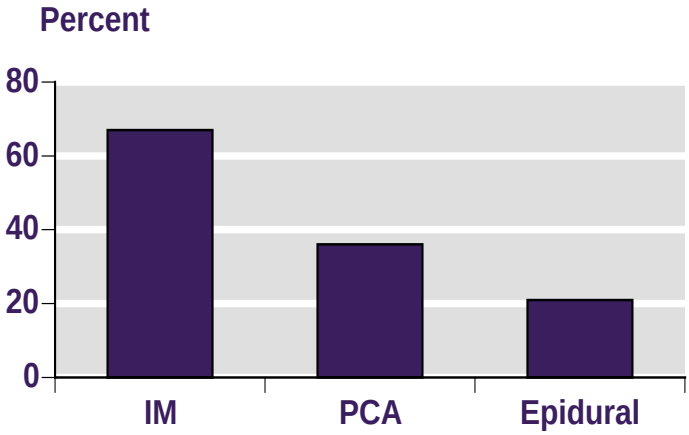


Figure 2: Moderate to severe pain on movement

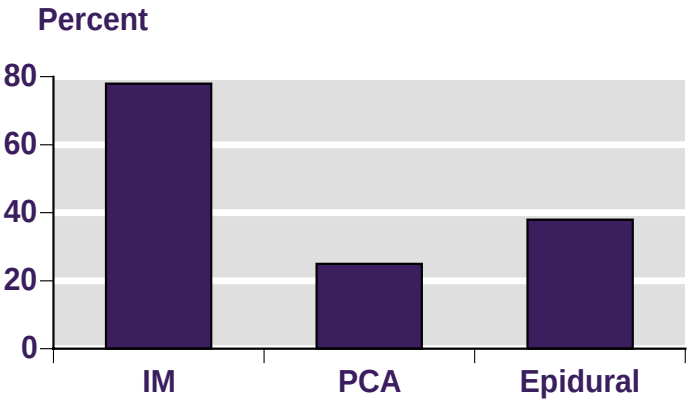
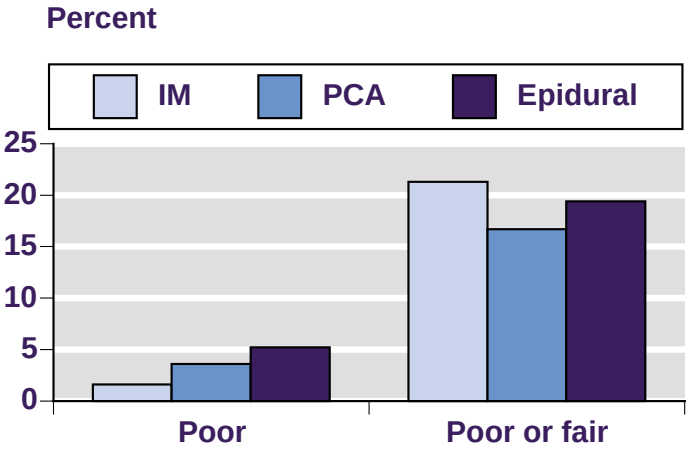


Figure 3: Poor or fair pain relief



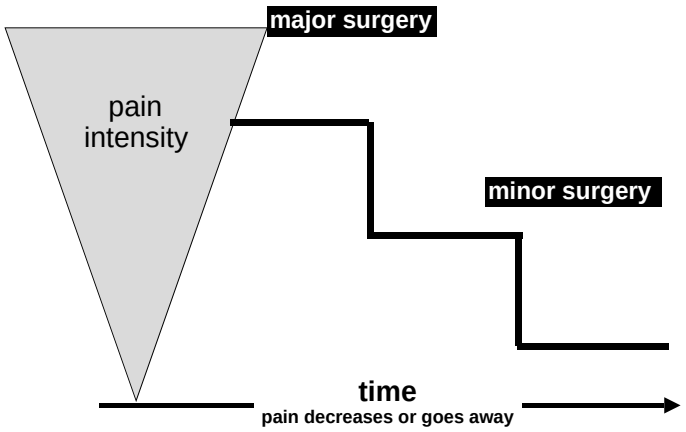
Comment

Though this review [4] gives some small evidence that postoperative pain treatment has got better with time, all sources generally agree that acute pain treatment still results in a significant number of patients having acute pain of moderate to severe intensity. In 1997, the UK Audit Commission proposed a standard whereby fewer than 20% of patients should experience severe pain after surgery after 1997, ideally reducing to fewer than 5% by 2002 [5]. On present evidence, usual practice is not delivering that expectation.

THE PATIENT JOURNEY

For the purposes of this essay we can put aside intraoperative analgesia and consider, for simplicity, the typical pain experience of a patient undergoing surgery. If the surgery is major abdominal, thoracic or orthopaedic surgery, then severe pain can be expected. If the surgery is minor, then less severe pain might be expected. In both cases the pain will go away with time, though that is likely to take longer with major surgery (Figure 4): what we have is an acute pain ladder of decreasing pain intensity. It should also be recognised that patients may not be able to swallow soon after surgery, when administration of analgesics other than by the oral route will be necessary.

Figure 4: Ladder of decreasing pain intensity



There is considerable between-patient variability. In several hundred patients undergoing minor orthopaedic surgery, most requested analgesia because of moderate or severe pain within three hours of surgery (Figure 5). For others the request was delayed by up to 15 hours, and 6% required no postoperative analgesia at all [6].

There are several things that can be done to alleviate pain [7] (Figure 6). Some involve higher technology interventions, such as epidural injections with opioid or local anaesthetic, or patient controlled analgesia. Others might be lower technology, like nerve blocks with local anaesthetic. An even lower technology would be intermittent intramuscular opioids. The lowest technology would be oral analgesics. All these might have their place at some part of our ladder of descending pain after surgery. There may be others we want to look at, like relaxation, or transcutaneous electrical nerve stimulation (TENS), or psychotherapy, or other interventions, all of which might potentially help some patients.

Figure 5: Not all patients need analgesics after surgery

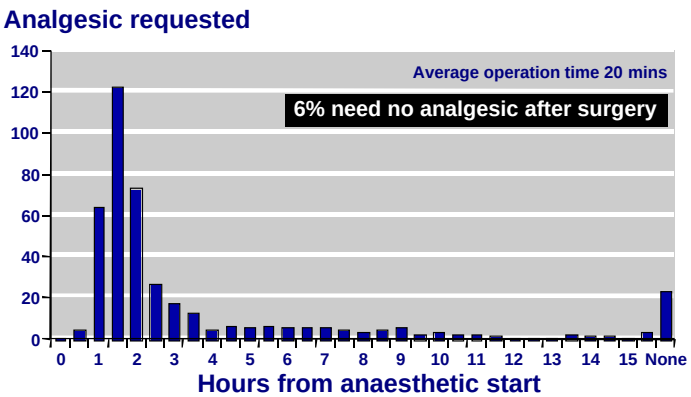


Figure 6: Treatment methods

Treatment	methods
Remove the cause	Surgery
	Splinting
Medication	NSAIDs ± paracetamol ± opioids
	Opioids (morphine)
Regional anaesthesia	Epidural infusion of local anaesthetic ± opioid
	Nerve blocks with local anaesthetic ± opioid
Physical methods	Physiotherapy
	Manipulation
	TENS
	Acupuncture
Psychological	Relaxation
	Hypnosis
	Psychoprophylaxis

What we have to do is to examine the evidence for each of the possible interventions that might have a place in the overall package of care. We may or may not choose to use them in particular patients, but we definitely want to know that interventions we might choose to use will work.

The evidence

It is now generally agreed that the highest quality evidence comes from good systematic reviews and meta-analysis of good randomised, double blind trials. Quality of both aspects minimises bias [8, 9]. Clinical trials in analgesia have traditionally been small, often with a few tens of patients. In this circumstance the random play of chance can have major effects on trial outcome [10]. For analgesic interventions, therefore, where large trials are not available, meta-analysis of high-quality small trials is essential to make sense of the data we have. Single small trials, however well done, can mislead [10].

How much information is enough?

While it is relatively easy to demonstrate that inadequate amounts of information can result in erroneous conclusions, the alternative question, how much information we need to avoid erroneous conclusions, is more difficult to answer. It depends on a number of things. Two important issues are the size of the effect you are looking at (absolute differences between treatment and control), and how sure you want to be.

A worked example using simulations of acute pain trials [10] gives us some idea. Using the 16% found in some standard pain trials as the rate with controls (because it happens to be what is found with placebo), it looked at event rates with treatment of 40%, 50% and 60%, equivalent to numbers needed to treat (NNTs) of 4.2, 2.9 and 2.3. The numbers in treatment and placebo group were each simulated in a computer from 25 patients per group (trial size 50) to 500 patients per group (trial size 1000). For each condition 10,000 trials were simulated and the percentage where the NNT was within ±0.5 of the true NNT counted.

The results are shown in Table 3. With 1000 patients in a trial where the NNT was 2.3, we could be 100% sure that the NNT measured was within ±0.5 of the true NNT; all trials of this size would produce values between 1.8 and 2.8. In a trial of 50 patients where the NNT was 4.2, only one in four trials would produce an NNT within ±0.5; the true value is between 3.7 and 4.7, and three-quarters of trials (or meta-analyses) of this size would produce NNTs below 3.7 or over 4.7.

The study also shows that to be certain of the size of the effect (the NNT, say), we need ten times more information just to know that there is statistical significance. For most analgesic trials, that means we need somewhere between 250 and more than 5000 patients, depending on the size of the effect.

Pain measurements

Pain is a personal experience, making it difficult to define and measure. It includes both the sensory input and any modulation by physiological, psychological and environmental factors. Not surprisingly there are no objective measures - there is no way to measure pain directly by sampling blood or urine or by performing neurophysiological tests. Measurement of pain must therefore rely on recording the patient's report.

Table 3: How much information is enough?

	Percent events with treatment		
	40	50	60
NNT	4.2	2.9	2.3
Group size			
25	26	37	57
50	28	51	73
100	38	61	88
200	55	81	96
300	63	89	99
400	71	93	99
500	74	95	100

With control the event rate was 16%

At least	
50%	within +/- 0.5
80%	within +/- 0.5
95%	within +/- 0.5

The assumption is often made that because the measurement is subjective it must be of little value. The reality is that if the measurements are done properly, remarkably sensitive and consistent results can be obtained. There are contexts, however, when it is not possible to measure pain at all, or when reports are likely to be unreliable. These include impaired consciousness, young children, psychiatric pathology, severe anxiety, unwillingness to co-operate, and inability to understand the measurements. Such problems are deliberately avoided in trials.

