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PAIN MANAGEMENT IN OUTPATIENT KNEE ARTHROSCOPY

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Abstract

Knee arthroscopy is probably the most common orthopaedic procedure performed. The objective of this thesis was to compare local anaesthesia with other used anaesthetic techniques for outpatient knee arthroscopy. The choice of postoperative local anaesthetic and the general postoperative pain pattern and management, as well as the general outcome were evaluated. Totally 642 patients were involved in three prospective randomized studies and one follow-up. In the first study patients were randomly allocated to either local (LA) (n=200), general (GA) (n=100) or spinal (SA) (n=100) anaesthesia. All patients were assessed and made self-assessments during the day of surgery and postoperatively. The surgeons were asked to grade the technical difficulty of the arthroscopic procedure on a VAS scale, and they also reported if the allocated anaesthesia was optimal, or, if not, which technique they would have preferred. In the second study 120 patients were studied comparing levobupivacaine 2.5 mg/ml (n=40), levobupivacaine 5 mg/ml (n=40), and lidocaine 10 mg/ml with adrenaline (n=40), administered intra-articularly at the end of surgery performed under light GA. Primary study endpoint was the need for any analgesics during the first 24 postoperative hours. In the third study 122 patients were randomised to either a NSAID (lornoxicam) (n=61), or a coxib (rofecoxib) (n=61) postoperatively after surgery in GA. Pain ratings and need for rescue medication were followed for four consecutive days. The fourth study is a questionnaire follow-up, six months after surgery, of all the enrolled patients in the first study.

Results. Ninety percent of the LA patients were satisfied with the procedure, although they stated statistically more intraoperative pain than the GA and SA patients. In 5 % of the LA patients the surgeon reported technical difficulties. If excess synovitis was present, LA did not seem to provide sufficient anaesthesia for surgery. Levobupivacaine 5 mg/ml was found to be an effective postoperative local anaesthetic in outpatient knee arthroscopy, providing superior postoperative analgesia as compared to lidocaine or a lower concentration of levobupivacaine. Twenty-five percent required, however, further analgesics during the first 24 hours after surgery. There was no difference in need for rescue analgesia (50 %), pain rating or side-effect profile between the patients receiving either a conventional NSAID or a selective cox-II-inhibitor. No repeat arthroscopies occurred in the SA or GA groups, three occurred in the LA group. The clinical course was altered by the repeat arthroscopy in only one case. There was no difference in the satisfaction rate between the anaesthesia groups six months after surgery.

Summary and conclusion. LA is a valid alternative to GA, or SA for outpatient knee arthroscopy in a selected group of motivated patients. The use of a long-acting local anaesthetic (levobupivacaine 5 mg/ml) intra-articularly, given immediately postoperatively, reduces experienced pain 24 hours after surgery. Still this must be combined with the access to oral analgesics for the coming 2-3 days in order to manage pain. We found no evidence for using the more expensive coxibes for the postoperative pain management. The choice of anaesthesia does not influence the frequency of repeat arthroscopy, satisfaction with the procedure, or recovery six months after surgery.

Keywords: local anaesthesia, arthroscopy, levobupivacaine, NSAID, coxibs, rearthroscopy