Measurement scales

Judgement of the patient rather than by the carer is the ideal. Carers overestimate the pain relief compared with the patient's version. A large number of measurement scales have been used. Only for very few has been any attempt to discuss systematically with patients what constitutes a worthwhile change. Despite this there are some commonly used measurement methods, some available for decades, that have proved to be reliable. Most acute pain analgesic studies include measurements of pain intensity and/or pain relief, and the commonest tools used are categorical and visual analogue scales.

Categorical and visual analogue scales

Categorical scales use words to describe the magnitude of the pain (Figure 7). They were the earliest pain measures [11]. The patient picks the most appropriate word. Most research groups use four words (none, mild, moderate and severe). Others were developed later. The commonest scale to measure pain relief has five categories (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 are then combined to produce means (rarely medians) and measures of dispersion (usually standard errors of means). 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 choice of a particular category when none describes the pain satisfactorily.

Visual analogue scales (VAS), lines with left end labelled "no relief of pain" and right end labelled "complete relief of pain", seem to overcome this limitation (Figure 8). Patients mark the line at the point corresponding to their pain. The scores are obtained by measuring the distance between

Figure 7: Categorical verbal rating scales

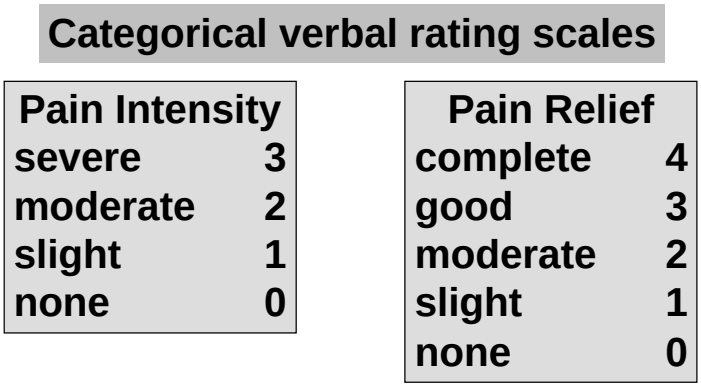
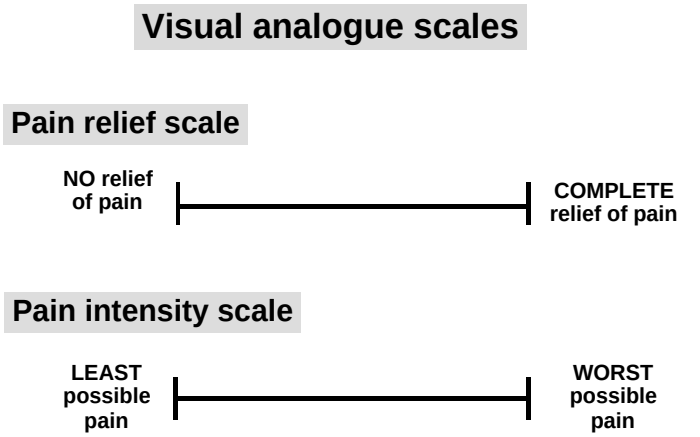


Figure 8: Visual analogue scales



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.

Pain relief scales are perceived as more convenient than pain intensity scales, probably because patients have the same baseline relief (zero) whereas they could start with different baseline intensity (usually moderate or severe). Relief scale results are thus easier to compare. They may also be more sensitive than intensity scales. A theoretical drawback of relief scales is that the patient has to remember what the pain was like to begin with.

Other tools

Global subjective efficacy ratings, or simply global scales, are designed to measure overall treatment performance. Patients are asked questions like "How effective do you think the treatment was?" and answer using a labelled numerical or a categorical scale. Although these judgements probably include adverse effects they can be the most sensitive discriminant between treatments [12]. One of the oldest scales was the binary question "Is your pain half gone?". Its advantage is that it has a clearer clinical meaning than a 10 mm shift on a VAS. The disadvantage, for the small trial intensive measure pundits at least, is that all the potential intermediate information (1 to 49% or how much greater than 50%) is discarded.

Analgesic requirements (including patient-controlled analgesia, PCA), special paediatric scales, and questionnaires like the McGill are also used. The limitation to guard against is that they usually reflect other experiences as well as or instead of pain [5].

Conventionally the time over which pain intensity and relief have been measured, and summary scores calculated, was four to six hours, because that was how long analgesics lasted. Occasional trials give information about time to remedication, a useful piece of information about the duration of analgesic effect.

Analysis of scale results - summary measures

In the research context pain is usually assessed before the intervention is made and then on multiple occasions afterwards. Ideally the area under the time-analgesic effect curve for the pain intensity (sum of pain intensity differences; SPID) or pain relief (total pain relief; TOTPAR) measures is derived (Figure 9). TOTPAR is measured by calculating the area under the curve for pain relief against time. If a patient had complete pain relief immediately, and sustained it for the full six hours of measurement, then the maximum TOTPAR would be attained (in this case a score of 4 points times 6 hours, giving a TOTPAR of 24, the maximum achievable). Another patient who had a score of 12 would have 50% of the maximum, or 50%maxTOTPAR (Figure 9).

Figure 9: Calculating TOTPAR and %maxTOTPAR

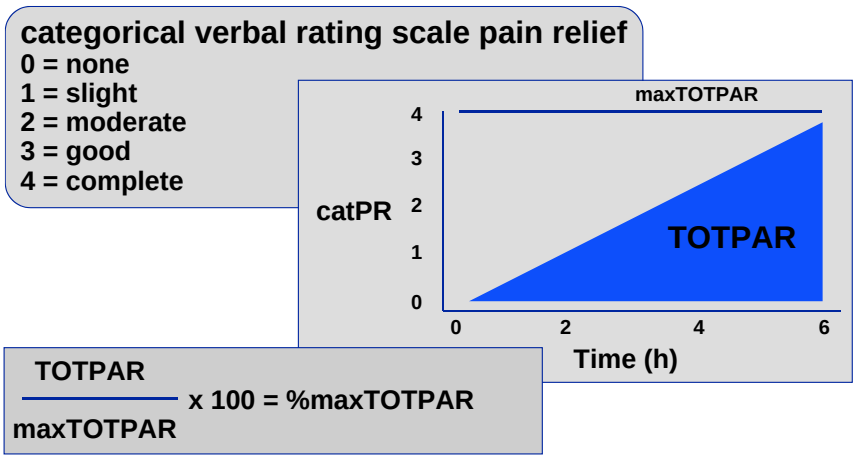
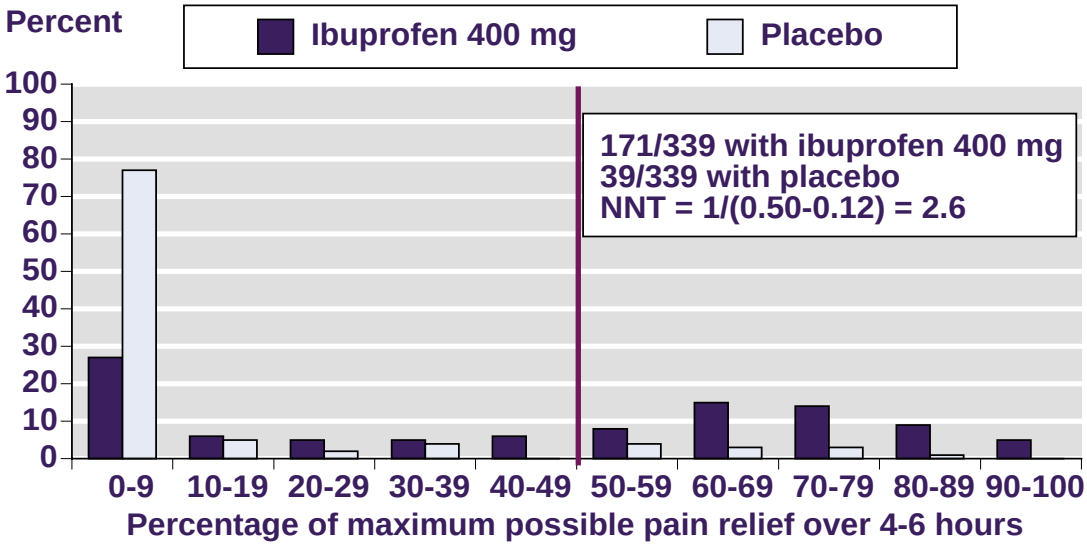


Figure 10: Individual patient results for ibuprofen and placebo



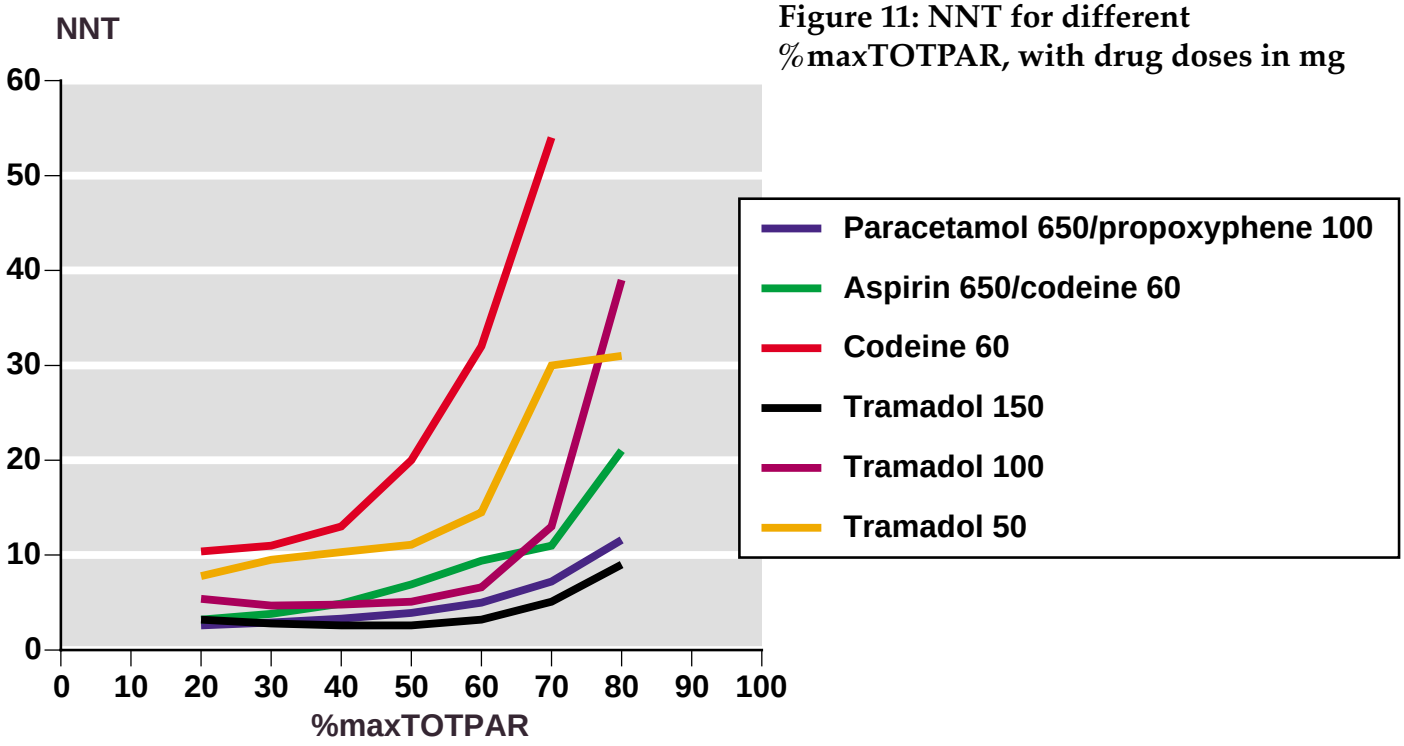
These summary measures reflect the cumulative response to the intervention. Their disadvantage is that they do not provide information about the onset and peak of the analgesic effect. If onset or peak are important then time to maximum pain relief (or reduction in pain intensity) or time for pain to return to baseline are necessary.

Acute pain trials

Measuring the efficacy of analgesics in acute pain is done in clinical trials that have been standardised over many years. Typically, patients in the first few days after an operation will develop pain that is moderate or severe in intensity and will then be given an analgesic or placebo. Pain will then be measured using standard pain intensity or pain relief scales over four to six hours. After a delay, usually of 60 to 90 minutes, those who do not have adequate pain relief will be given additional analgesia (often called "escape" analgesia). For these patients it is usual to make no additional pain measurements, but for all subsequent pain intensity measures to revert to the initial pain intensity, and for all subsequent pain relief measures to revert to zero. This process ensures that analgesia from escape analgesic is not wrongly ascribed to the test intervention.

A variety of pain outcomes can be chosen as the outcomes of the trial and commonly several are reported, like summed pain intensity difference (SPID) or total pain relief (TOTPAR), or their visual analogue equivalents. For the purposes of meta-analysis the most commonly used outcome has become the percentage of patients in a treatment arm who achieve at least 50% of the maximum available pain relief (%maxTOTPAR). Methods have been developed and validated with independent data sets that reliably allow conversion of a variety of outcomes measures to %maxTOTPAR [13-15].

Figure 11: NNT for different %maxTOTPAR, with drug doses in mg



The distribution of results from individual patients in 339 given placebo and 339 given ibuprofen 400 mg can be seen in Figure 10. The distribution is skewed. Choice of half pain relief (or, in this case, the number of patients who achieve at least 50% maxTOTPAR) gives the number of patients achieving the outcome with placebo and with ibuprofen 400 mg. This allows the calculation of an NNT for this outcome.

It is important to mention the danger inherent in using mean values for a skewed distribution like this. Obviously a mean (average) imperfectly represents what is actually happening, and using means results is nonsense. An example was an apparent confirmation of the observation that the placebo response was a fixed fraction of the active, a result that disappeared when medians were used instead [16].

Half pain relief over four to six hours is a high hurdle, and has been shown to distinguish between more and less effective analgesics (Figure 11) [17]. Although the outcome of half pain relief was chosen merely because it is half way between 0% and 100%, similar discrimination can be seen over a wide range of cut points from about 20% to 60% of maximum pain relief (Figure 10). Lower and higher values lose discrimination because all or none of the treatments can meet the outcome.

Pain models

A number of different clinical situations have been used to measure the efficacy of analgesics in acute pain, including third molar dental extraction, orthopaedic or general surgery. We are reasonably sure [18] that analgesics do not behave differently in different acute pain models, though clearly some clinical situations (older patients, renal or hepatic dysfunction) can affect pharmacokinetics and metabolism. Patients with severe kidney or liver disease are understandably never included in clinical trials of analgesics.

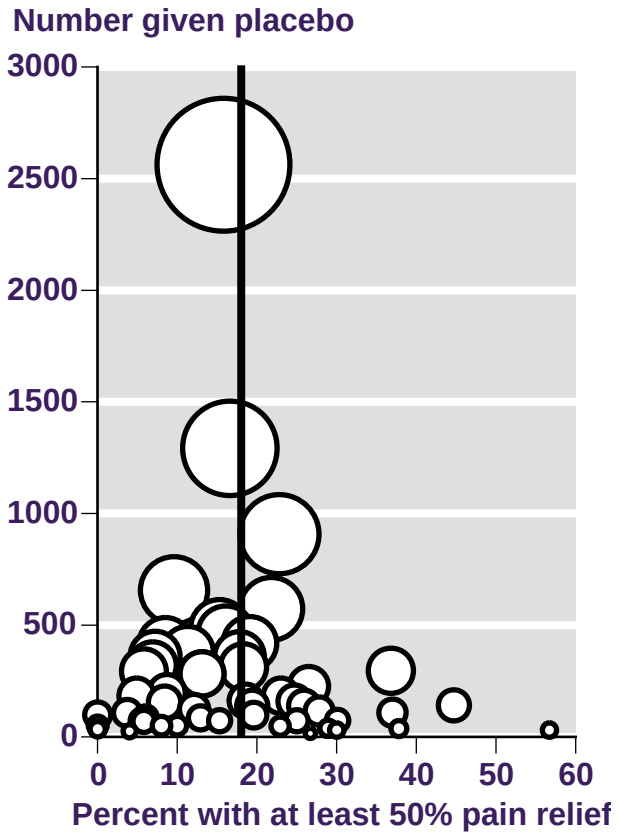
Placebo

There are occasionally ethical objections to use of placebo in acute pain trials (though registration authorities currently mandate it). Some patients given placebo obtain significant pain relief (Figure 10), not because placebo "produces" pain relief, but rather because these are patients whose pain, though initially moderate or severe, was not long lasting. Some people given analgesics conversely get no pain relief.

In reality, if pain is unrelieved after a short interval, additional analgesia is available to all patients in the trial, whether they have been given placebo or active treatment. This reflects what tends to happen in the real world, where additional analgesia can be given; treatment may even be better in clinical trials because there is always a nurse and/or doctor on hand to administer escape analgesia when needed. Moreover, there are good reasons why some acute pain studies would be unethical without a placebo, because they would not be able to produce a sensible result [19].

A major source of variability in the proportion of people with acute pain achieving adequate pain relief in clinical

Figure 12: Placebo responses in 56 meta-analyses in acute pain



trials is the size of the trial. In an analysis of 56 meta-analyses with over 12,000 patients given placebo in acute pain trials, 18% had more than 50% maxTOTPAR (Figure 12). Analyses with over 500 patients given placebo were in reasonable agreement. Smaller meta-analyses could be widely different, from 0% to almost 60%.

Comment

Because pain is so obviously subjective, randomised and double blind trials to avoid both selection and observer bias have been usual for about 50 years, though not universally. This has provided a wealth of information for systematic reviews and meta-analysis, and the source of material to develop and test methods. Yet there is no reason for complacency, because many individual trials today have deficiencies in design, in validity, in size, and especially in the utility of outcomes chosen.

EARLY INTERVENTIONS FOR ACUTE PAIN

Early intervention after surgery usually (though not exclusively) demands the use of opioids because they allow titration of dose to effect. Titration can be achieved by the patient using devices like patient controlled analgesia (PCA). Titration can also be achieved by using lower technology early interventions like intermittent intramuscular opioids or NSAIDs. Or the anaesthetist may choose different routes of administration, like epidural opioids or local anaesthetic.

The real-world effectiveness of some of these techniques has been examined in a systematic review [4], and it shows that the incidence of moderate to severe pain at rest or on movement, or severe pain, or poor or fair pain relief is high with all these techniques (Table 4). Much of the information comes from audit data, and not from randomised trials. But it was derived from nearly 20,000 patients. Nor do pain or pain relief measures give the complete picture. For epidural techniques, for instance, premature catheter dislodgement represents a form of failure. The overall mean incidence of premature catheter dislodgement was 5.7% (95% confidence interval 4.0 to 7.4%) in 13,629 patients.

Patient controlled analgesia

A problem with many randomised studies of higher technology analgesia methods is that they often have poor reporting quality, so that the charge of bias cannot be excluded. For instance, a systematic review found 32 trials comparing PCA with conventional intermittent subcutaneous, intravenous or intramuscular opioids [20]. But of these, 27 had quality scores (2/5 on a validated scale) that have been associated with overestimation of treatment effect.