Swedish summary
Sammanfattning på svenska

Knäartroskopi (titthålsoperation av knäleden) är sannolikt det mest förekommande ortopediska ingreppet inom dagkirurgi. Syftet med denna avhandling är att jämföra lokalbedövning med andra bedövningar (anestesier) för knäartroskopi, både ur patientens och operatörens synvinkel. Vidare att utvärdera förekomsten av smärta och effekten av olika former av smärtbehandling efter operationen (lokalbedövning och tabletter) samt slutligen det kirurgiska resultatet av ingreppet.
Totalt studerades 642 patienter i fyra olika studier, varav tre är prospektivt randomiserade. I den första studien lottades patienter till lokalbedövning (lokal anestesi, LA), narkos (generell anestesi, GA) eller ryggbedövning (spinal anestesi, SA). Smärta under och efter operationen, liksom eventuella kirurgiska svårigheter noterades. Både patient och utförande kirurg rapporterade om de var nöjda eller ej med den aktuella bedövningsformen.
I den andra studien lottades patienterna till någon av tre olika lokalbedövningsmedel för injektion i knäleden efter operationen. Under själva artroskopin fick samtliga patienter narkos.
I den tredje studien fick patienterna antingen en vanlig antiinflammatorisk medicin (NSAID), eller en coxib (som inte ska ge så mycket magbiverkningar som de vanliga NSAID), som smärtstillande efter operationen.
I den fjärde undersökningen utvärderades de patienter, som lottats till olika bedövningsformer, sex månader efter knäartroskopin. Patienterna fick med en enkät rapportera om de var återställda och om de fortfarande var nöjda med valet av bedövning. Vidare efterforskades behovet av reoperationer.
Resultat. Nittio procent av patienterna som opererades i LA var nöjda med bedövningen, trots att signifikant fler patienter upplevde smärta än de patienter som opererades i GA eller SA. I 5 % av LA patienterna rapporterade operatören tekniska svårigheter. Om knät var kraftigt svullet inför operationen, ökade risken för att LA inte räckte som bedövning för att genomföra operation. Levobupicavaine 5 mg/ml var det lokalbedövningsmedel som gav bäst smärtlindring första dygnet efter knäartroskopin och minst behov av smärtstillande tabletter efter operationen. Det var ingen skillnad mellan de olika anti-inflammatoriska medicinerna som gavs efter operationen, traditionella NSAIDs gav lika bra och säker smärtstillning som coxiber. Bedövningsformen påverkade inte slutresultatet av knäartroskopin sex månader senare. Tre LA patienter hade blivit omopererade, men i endast ett av dessa fall förändrades behandlingen av den andra operationen, som utfördes i narkos.
Sammanfattningsvis är lokalbedövning ett alternativ till narkos eller ryggbedövning för titthålsoperation av knäleden i utvalda och motiverade patienter. Långverkande lokalbedövningsmedel injicerat i leden omedelbart efter operationen ger god smärtlindring det första dygnet efter operationen. Detta bör dock kompletteras med tillgång till värktabletter under de första 2-3 dagarna efter ingreppet. Det finns inga skäl att rutinmässigt använda mer kostsamma anti-inflammatoriska tabletter för smärtlindring efter operationen. Valet av bedövningsform påverkar inte utfallet sex månader efter operationen.

List of original papers

This thesis is based on the following papers, which will be referred to in the text by their Roman numbers (Paper I-IV)

I

Jacobson E, Forssblad M, Rosenberg J, Westman L, Weidenhielm L. Can Local Anesthesia be recommended for routine use in elective knee arthroscopy ? A comparison between local, spinal and general anesthesia. Arthroscopy 2000 16(2):183-90.

II

Jacobson E, Assareh H, Cannerfelt R, Anderson R, Jakobsson J. The postoperative analgesic effects of intra-articular levobupivacaine in elective day-case arthroscopy of the knee. A prospective, randomized, double blind, clinical study. Knee Surg Sports Traumatol Arthrosc 2006 14:120-124.

III

Jacobson E, Assareh H, Cannerfelt R, Renström P, Jakobsson J. Pain after elective arthroscopy of the knee; A prospective, randomised study comparing conventional NSAID to coxibe. Accepted for publication in Knee Surgery Sports Traumatology Arthroscopy.

IV

Jacobson E, Forssblad M, Weidenhielm L, Renström P. Knee arthroscopy with the use of local anesthesia – an increased risk for repeat arthroscopy ? A prospective randomized study with a six-month follow up. Am J Sports Med 2002:30 ; 61-65.

Contents

Abbreviations

ASA	**American Society of Anaesthesiologists**
Coxibs	**Selective cycloxygenase-II-inhibitors**
GA	**General Anaesthesia**
LA	**Local Anaesthesia**
NSAID	**Non Steroid Anti Inflammatory Drug**
SA	**Spinal Anaesthesia**
SEK	**Swedish crowns (currency)**
SD	**Standard Deviation**
VAS	**Visual Analogue Scale**

Introduction

Knee arthroscopy

History and technique

The first reported knee arthroscopy was performed by the Swiss surgeon Eugen Bircher in 1921. At the same time Takagi in Japan also was exploring joints with endoscopy, and his pupil Watanabe in 1957 did the first operative knee arthroscopy. However, it was first in the 1970s that arthroscopic meniscectomy was described by several authors from different parts of the world.