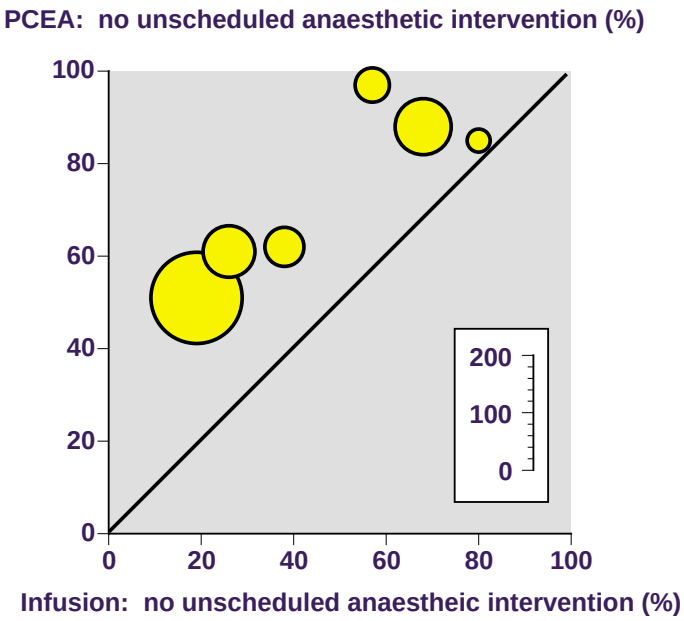
How then do we treat the information that, for dichotomous efficacy information, patients using patient-controlled devices had more satisfaction (82%) than those having conventional analgesia (68%), with a number needed to treat for one more patient to be satisfied of 8 (5 to 15)? Does this show a real improvement with a higher technology intervention, or a bias imparted by enthusiasts? The reality is that we do not know, but the systematic review of audit data [4] suggests that there was little difference.

Higher quality studies can be done. A systematic review of patient controlled epidural analgesia for labour found that five of nine studies had quality scores of 3/5 or more [21]. Pain scores were not reported, but in five studies, the number of women who needed a clinician top up of the

Table 4: Systematic review of pain outcomes with three early interventions for acute pain

Pain outcome	Technology	95% confidence interval of percentage
Moderate - severe pain at rest	Intermittent intramuscular	58-76
	PCA	31-40
	Epidural	18-24
Moderate-severe pain on movement	Intermittent intramuscular	too little data
	PCA	8.4-42
	Epidural	30-45
Severe pain	Intermittent intramuscular	19-39
	PCA	12-21
	Epidural	15-23
Poor pain relief	Intermittent intramuscular	too little data
	PCA	1.8-5.4
	Epidural	3.7-6.8
Poor or fair pain relief	Intermittent intramuscular	14-29
	PCA	12-21
	Epidural	15-24

Figure 13: Patient controlled epidural analgesia for labour



epidural for analgesia was reported (Figure 13). In women with continuous epidural infusion, 41% did not need a top up. In women with patient controlled epidural analgesia only 69% did not need a top up. The relative risk was 1.7 (1.4 to 2.0) and the number of women needed to be treated with patient controlled epidural analgesia rather than continuous epidural infusion to prevent one needing an unscheduled top up was 3.6 (2.8 to 5.2).

There was some evidence of decreased motor weakness in four trials with 300 patients. Here no motor weakness was seen in 90% of women receiving patient controlled epidural analgesia compared with 80% in those receiving continuous epidural infusion. The NNT for one women to be free of motor weakness was 9 (5.3 to 43).

Table 5: NNTs for IM opioid and NSAID

Drugs and dose (mg)	Number of Trials	Number of Patients	NNT (95% CI)
Morphine 10	15	946	2.9 (2.6 to 3.6)
Pethidine 100	8	364	2.9 (2.3 to 3.9)
Ketorolac 10	2	142	5.7 (3.0 to 5.3)
Ketorolac 30	5	359	3.4 (2.5 to 4.9)

NNTs for injected analgesics

For both injected opioids and NSAIDs, NNTs have been calculated for various drugs and doses compared with placebo (Table 5). The trials were all randomised and double blind, and compared single doses of injected opioid or NSAID with injected placebo [22, 23]. NNTs for commonly-used doses of morphine, pethidine and ketorolac were about 3. Adverse events for opioids included significantly more drowsiness or somnolence and dizziness or lightheadedness than placebo.

Adverse effects of higher technology interventions

There is good evidence from a large study of hospital adverse drug events (ADE) in two top Boston hospitals that

Table 6: Adverse events at Boston hospitals associated with analgesic techniques

Event	Number	Rate per 100 admissions	Number per hospital per year
All ADEs	247	6.5	1923
Due to analgesics	73	1.9	568
Due to opiates	57	1.5	444
Preventable ADEs due to pump or device malfunction	9	0.2	70

Table 7: Adverse event risk in a review of 44 audits and over 30,000 patients

Event description	Number of cases	Total number	Risk
Cauda equina with epidural	1	5602	1 in 5601
Meningitis with epidural	2	2287	1 in 1144
Intravascular migration	3	1062	1 in 354
Intradural migration	5	4958	1 in 992
Potential severe complications of infusion device	16	3016	1 in 189
Accidental epidural opioid overdosing	2	2827	1 in 1414
Accidental PCA overdosing	3	2922	1 in 974

high-technology analgesia contributes to harmful or potentially harmful events [24]. In a six-month study period, there were 4,031 admissions to study units, comprising 21,412 patient-days (about 10% of the 214,000 patient days in adult, nonobstetric units at the two hospitals). There were 247 ADEs and 194 potential ADEs, many of which were associated with analgesia (Table 6). Extrapolated, this amounted to 1900 ADEs per hospital per year, with 6.5 ADEs and 5.5 potential ADEs for every 100 admissions. Of all ADEs, 1% were fatal, 12% life-threatening, 30% serious and 57% significant.

A recent review of acute pain services confirms that potential serious harm can arise from using higher technology analgesic methods [25]. The review of 44 audits with about 84,000 patients was careful to document the occurrence of harm. The risks of particular harms for epidurals and infusion devices are given in Table 7. Some of these risks are small, but taken together there is clearly a need both for caution and for vigilance when using these higher technology methods. Other studies suggest that the risk of persistent neurological sequelae after an epidural is about 1 in 5,000 [26].

Comment

The information we have seems to concentrate on inadequacy of trials, on patients in whom there has been a lack of effect, and of the risks involved, especially with higher technology early interventions for acute pain. Perhaps this is unfair, and we should regard this particular cup as half full rather than half empty.

Many patients will have a good or adequate pain experience after surgery, and the trick is making it better for those who do not. Often this is not just an issue of the efficacy of particular technologies, but the effectiveness with which those technologies are deployed. That is as much, or more, issues of resource and management as it is of evidence. These three should be improved together.

Later interventions for acute pain: oral and intramuscular analgesics

For oral and intramuscular analgesics we now have a number of meta-analyses that compare analgesic with placebo. The systematic reviews were of randomised, double-blind, single-dose studies in patients with initial moderate to severe pain. Each review chose to use the same standardised and validated pain measurements. Each review chose to report the same outcome, of patients with at least 50% maxTOTPAR over four to six hours. So each review uses unbiased data, similar patients, with the same outcome measured in the same way over the same period of time, and with analgesic always compared with placebo.

When we have information like this we are justified in making comparisons between one analgesic and another. It is often said that to make comparisons we need direct head-to-head trials. If so, we would wait for ever, because there are no such trials of sufficient size to have any value. The analogy here is with a 100-metre race. We can have an Olympic champion, the first of several people running together in the same race. Or we can have a world record holder, who has won the fastest race ever against the clock. For world record holders, we have to know that the conditions are the same for everyone, everywhere.

Analgesic league table

The Oxford league table of analgesics (Table 8, for commonly used doses) works because it has done just that, assured that conditions are the same. Only like is compared with like, and there is a common comparator throughout, namely placebo. Readers who want to see individual meta-analyses and their references, and for drugs and doses not commonly used, should visit ***Bandolier's*** Oxford Pain Internet site (http://www.jr2.ox.ac.uk/bandolier/booth/painpag/index.html), where information on updated reviews is kept.

Information can be presented in a number of formats. The definitive source is Table 8 (updated mid 2002), which has the number of patients in the comparison, the percent with at least 50% pain relief with analgesic, the number-needed-to-treat (NNT) and the high and low 95% confidence interval. Also presented is a simplified table (Table 9) with information on common doses of common analgesics. Two figures (Figures 13 and 14) present information on common analgesic doses giving NNTs, and in terms of percentages of patients achieving at least 50% pain relief.

Understanding the NNT league table

Analgesic efficacy is expressed as the NNT, the number of patients who need to receive the active drug for one to achieve at least 50% relief of pain compared with placebo over a 4-6 hour treatment period. The most effective drugs have a low NNT of just over 2. This means that for every two patients who receive the drug one patient will get at least 50% relief because of the treatment (the other patient

Table 8: Full version of Oxford acute pain table

The Oxford league table of analgesic efficacy

Numbers needed to treat are calculated for the proportion of patients with at least 50% pain relief over 4-6 hours compared with placebo in randomised, double-blind, single-dose studies in patients with moderate to severe pain. Drugs were oral, unless specified, and doses are milligrams. Shaded rows are intramuscular administration

Analgesic	Number of patients in comparison	Percent with at least 50% pain relief	NNT	Lower confidence interval	Higher confidence interval
Ibuprofen 800	76	100	**1.6**	1.3	2.2
Ketorolac 20	69	57	**1.8**	1.4	2.5
Ketorolac 60 (intramuscular)	116	56	**1.8**	1.5	2.3
Diclofenac 100	411	67	**1.9**	1.6	2.2
Piroxicam 40	30	80	**1.9**	1.2	4.3
Paracetamol 1000 + Codeine 60	197	57	**2.2**	1.7	2.9
Oxycodone IR 5 + Paracetamol 500	150	60	**2.2**	1.7	3.2
Bromfenac 25	370	51	**2.2**	1.9	2.6
Rofecoxib 50	675	54	**2.3**	2.0	2.6
Diclofenac 50	738	63	**2.3**	2.0	2.7
Naproxen 440	257	50	**2.3**	2.0	2.9
Oxycodone IR 15	60	73	**2.3**	1.5	4.9
Ibuprofen 600	203	79	**2.4**	2.0	4.2
Ibuprofen 400	4703	56	**2.4**	2.3	2.6
Aspirin 1200	279	61	**2.4**	1.9	3.2
Bromfenac 50	247	53	**2.4**	2.0	3.3
Bromfenac 100	95	62	**2.6**	1.8	4.9
Oxycodone IR 10 + Paracetamol 650	315	66	**2.6**	2.0	3.5
Ketorolac 10	790	50	**2.6**	2.3	3.1
Ibuprofen 200	1414	45	**2.7**	2.5	3.1
Oxycodone IR 10+Paracetamol 1000	83	67	**2.7**	1.7	5.6
Piroxicam 20	280	63	**2.7**	2.1	3.8
Diclofenac 25	204	54	**2.8**	2.1	4.3
Dextropropoxyphene 130	50	40	**2.8**	1.8	6.5
Bromfenac 10	223	39	**2.9**	2.3	4.0
Pethidine 100 (intramuscular)	364	54	**2.9**	2.3	3.9
Tramadol 150	561	48	**2.9**	2.4	3.6
Morphine 10 (intramuscular)	946	50	**2.9**	2.6	3.6
Naproxen 550	169	46	**3.0**	2.2	4.8
Naproxen 220/250	183	58	**3.1**	2.2	5.2
Ketorolac 30 (intramuscular)	359	53	**3.4**	2.5	4.9
Paracetamol 500	561	61	**3.5**	2.2	13.3
Paracetamol 1500	138	65	**3.7**	2.3	9.5
Paracetamol 1000	2759	46	**3.8**	3.4	4.4
Oxycodone IR 5 + Paracetamol 1000	78	55	**3.8**	2.1	20.0
Paracetamol 600/650 + Codeine 60	1123	42	**4.2**	3.4	5.3
Ibuprofen 100	396	31	**4.3**	3.2	6.3
Paracetamol 650 + Dextropropoxyphene (65 mg hydrochloride or 100 mg napsylate)	963	38	**4.4**	3.5	5.6
Aspirin 600/650	5061	38	**4.4**	4.0	4.9
Paracetamol 600/650	1886	38	**4.6**	3.9	5.5
Ibuprofen 50	316	31	**4.7**	3.3	7.9
Tramadol 100	882	30	**4.8**	3.8	6.1