Sweden has a long tradition in knee arthroscopy after early attempts of Wiberg in the 1940s. Eriksson and Gillquist are two true pioneers of the 70s in the field. During the last 35 years the technique has developed enormously and arthroscopy has been called one of the greatest contributions in orthopaedic surgery of this century.

Knee arthroscopy is most commonly performed using two portals and a continuous pressure-irrigation system with saline. A third lateral, proximal portal for an outflow cannula can be used when extreme lavage of the joint is necessary, or if joint pathology demands surgical access from another direction. This third portal should be avoided, if possible, since it causes additional pain, both intra- and postoperative. The use of tourniquet is very seldom necessary, and it should not be applied as a routine, as it may cause more pain and may enhance thrombosis formation.

If the patient's history indicates increased risk for thrombosis the use of thromboprofylaxis should be generous. The most feared adverse events in outpatient knee arthroscopy, besides infection, are the thromboembolic complications.

Today there is no generally accepted golden standard, when it comes to intraoperative anaesthesia or postoperative pain therapy in outpatient knee arthroscopy. A variety of drugs, techniques, and prescription routines are used.

From in-hospital to office-based

Knee arthroscopies are today performed on regular basis at most orthopaedic clinics throughout the world (Bonicalzi et al 1995, Dahl et al 1997, Fairclough et al 1990, Goranson et al 1997, McGinty ed 1996, Pellaci et al 1996, Schafer et al 2003). It has turned from an in-hospital, to an outpatient procedure, at some clinics even performed in an office based setting, with a minimum of technical and staff set-up (Forssblad 2004). This has been possible thanks to the advances of the technique, but the introduction of new and safe anaesthetics and analgesics have most certainly also had an influence.

The general trend is to transfer, whenever feasible from in-hospital to day-case surgery, in order to reduce the requirement of hospital resources and cost.

This transition puts, however, demands on knowledge and skills both in the intra-operative management to facilitate a fast recovery and early mobilisation, as well as in pain management to accomplish an acceptable postoperative course in knee arthroscopy.

Making the incision for the anterolateral portal for the arthroscope.

Pain management

Pain and pain management in outpatient knee arthroscopy can be divided in three periods; the pre- intra- and postoperative period.
There are several factors to consider, all having potential influence on pain perception.

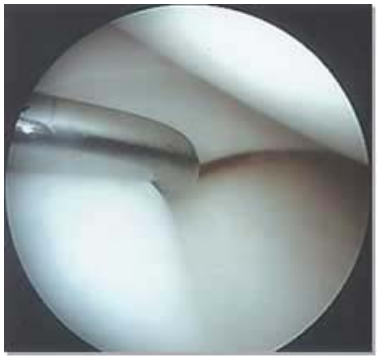
Period	*Considerations regarding pain*
Preoperative	**Information of procedure** **choice of anaesthesia**
Intraoperative	**confident milieu** **choice of anaesthesia** **equipment** **surgical trauma** **duration of surgery** **tourniquet**
Postoperative	**choice of local anaesthetic** **choice of analgesics** **mobilisation** **confident milieu**

Having in mind that elective knee arthroscopy is one of the most common procedures, it seemed interesting and important to explore the pain management both during the intra- and postoperative period, as well as to find out if the chosen anaesthesia had any influence on the outcome. The preoperative period, including information regarding the procedure to the patient, has not been the focus of the present thesis. It is important to remember that also this may have a decisive impact on both the outcome, and pain experience. It is no doubt that expectations of the patients may have major influence on the overall evaluation of the procedure. A well-informed patient is of course better off, than a badly informed and motivated.

Intraoperative period

Local anaesthesia for outpatient knee arthroscopy has been used for a couple of decades (Buckley et al 1989, Eriksson et al 1986, Fruensgaard et al 1990, Hultin et al 1992, Lorentsen et al 1997, Ramanathan 1998, Shapiro et al 1996, Tsai et al

1993, Williams et al 1997, Yacobucci et al 1990), still a vast majority of these elective knee arthroscopies are performed under anaesthesias demanding both preoperative, as postoperative advanced considerations, as well as risks for complications. All anaesthetic techniques carry theoretical risks; for example general anaesthesia has by itself a mortality rate not to forget, and there are always hazards as aspiration to look out for. Not all patients can cope with anaesthesias with systemic involvement. Many patients fear spinal anaesthesia as it seems scary to become paralyzed (Shevde et al 1991). There is also a risk for postspinal headache. However recent studies from Finland report effective low dose SA for outpatient knee arthroscopy (Korhonen et al 2005).
Today local anaesthesia is not offered as a standard procedure at most hospitals. A common opinion is that it is painful for the patient, and technically difficult for the surgeon; resulting in recurrent surgery in more powerful anaesthesias. Many think that the only reason for using LA is to save money, as it demands less staff resource, time and drugs (Forssblad et al 2004, Linter et al 1996, Rockborn et al 2000, Trieshmann et al 1996,). But there are other interesting factors to consider; such as the risk for the patient and that the patient can be engaged and informed during the process, facilitating a smoother postoperative course.



Intra-operative probe testing of medial meniscus

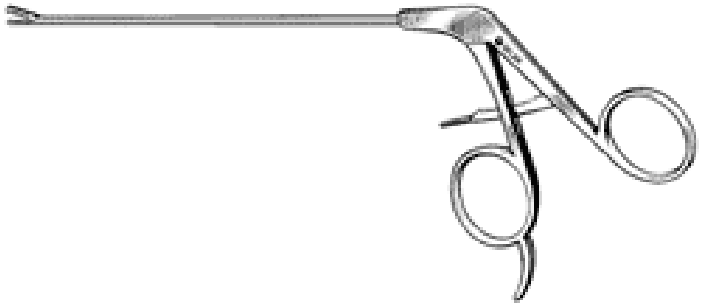
Postoperative period

The postoperative course can be divided into different parts, early recovery, recovery to street fitness, recovery to ordinary life function and surgical outcome.

- Early recovery includes return of basic vital functions, spontaneous breathing, stable circulation and regain of all protecting reflexes.
- Street fit or ready for discharge includes also return of cognition, ability to ambulate without pain or emesis (Chung et al 1995).
- Return to ordinary life functionality includes ability to do basic every day activities including at least desk associated work.
- Surgical outcome includes end surgical knee function.

Important parts in the overall patient management are to minimize pain and discomfort. For the outpatient patient this should be achieved without compromising safe ambulation and discharge from the hospital facility.
As day surgery increases worldwide efforts are made to provide not only an optimal intraoperative environment for both patient and surgeon, but also to facilitate a rapid return to normal daily life functions with a minimum of side effects and highest degree of safety is nowadays of vital importance. Pain and emesis are the major symptoms recalled after day surgery (Apfelbaum et al 2003, Carroll et al 1995). Both are not only mandatory comfort considerations but have also economical and practical consequences for the patient as well as the dimensioning and manning of recovery room facilities.
Postoperative pain management is continuously improving partly due to the introduction of new drugs that are safe and more effective but also by optimizing complementary analgesic methods and sites of action. This multi-modal analgesia has become the golden standard for pain management and is particularly essential after day surgery (Redmond et al 2003, Shang et al 2003) The optimal combination of the various components of local anaesthetics, peripheral and central acting analgesics is not well established and must be tailored to each particular type of surgery (Kalso et al 1996).
In outpatient surgery, methods to obtain safe and efficacious pain relief also after discharge are demanded, not the least to allow early mobilisation (McQuay et al

1998, Schafer et al 2003). There is today no consensus as to the pain management immediately postoperatively, and after discharge.



Surgical punch for meniscal resection.

Aims of the thesis

- To evaluate and compare local anaesthesia intraoperatively with other used anaesthetic techniques for outpatient knee arthroscopy with special reference to the patient's , as well as the surgeon's subjective experience
- To compare the postoperative (24 hours) analgesic effect of different local anaesthetics administered intra-articulary after outpatient knee arthroscopy
- To map (describe) the postoperative pain pattern in (following) outpatient knee arthroscopy
- To compare a conventional NSAID to a coxib as postoperative analgesic in outpatient knee arthroscopy
- To study the impact of anaesthetic technique used on the overall surgical outcome following elective knee arthroscopy

Ethical considerations

Study I & IV

These studies were approved by the ethical committee at the Karolinska Hospital, diary number 96-074

Study II

This study was approved by the ethical committee at the Karolinska Hospital, diary number 03-031