Table 9: Oxford acute pain league table for common analgesics and doses

The Oxford league table of analgesic efficacy

Numbers needed to treat are calculated for the proportion of patients with at least 50% pain relief over 4-6 hours compared with placebo in randomised, double-blind, single-dose studies in patients with moderate to severe pain. Drugs were oral, unless specified, and doses are milligrams. Shaded rows are intramuscular administration

Analgesic and dose (mg)	Number of patients in comparison	Percent with at least 50% pain relief	NNT	Lower confidence interval	Higher confidence interval
Paracetamol 1000 + Codeine 60	197	57	**2.2**	1.7	2.9
Rofecoxib 50	675	54	**2.3**	2.0	2.6
Diclofenac 50	738	63	**2.3**	2.0	2.7
Naproxen 440	257	50	**2.3**	2.0	2.9
Ibuprofen 400	4703	56	**2.4**	2.3	2.6
Pethidine 100 (intramuscular)	364	54	**2.9**	2.3	3.9
Morphine 10 (intramuscular)	946	50	**2.9**	2.6	3.6
Naproxen 550	169	46	**3.0**	2.2	4.8
Naproxen 220/250	183	58	**3.1**	2.2	5.2
Ketorolac 30 (intramuscular)	359	53	**3.4**	2.5	4.9
Paracetamol 500	561	61	**3.5**	2.2	13.3
Paracetamol 1000	2759	46	**3.8**	3.4	4.4
Paracetamol 600/650 + Codeine 60	1123	42	**4.2**	3.4	5.3
Paracetamol 650 + Dextropropoxyphene (65 mg hydrochloride or 100 mg napsylate)	963	38	**4.4**	3.5	5.6
Aspirin 600/650	5061	38	**4.4**	4.0	4.9
Paracetamol 600/650	1886	38	**4.6**	3.9	5.5
Tramadol 100	882	30	**4.8**	3.8	6.1
Tramadol 75	563	32	**5.3**	3.9	8.2
Aspirin 650 + Codeine 60	598	25	**5.3**	4.1	7.4
Paracetamol 300 + Codeine 30	379	26	**5.7**	4.0	9.8
Tramadol 50	770	19	**8.3**	6.0	13.0
Codeine 60	1305	15	**16.7**	11.0	48.0
Placebo	>10,000	18	**N/A**	N/A	N/A

may or may not obtain relief but it does not reach the 50% level).

The NNT is treatment specific, and is drug, dose, and context specific. In these special circumstances NNT is useful for comparison of relative efficacy. Because the NNT comparisons here are against placebo, the best NNT of 2 means that 50 of 100 patients will get at least 50% relief specifically because of the treatment who would not have done with placebo. Another ten to twenty will have had adequate pain relief with placebo giving them at least 50% relief. With ibuprofen 400 mg, therefore, about 60 of 100 in total will have effective pain relief. For comparison, with 10 mg intramuscular morphine about 50% of patients get more than 50% pain relief. Because the effect of placebo is added in when looking at percentages with the outcome of at least 50% pain relief, the comparisons between analgesics are not as stark as with NNT.

Effective relief can be achieved with oral non-opioids, non-steroidal anti-inflammatory drugs, coxibs and combinations of paracetamol and codeine. For paracetamol 1 g the NNT is nearly 4. Combination of paracetamol 1000 mg with codeine 60 mg improves the NNT to 2. Ibuprofen 400 mg is better at 2.4 and diclofenac 50 mg and rofecoxib 50 mg at about 2.3. NSAIDs generally do well with lower (better) NNTs.

Figure 14: NNTs for some common analgesics in acute pain

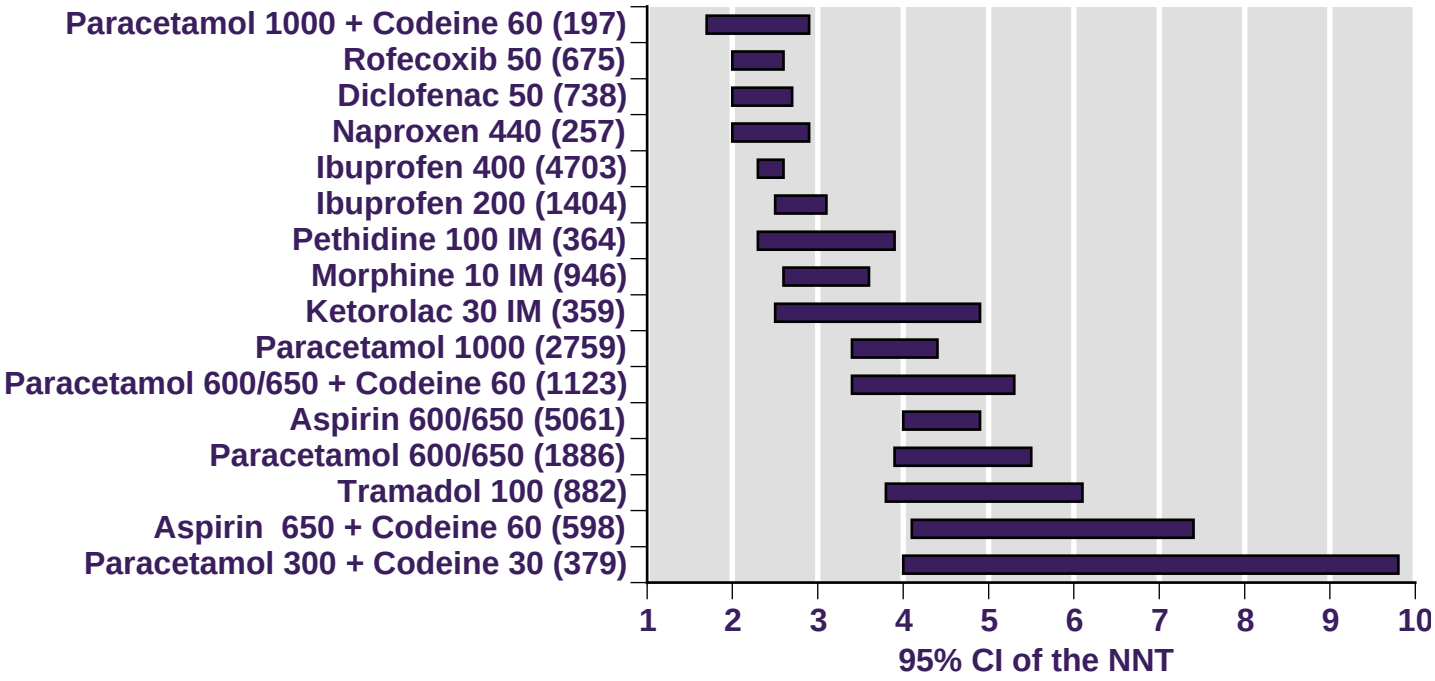
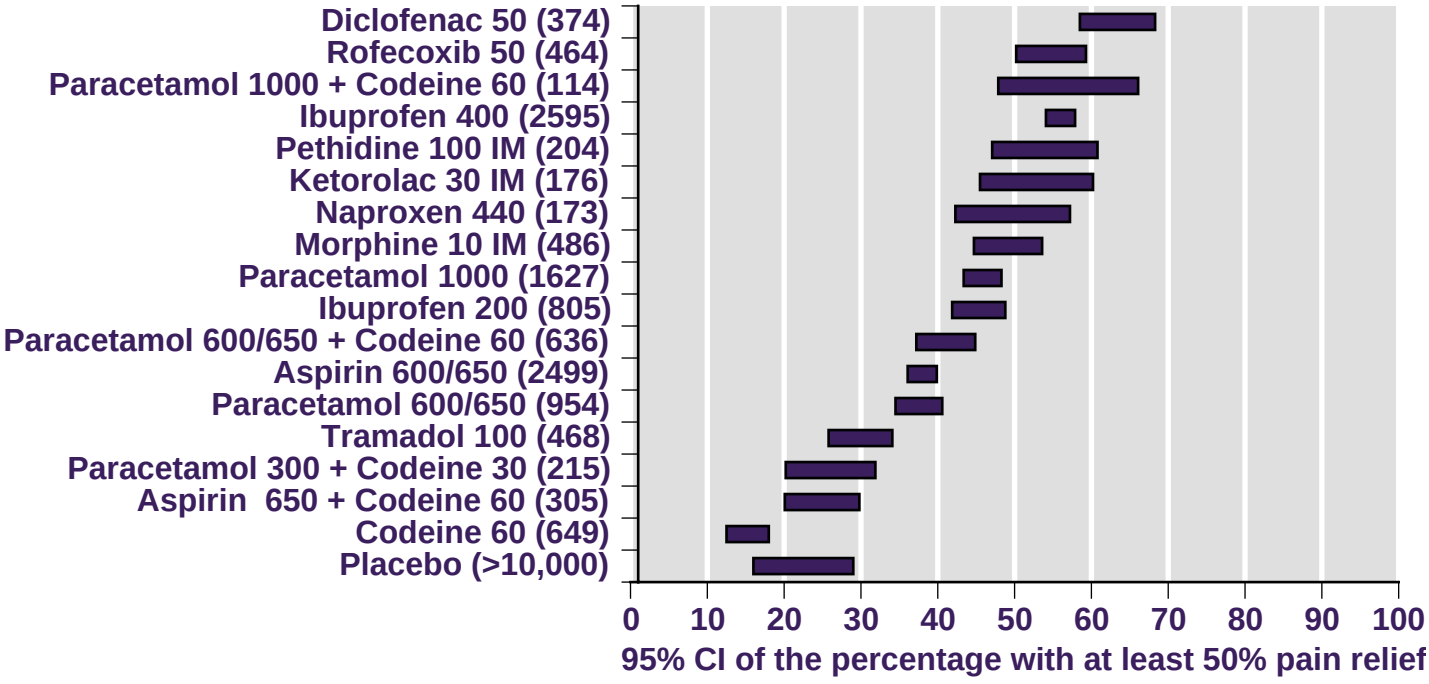