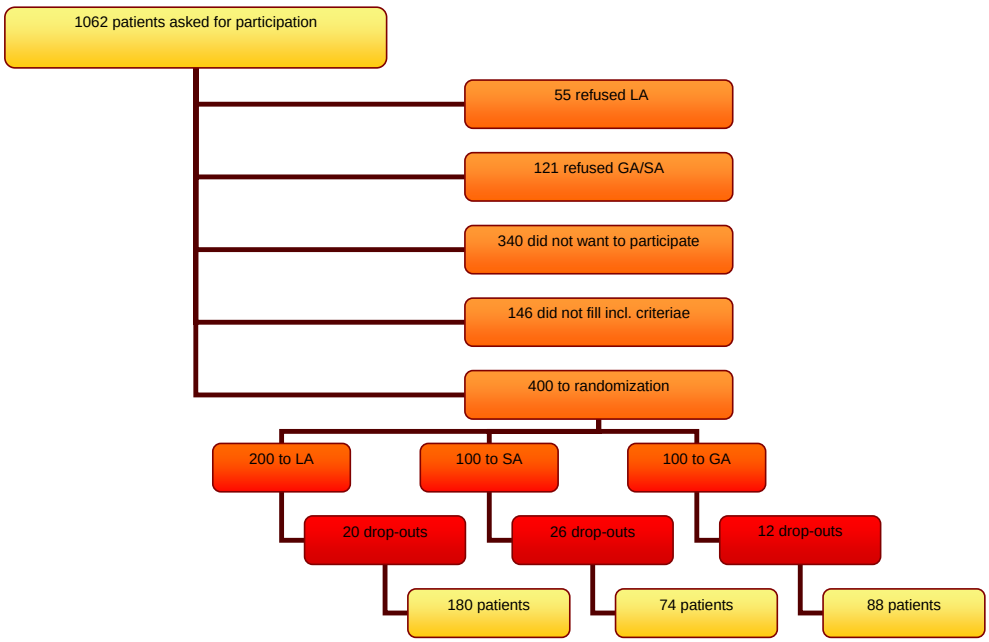
Study III

This study was approved by the ethical committee at the Karolinska Hospital, diary number 03-133

Materials and Methods

This thesis includes three prospective, randomized studies and one follow-up study of a total of 642 patients.
The visual analogue scale (VAS) was used as the tool for measurements of subjective effects (pain) since it is well documented (Collins et al 1997, Rosier et al 2002), in addition (study II, III) the need for rescue analgesics was registered.

Study I (prospective, randomised, none-blinded, study)
Four hundred patients were randomized to local (LA) (n=200), general (GA) (n=100) or spinal (SA) (n=100) anaesthesia. Of the 1062 patients asked to participate in the study, 516 did not want to, and of these 55 rejected the idea of risking having surgery in LA. One-hundred-and- twenty-one did not want to be in the study due to risking having a more advanced anaesthesia as GA or SA. Inclusion criterias were ASA I-II, knee range of motion 0-90 degrees; exclusion criterias neurological/neuromuscular disorder, local infection at planned injection site, allergy to amide LA and allergy to NSAIDs. No meniscal repairs, ACL reconstructions or rearthroscopies were included. The anaesthetic procedures were standardized, as the analgesics postoperatively.
All patients were assessed during the day of surgery at the hospital, and the patients made self-assessments the two following days.
A visual analogue scale (VAS) 0 – 100 mm was used to assess pain and nausea as well as to grade the technical difficulty of the arthroscopic procedure.
The postoperative analgesic consumption, the patient's opinion of the anaesthesia method used, and postoperative sick-leave were reported two days after surgery. The surgeons also reported if the allocated anaesthesia was optimal, or, if not, which technique they would have preferred. Adverse events during the procedure were also registered.



Study I - randomisation

Study II (prospective, randomised, single/patient blinded study)
One-hundred-and-twenty ASA I-II patients scheduled for primary elective knee arthroscopy were randomized into 3 groups, 40 patients each; levobupivacaine 2.5 mg/ml, levobupivacaine 5 mg/ml or lidocaine 10 mg + 5 µg/ml adrenalin.
Prior to surgery 7 ml of the randomized local anaesthetic was injected in the skin for portal placement and 13 ml was injected intra-articularly at the end of surgery. Patients taking analgesics pre-operatively were excluded. No premedication was given. All patients had a standardized light general anaesthesia.
Primary study variable was any need for oral analgesia during the first 24 hours after surgery. VAS and need for analgesics were recorded at the hospital and after discharge, all patients completed a questionnaire about pain and the need for any analgesia during the first 24 postoperative hours.