Figure 15: Patients with at least 50% pain relief for some common analgesics in acute pain



Many doses of NSAIDs have NNT values of between 2 and 3, and the point estimate of the mean is below that of (i.e. better than) 10 mg of intramuscular morphine, even though the confidence intervals overlap. The simple analgesics, aspirin and paracetamol, are significantly less effective than 10 mg intramuscular morphine. The point estimates of the NNT are higher, and there is no overlap of the confidence intervals. Weak opioids perform poorly in single doses on their own. Combining them with simple analgesics improves analgesic efficacy.

Validity of the league table

There is internal validity of the indirect comparisons from dose-response relationships. In all cases where there is sufficient information, higher doses provide better analgesia and lower NNTs, as with diclofenac, ibuprofen, paracetamol and tramadol. External validity comes from a systematic review that compared paracetamol and NSAIDs in head-to-head trials, and found that NSAIDs were demonstrably better than 1000 mg paracetamol, at least in dental pain models [27].

Validation of the low NNT for paracetamol 1000 mg plus codeine 60 mg comes from a variety of other sources [28]. While the NNT was established only from 197 patients in three trials, other data could be found that gave credence to the figure. Computer simulation of randomised trials demonstrated 92% confidence that the simulated NNT was within ±0.5 of the underlying value of 2.2 with this number of patients.

The result was supported by a rational dose-response relationship for different doses of paracetamol and codeine in 17 additional trials with 1,195 patients. Three controlled trials lacking a placebo and with 117 patients treated with paracetamol 1000 mg and codeine 60 mg had 73% (95%CI 56% to 81%) of patients with at least 50% pain relief, compared with 57% (48% to 66%) in placebo controlled trials. In each of six trials in acute pain that were omitted because of design issues, like the use of different pain measures or multiple dosing regimens, paracetamol 1000 mg and codeine 60 mg was shown to be better than placebo or comparators for at least one measure.

The analgesic league table of indirect comparisons concentrates on placebo-controlled studies, which is fine when there is sufficient evidence. When numbers are small, additional evidence from other studies should be sought.

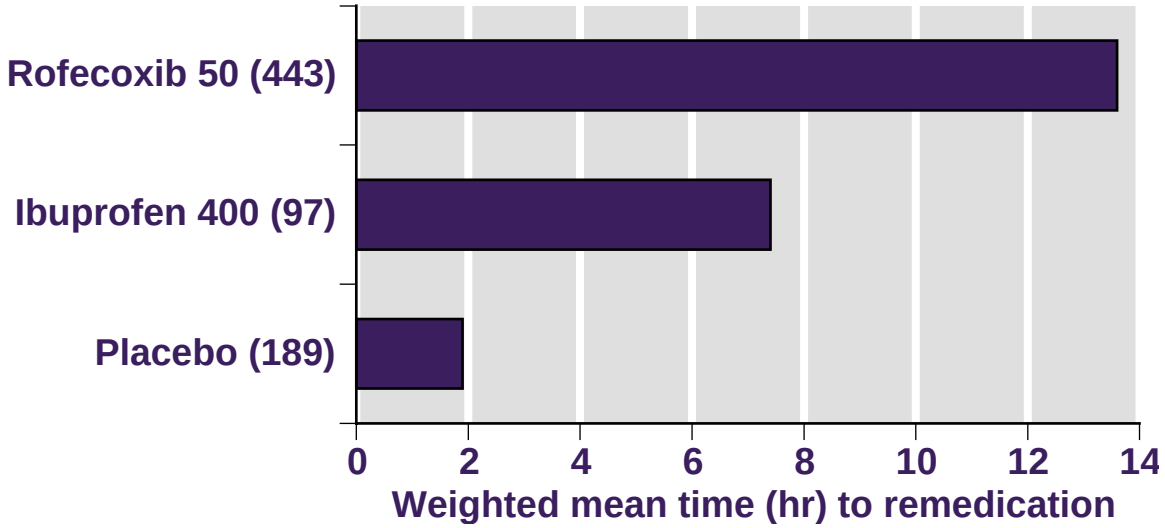
Drawbacks of the league table

Some analgesics may not appear in the league table at all because they had no statistical benefit over placebo. For many of the doses or drugs, a real problem is small numbers, resulting in wide confidence intervals, and low confidence in the result, especially when the NNTs are above 4.

But the issue of size is a relative drawback. Small trials (or small data sets) cannot accurately estimate the magnitude of the analgesic effect. To know that the NNT of an analgesic is 3.0 with a confidence interval of 2.5 to 3.5 we need at least 1000 patients in a comparative trial. But if the NNT is 2.3, we need only 400 patients. And if the NNT is 4 or more, we probably need in excess of several thousand patients (Table 3). In Table 8 we have adequate information for most of the popular doses of analgesics.

So as you contemplate the numbers, be conscious of the amount of information upon which NNTs and percent of patients with at least 50% pain relief are based. In practice any comparison with more than 250 or so patients is prob-

Figure 16: Remedication time for rofecoxib 50 mg, ibuprofen 400 mg and placebo



ably adequate. The information is presented here, warts and all, so that professionals and public can make their own assessments.

What is missing?

Some analgesics used commonly outside the UK may not be represented. Work is ongoing to plug these gaps, but so often the randomised trials (placebo-controlled, randomised, double-blind and with proper outcome measures and entry criteria), have not been done. New analgesics are becoming available (like the selective COX-2 inhibitors) and not all completed trials are published in their full form yet, making judgement of their efficacy difficult. But a number of reviews of coxibs in acute pain have been registered with the Cochrane Collaboration, and will eventually provide updated information.

Adverse effect information from single-dose analgesic trials is rarely helpful with simple analgesics and NSAIDs, though it may be much more helpful with opioids. A problem is that methods of reporting adverse events in single-dose clinical trials change the events reported and their frequency [29]. Lessons about adverse effects of analgesics, especially less frequent and more harmful, better come from epidemiological studies of continuous use.

A limitation of information about single-dose analgesic trials is that of outcome. Most report SPID or TOTPAR, but these are not intuitively helpful. NNTs and percentages of patients with at least 50% maxTOTPAR are improvements, but again can be limiting in applicability for some professionals. What seems to be needed is an outcome more relevant on wards and to nurses. That could be something as simple as the time after a dose when the patient needs another dose because the pain has come back – the time to remedication. The problem is that this is an outcome rarely reported.

An example of how this could be relevant comes from a systematic review of published trials of rofecoxib 50 mg [30]. Here median time to remedication could be calculated for rofecoxib 50 mg and ibuprofen 400 mg (Figure 16). These have similar NNTs for the number of patients with at least 50% maxTOTPAR over 4-6 hours compared with placebo (2.3 and 2.4 respectively). But rofecoxib 50 mg had a much longer duration of action, underscoring the once-daily licence, with a mean weighted remedication time of 13.6 hours compared with 7.4 hours for ibuprofen 400 mg.

Comment

For oral analgesics we have a wealth of knowledge from systematic reviews and meta-analyses. Even so there are limitations in utility, mainly because of the outcomes. Despite this we have a solid body of evidence with which to work.

League tables do not (or at least should not) tell us what to do, but they should make deciding what to do easier, and help us make choices for individual patients and for care pathways.

Other interventions that do or do not work

There are many possible interventions that can be used in the relief of pain. Not all may have been the subject of clinical trials, let alone systematic reviews, but that need not relegate them to the dustbin. Knowing that there is evidence for efficacy or lack of it, or harm or lack of it, will be useful in making choices. Though not exhaustive, a brief survey of technologies known either to work or not work is helpful.

Interventions that work

Epidural analgesia is associated with pain relief during labour, and this is likely to be more effective than alternative treatments [31]. However, it is likely that epidural blocks lengthen labour and result in increased rates of operative vaginal delivery. Epidural block maintained beyond the end of the first stage is associated with an NNT for assisted vaginal delivery is 9.6 (6.7 to 17) compared with control treatments. More information is needed to establish the effects of epidural blocks on longer-term effects in women and babies.

Intrathecal morphine 0.1 to 0.2 mg significantly decreased postoperative pain and decreased the need for postoperative analgesia compared with spinal anaesthesia alone for women undergoing caesarean section [32]. These benefits are of clinical relevance, though women experienced more adverse effects, including pruritus, nausea and vomiting.

Less information was available for other opioids, making direct comparisons difficult. It is likely that fentanyl and sufentanil are less effective than morphine, but are also associated with less harm, although it is unclear whether this is of clinical relevance. Concerning the efficacy of intrathecal opioid use for intraoperative analgesia, evidence suggests that this is of benefit. However, based on the observation that only 24% required additional analgesia intraoperatively, routine use of intrathecal opioids to reduce intraoperative analgesia may be inappropriate in some cases.

Based on the evidence within the review, reviewers recommend the drug of choice as 0.1 mg intrathecal morphine. For every 100 women with 0.1 mg intrathecal morphine added to spinal anaesthetic, 43 will experience pruritus, 10 will experience nausea and 12 will experience vomiting postoperatively, all of whom would not have experienced these adverse events without intrathecal morphine.

Incisional local anaesthetic is effective in relieving postoperative pain after inguinal herniotomy up to about seven hours [33]. For hysterectomy, cholecystectomy and other major/minor surgical procedures, there was a lack of evidence for effectiveness. This may be due in part to inadequate trial design, and further trials are needed before recommendations can be made.

Interventions that do not work

Systematic reviews have shown that a number of techniques have no effect, or little effect, or have no solid evidence to back their use. A brief summary of some of these follows:

- TENS is not effective in the relief of postoperative pain. Patients should be offered effective methods of pain relief [34].
- TENS does not alleviate labour pain nor reduce the use of additional analgesics. Women should be offered effective interventions for relief of labour pain [35].
- There is no convincing evidence for the effectiveness of acupuncture in relieving clinical dental pain [36], despite a review suggesting that it does work [37].
- Convincing evidence for the efficacy of relaxation is lacking. More trials of better quality are needed [38].
- Cannabinoids are not effective in acute pain, based on limited evidence [39].
- NSAIDs given by injection or by rectal administration are no more effective than NSAIDs given by mouth [40].

Other topics of interest

Topics of interest frequently arise, gain a currency, and then die away or not as the evidence grows. Out of interest it is worth taking a quick look at three: intra-articular opioids, pre-emptive analgesia, and gender differences.

Intra-articular opioids

There have now been several systematic reviews, but the latest [41] is of most interest. Six different doses (1-10 mg) of intra-articular morphine were compared with placebo. In the immediate postoperative period (0-2 hours) 7/15 sensitive trials were positive, in the early postoperative period (2-6 hours) 8/12 sensitive trials were positive and in the late postoperative period (6-30 hours) 10/13 sensitive trials were positive.

Most positive studies had used higher doses (3-5 mg) compared with negative studies that had mainly used 1 mg. Two studies using PCA consumption of analgesics as an outcome were also positive. The only sensitive study of four dose-response comparisons indicated that 5 mg of IA morphine was more effective than 1 mg. The only sensitive study of three cross-route comparisons showed no difference between 5 mg of IA and 5 mg of intramuscular morphine.

The analysis of sensitive studies indicated that 5 mg of IA morphine injected into the knee joint provides postoperative pain relief for up to 24 hours. A minimum of 30% of the maximum possible pain intensity was needed for an analgesic effect to be detected in a study.

Pre-emptive analgesia

Pre-emptive analgesia is all about giving analgesics before the pain, with the intention that postoperative pain or postoperative use of opioids will be reduced. A comprehensive systematic review and meta-analysis [42] has shown clearly that none of our current approaches to pre-emptive analgesia are of any value. A possible exception may be newer coxibs with longer duration of action, but there are no present trials of sufficient size or quality that suggest this is the case.

Gender differences

A gender difference between men and women in their endocrine and analgesic response to a surgical insult has been known for some decades [43]. While age and race may contribute to different responses to morphine, gender did not, in a summary of studies [44]. We can be sure also that gender has no effect on the analgesic response of 400 mg of ibuprofen, based on meta-analysis of trials, and on individual patient data [45].

Comment

Systematic reviews and meta-analyses are helping us to differentiate between those interventions backed by enthusiasm, but not much evidence, and those backed by enthusiasm, lots of evidence of lack of effect, but where the search goes on for some goal-post moving effort that will change things.

Both are dangerous. The first for the obvious reason that no evidence of efficacy also means no evidence about harm. The second is dangerous because it attracts attention to pointy-headed academic questions that are of little or no practical relevance. Practical relevance is, or should be, the most important thing.

PULLING IT ALL TOGETHER

There is an old adage that if the patient can swallow it is best to give drugs by mouth. There is no evidence that NSAIDs given by injected or rectal routes give any better analgesia than oral doses [40]. If the patient cannot swallow, injected opioids or NSAIDs would often be appropriate, though there appears to be little choice between them in efficacy.

It may come down to the main concerns of adverse events with NSAIDs, which in acute pain are renal failure and coagulation problems. Acute renal failure can be precipitated in patients with pre-existing heart or kidney disease, those on loop diuretics, or those who have lost more than 10% of blood volume. NSAIDs can cause lengthening of the bleeding time, usually within the normal range, though there is little evidence that they cause increased blood loss. Increased bleeding should not occur with coxibs, which do not inhibit platelets. The main choice may come down to the fact that opioid dose can be titrated to effect.

Opioids

For this reason and others, opioids are the first line treatment for severe acute pain, and most information is available for injected morphine. Adequate doses are often withheld because of traditions, misconceptions, and fear. Doctors and nurses fear addiction and respiratory depression. Over 100,000 patients were followed up for a year after opioids were given for acute pain, and just four were considered addicts (in North America) [46].

Irrespective of the route, opioids used for people who are not in pain, or in doses larger than necessary to control pain, can slow or even stop breathing. The key principle is to titrate the dose against the desired effect – pain relief – and minimise unwanted effects (Figure 17). If the patient is still complaining of pain and you are sure that the drug has all been delivered and absorbed, then it is safe to give another, usually smaller, dose (five minutes after intravenous, 60 minutes after subcutaneous or intramuscular, 90 minutes after oral morphine). If the second dose is also ineffective, then repeat the process or change the route of administration to achieve faster control. Delayed release formulations, oral or transdermal, should not be used in acute pain because delayed onset and offset are dangerous in this context.

Figure 17: Titrating dose to effect

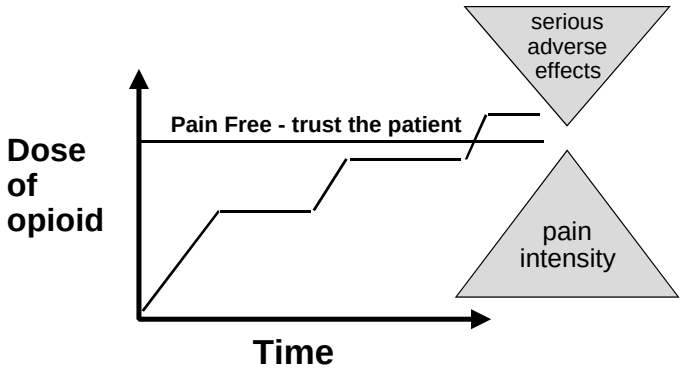
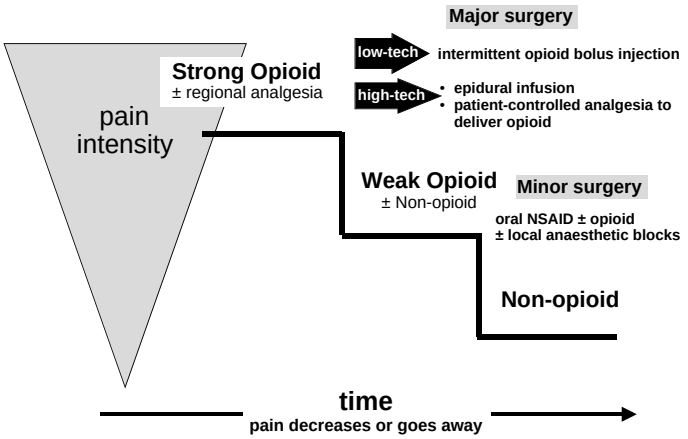


Figure 18: Descending ladder of acute pain



In renal dysfunction, the active metabolite of morphine, morphine-6-glucuronide, can accumulate and result in greater effect from a given dose. Accumulation can be a problem in unconscious intensive care patients on fixed dose schedules when renal function is compromised [47]. Pethidine has a specific disadvantage in that in multiple doses the metabolite norpethidine can accumulate and act as a central nervous system irritant, ultimately causing convulsions, especially in renal failure [48].

The acute pain ladder

The acute pain ladder of Figure 4 can now become the acute pain ladder of Figure 18, with some of suggestions about what treatments may be appropriate when. It cannot, nor ever can be comprehensive because there will be circumstances in which different considerations apply. But for most patients, the decreasing pain ladder will be a useful guide.

Getting the management right

One of the major initiatives to improve pain in hospitals has been the introduction of acute pain services [49]. In a survey of 105 hospitals in 17 European nations, only 34% had acute pain services but over half of anaesthetists were dissatisfied with postoperative pain management on surgical wards. A review of 44 acute pain service audits [25] reporting on 84,000 patients showed that most reported less pain at rest (by 0-27%) and on movement (by 19-64%). Postoperative nausea and vomiting was somewhat less frequent and there was some evidence that postoperative sedation was less at hospitals with an acute pain service.

Some examples show how pain management has been improved.

1 Improving postoperative care

One of the best examples of how simple changes can make a difference comes from an initiative from Cardiff [50]. Following a survey of all NHS hospitals, units were identified where there was no formal mechanism for postoperative pain management. A representative hospital was chosen from each NHS region, from small district hospitals to teaching hospitals.

The project had four stages:

1 An initial survey of 100 postoperative surgical inpatients or a one-month survey. Patients were interviewed at 24 hours and four days to record complications and pain using a standardised questionnaire.
2 A programme of education for all staff led by a lead clinician and nurse. Education consisted of the use of a four point verbal rating scale and an algorithm to allow a flexible and safe provision of intermittent intramuscular opioid use after surgery. Patients with moderate or severe pain were managed according to sedation, respiratory rate, blood pressure and time since last dose.
3 Standard guidelines were introduced, initially in two surgical wards.
4 After four to six months, a repeat survey was undertaken.

There was information from 1,416 patients in the first survey and 1,322 in the second. Surgery types included gynaecological, orthopaedic, general, urological and vascular. Operations were classed as major, intermediate and minor. The demographics of patients were similar in terms of sex distribution, age, and proportions of major, intermediate and minor surgery.

More patients (73%) received information about pain and its relief in the second survey than in the first (46%). More patients found their pain better than expected in the second survey than in the first. Pain at rest, on movement, and on deep inspiration was better in the second survey, with fewer patients having moderate or severe pain (Table 10). The proportion with severe pain on movement fell from 37% to 12%. Moderate to severe nausea fell from 37% in the first survey to 23% in the second, and moderate to severe vomiting fell from 22% to 12%. There was also a reduction in the number of patients reporting postoperative complications by the fourth day, particularly chest infection, constipation and paralytic ileus.