Study III (prospective, randomised, single/patient blinded study
One-hundred-and-twenty-to ASA I-II patients scheduled for primary elective knee arthroscopy in general anaesthesia were enrolled in the study. The patients were randomly allocated to receive a conventional NSAID (lornoxicam; *Xefo*©) or a coxibe (rofecoxib;*Vioxx*©) by envelope technique. The need for rescue analgesia, and pain ratings during the four first postoperative days were followed. A questionnaire, including VAS scales (non- interrupted, 0-10 cm) was used. All patients were anaesthetised according to standard departmental routines. In the recovery room all patients were given orally 1 g paracetamol and an anti-inflammatory agent in accordance to randomisation as soon as possible after waking up. Pain assessments (VAS scale) were made frequently. At discharge all patients were asked to fill in the questionnaire and were given a package of randomised drug treatment for the following four days (8 mg lornoxicam twice daily, or 50 mg rofecoxib once daily) and were instructed to take this therapy regardless of pain, in order to facilitate the recovery process. The need for rescue medication, pain grading and occurrence of side effects were recorded on a questionnaire that was send back to the hospital for evaluation.

Study IV (post-intervention follow-up study)

Six months after surgery all 342 enrolled and included patients in study I, were asked to complete a questionnaire, and all of their medical records were reviewed. Questions were made both on the total experience of the surgical event, and on any remaining knee problems, or need for recurrent surgery.

Statistics

Study I

Median values, arithmetic mean values and standard deviations (SD) were calculated. Kruskal-Wallis test and Wilcoxon's rank sum test were used to test the results of the VAS-measurements, and a Chi-square test was used to test the other nonparametric data.

Study II

The number of patients studied was chosen after power analysis based on previous experience and that we considered at least a 30% reduction in analgesia free patients to be clinically relevant. Patient demographics were given as the mean and standard deviation, and differences between groups were studied by means of analysis of variance. Need for rescue medication and VAS grading at 24 hours was given as median and range and differences were studied using the Kruskal-Wallis test or contingency table analysis.
$P < 0.05$ was considered statistically significant.

Study III

Patient demographics are presented as mean and standard deviations. VAS ratings and need for rescue analgesia values are presented as median and range. Differences between groups were studied by non-parametric tests; Chi-square test or Mann-Whitney U-test when appropriate. The number of patients (61 in each group) was determined by a power analysis based on the assumptions; a response rate *no need for rescue analgesics* in the conventional NSAID group of 45%, and a clinical relevant further reduction being an absolute increase of 15%, corresponding to 60% of patients not requiring rescue analgesia during the first postoperative day with a power of 90 % at $p < 0.05$.

Study IV

Differences between the groups were assessed using a chi-square test, Kruskal-Wallis test or Fischer's exact test were used to test the data. $P < 0.05$ was considered significant.

Summary study I-IV

	Study I	*Study II*	*Study III*	*Study IV*
Type of study	*Prospective, randomised*	*Prospective, randomised*	*Prospective, randomised*	*Follow-up*
Aim	*Choice of anaesthesia for arthroscopy*	*Choice of LA postop*	*Postop analgesia – choice and pain pattern*	*Outcome*
No of patients	*342*	*120*	*122*	*324*
Age years	*43.2 (20-78)*	*45 (18-69)*	*48 (18-70)*	*43.2 (20-78)*
Anaesthesia	*LA, GA or SA*	*GA*	*GA*	*LA, GA or SA*
Studied period	*Perioperative – 3 days*	*Postoperative - 24 hours*	*Postoperative – 4 days*	*6 months*
Pain measurement	*VAS + questionnaire*	*VAS + rescue analgesics*	*VAS + rescue analgesics*	*VAS + questionnaire*
LA post op	*+*	*+*	*+*	*+*
Postop analgesic	*paracetamol*	*etoricoxib*	*rofecoxib*	*paracetamol*
Rescue analgesic	*paracetamol*	*paracetamol*	*paracetamol (dextropropoxiphene)*	*paracetamol*

Results

Study I

Patients

Of the 400 patients, 58 (15 %) were excluded *after* randomisation; 20 in the LA group, 26 in the SA group, and 12 in the GA group. The main reason were patients declining surgery/or surgery was no longer needed (9 (LA), 9 (SA), 4 (GA)). It should be noticed that 176 patients dropped–out *before* randomization owing to the possibility of getting a non-wished anaesthesia. Of these 55 rejected the idea of surgery under LA, the rest wanted LA, i.e. rejected GA or SA.