2 Improving day case pain relief

Also from Cardiff comes useful information about the benefits of getting pain relief after day case surgery right [51]. In an eight week period in 1993, 150 adults having surgery in a day surgery unit in Cardiff (general surgery, gynaecology, ophthalmic or ENT) were audited using a postal questionnaire for pain at home after their operation. At 24 and 72 hours they rated their pain as mild, moderate or severe, and recorded analgesic drugs used over three days. The hospital had an analgesic prescribing policy which covered about half these patients.

Table 10: Implementing acute pain management

Situation	Percent of patients	
	First survey	Second survey
Pain at rest	32	12
Pain on movement	76	53
Pain on deep inspiration	41	22

The results of the audit showed that of the 111 usable questionnaires returned, 29 patients (26%) reported severe pain at least one time, and 12 patients (11%) contacted their GP or were readmitted to hospital because of poor pain control. For some operations (hernia repair, for instance), almost all the patients had severe pain and over a third sought GP advice or were re-admitted.

Briefly, the prescribing policy was revised to include 'missing' procedures. Procedures were ordered into those where mild pain was expected (cataracts, for example), moderate pain was expected (varicose veins, for example), or severe pain was expected (hernia repair, for example). Prescribing policy was adjusted to take account of the expected pain level:

- Mild pain: Paracetamol 1000 mg four times a day
- Moderate pain: Co-codamol 1 or 2 tablets four times a day
- Severe pain: Co-codamol 1 or 2 tablets four times a day plus naproxen 500 mg twice a day (with, of course, appropriate adjustments for certain patients with ulcers or asthma).

In addition a system of 'rubber-stamping' prescription forms was devised so that appropriate prescriptions were given for appropriate operation types.

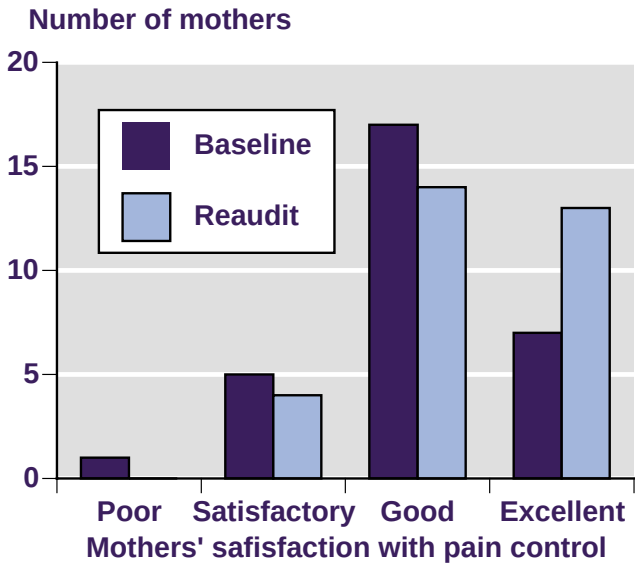
An audit of 200 patients over a 10 week period in 1994 showed that the prescribing policy was followed in 89% of cases. There were 130 returned questionnaires. They showed that the number of patients reporting severe pain at 24 or 72 hours at home had been reduced almost to zero (about 10% reporting severe pain in but four of 12 operation types). No patient had cause to contact their GP for provision of postoperative pain relief.

3 Do-it-yourself pain control

This rather small audit-reaudit and action sandwich originally stemmed from the observation that after caesarean section mothers were often had too much pain or were too affected by their analgesic to look after their babies. As a result a new protocol, based on evidence, was introduced. Key features of the protocol were the introduction of formal pain assessments, the use of pre-printed prescription labels to apply to drug charts and the introduction of self-medication by mothers. There was also an education programme introduced by professionals from the Acute Pain Service by individual face-to-face sessions (doctor to doctor, nurse to nurse) rather than through seminars.

A reaudit showed that maternal function was much improved. Only seven mothers were not caring for their babies with just one giving pain as the reason (the other six were in SCBU). In the baseline survey, the numbers were 13 and 10 respectively. The incidence of severe pain at rest and on movement was down by about 30%. Mothers were more satisfied with their pain control. Over 40% (13) rating pain control as excellent compared with about 20% (7) in the baseline. Good or excellent pain control predominated, and poor control had been eliminated (Figure 19).

Figure 19: DIY pain control in Warwick



Comment

The message that comes through in managing acute pain is to do the simple things well, to make sure that everyone on the team is in the team, to have champions, to make sure that the people on the front line have tools to do the job, and to reaudit to make sure that changes stick. It also needs to be emphasised that change is a good thing, especially as more or better evidence comes alone, or as staff turn over, or as organisations change.

And it is always worthwhile thinking about others who might be involved, but about whom you have forgotten. For day case surgery, that now should include GPs. In perhaps a first survey of GPs' views on the subject, general practitioners in Lorraine (2,199) who were active or retired were sent a postal questionnaire with 10 questions about postoperative pain after ambulatory surgery. The response rate was 44%.

The potential risk of a patient needing a postdischarge intervention once home was a major concern to 74%, and that of encountering inadequate acute postoperative pain control at home to 65%. Communication with surgical units was poor, with 73% of GPs never receiving instructions about rescue analgesia, and 80% with no information about communication with a designated specialist about pain management. The frequency of patient contact because of inadequate pain relief after ambulatory surgery is shown in Table 11. Many GPs saw at least one patient a month, and about two thirds of GPs wanted much more scientific information, guidelines, training and contact with specialists.

Table 11: GP visits for postoperative pain in Lorraine

Frequency	Percent
More an once a week	5.7
Less than once a week	32
Less than once a month	48
Less than once a year	12
Never	2.5

Chronic pain after surgery

Chronic pain is a possible, if often overlooked, adverse outcome of surgery.

Systematic review

A systematic review [54] has examined the incidence of chronic pain after surgery and suggests that it is common. The review searched OVID to January 1999 for articles linking persistent pain to surgery. Authors' databases and references were also examined. For inclusion articles had to have information about pain 12 weeks or longer after surgery. Generally, studies smaller than 50-100 patients were excluded, apart from amputation studies where studies with 25 patients were accepted.

Chronic pain after surgery was common. Many studies had information to one year or longer, and many compared different surgical approaches, or anaesthesia. The results shown in Figure 20 use data from studies closest to one year after surgery, and combine surgical approaches when reported separately. Where several types of chronic pain were reported (like chest pain, arm pain, or phantom breast for breast surgery), the pain at or close to the site of operation was taken. The figures for breast pain include mastectomy, lumpectomy, breast augmentation and reduction.

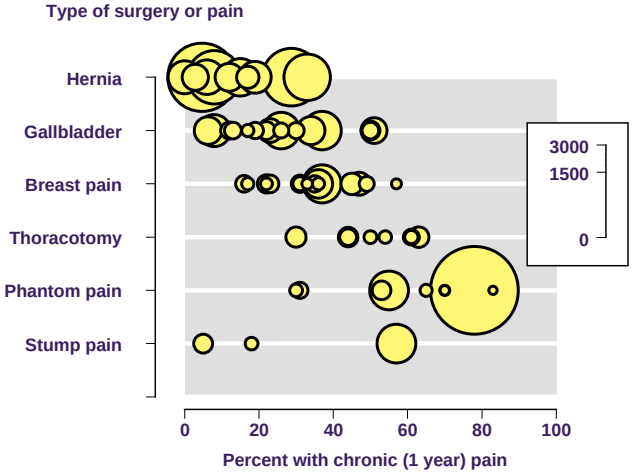
Phantom limb pain was common, but high rates of chronic pain were reported for all surgery. Even in the lowest incidence, hernia repair, rates varied from 0% to 29%.

Predictive factors included pre-operative pain, repeat surgery, a surgical approach with risk of nerve damage, acute and severe post-operative pain, radiation, chemotherapy and a variety of psychological and depressive symptoms.

Functional impairment

More than 95% of all hernia operations performed in Denmark are reported to the Danish Hernia Database. In a two-month period in 1998 1,652 patients had surgery for inguinal

Figure 20: Percentage of patients with chronic pain about a year after surgery



or femoral hernia, and 1,443 questionnaires were mailed one year after surgery. The first questionnaire established the incidence of pain, and the second characterised the pain and its effect on function [55].

There was an 81% response to the first questionnaire. Twenty-nine percent reported having pain in the area of the hernia within the past month, and 11% reported that the pain impaired work or leisure activities. Only 4.5% (1 in 6) had sought medical advice or received treatment for the pain.

Comment

How much pain there is, and its location and nature, determine how important chronic pain is after surgery. Even the lowest figure of 1 in 20 patients needing treatment or advice for pain one year after surgery has large resource implications. Postoperative breast pain occurred not just after mastectomy, but after lumpectomy, and after breast augmentation and reduction, which are elective procedures.

Two issues emerge. The obvious one is to find out more about what influences the incidence of chronic pain after surgery, and do something about it. The other is to make patients aware that surgery can have longer-term consequences.

Health economics of acute pain management

This is a confused and confusing area, complicated by large differences in healthcare systems, and without being informed by large systematic studies. There is clear need for more thinking and better studies. This is the only conclusion of reviews of the economic considerations of PCA [56] or opioid strategies [57].

The cost of medicines is probably one of the least expensive items. For instance, in a randomised educational intervention study in the USA [58], the median cost of postoperative pain medications over the patient hospital stay was $9.46 per patient. The highest per-patient cost was $23 for knee replacement surgery and the lowest about $4 for minor abdominal or orthopaedic surgery, though with large inter-patient variation.

Most stress is likely to be on larger cost items, like length of stay. Though some studies have linked better pain control to shorter length of stay [52], or to preventing re-admission after day-case surgery [51], costs have not generally been measured. There are studies that relate re-engineering of surgical services to reduced length of stay and have shown benefits like reduced rates of wound infection [59] or, indeed, total costs [60], but neither was particularly related to control of postoperative pain. On the other hand, large (more than 12,000 patient) US surveys on overall costs of surgery suggest that reducing length of stay by one day reduces total costs by 3% or less [61].

Comment

We do not know that better pain control reduces costs. But neither is it likely to increase them dramatically. Doing the simple things well can generate great benefits for patients without recourse to expensive high-technology interventions.

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