Performed surgery

In the study, 25 of 180 LA patients, 16 of 88 GA patients and 8 of 74 SA patients had only a diagnostic procedure. A vast majority of the patients had intra-articular procedures performed, most commonly a partial meniscus resection (67%).

Duration of surgery

There was no significant difference in the duration of surgery between the three groups. The median surgery time in LA was 12 minutes, in SA 15 minutes and in GA 13 minutes.

Opinion of the surgeons

The surgeon assessed the technical difficulty on the VAS (0-100 mm) to be more intense during surgery in the LA group (median 10 mm, range 0 - 93 mm) as compared with the SA group (median 4 mm, range 0 – 71 mm) and GA group (median 4 mm, range 0 – 88 mm). ($p < 0.05$).

The performing surgeon also estimated the patient's pain as more intense during surgery in the LA group (median 8 mm) compared with the SA group (median 0 mm) and the GA group (median 0 mm) ($p < 0.0001$).

In 29 patients (16 %) the surgeon did not consider the LA to be the optimal anaesthetic technique. The median VAS pain score for these patients during surgery was 34 mm (range 0-100 mm). In nine of these there were technical

difficulties; as a narrow joint capsule or need for extensive surgery. In five cases excess synovitis were considered a problem, and made LA less optimal. In another five patients, vasovagal reactions, probably pain induced, occurred.In 21 SA (28%) and 18 GA (20%) patients the anaesthesia used was not optimal since the procedure was short and easy. Technical problems were never reported in the SA or GA group.

Experience of the surgeons

It should however be noted that the performing surgeons in this study were not all on the same experience level. The less experienced surgeon had longer duration of surgery which caused more pain during surgery; however this was not a significant difference.

Intra- and postoperative pain

There was a significant difference between the LA, SA and the GA groups in respect of intraoperative pain. The median VAS score for the LA patients was 6 mm (range 0-100 mm) compared to 0 mm (range 0-52 mm) for the SA patients. The GA patients experienced no pain.

In the LA group 47 % did not use analgesics postoperatively compared with 26% in the SA group, and 56 % in the GA group, a significant difference. More patients in the SA group used analgesics compared with the LA group ($p<0.1$) and GA *group* ($p<0.0001$).

Dissatisfaction with anaesthesia

In the LA group 21(12 %) patients of 180 would have preferred another form of anaesthesia. In eight of these patients the surgeons also considered the used anaesthetic technique not optimal. In five of these the surgeon indicated that excess synovitis was the problem. Of the 21 LA patients, seven did not want to have the same anaesthetic procedure again. The median postoperative VAS score for this group of patients was 16 mm (range 0-100 mm). This indicates that the patient's experience of LA involves more than pain and nausea.

Return to work

No major complications were seen, and the number of patients who returned to work in 3 days postoperatively, was 120 (67 %) in the LA group, 44 (59 %) in the SA group, and 56 (64%) in the GA group. (n.s.)

Study II

Surgery was uneventful and all patients were discharged home within 3 hours. The number of patients who required any analgesia in the recovery room was lower for those given levobupivacaine 5 mg/ml and lidocaine 10 mg/ml than for the group receiving 2.5 mg/ml levobupivacaine ($p < 0.001$). No patients needed rescue medication during the stay in the recovery area.

	Lidocaine 10 mg/ml, n=40	**Chirocaine 2.5 mg/ml, n=40**	**Chirocaine 5 mg /ml, n=40**
No analgesics in recovery area	36 (90 %)	23 (58 %)	35 (88 %)

The number of patients not needing any oral analgesics during the entire 24-hour follow-up period was lower for those who received the higher levobupivacaine 5 mg/ml dose as compared to the levobupivacaine 2.5 mg/ml and lidocaine 10 mg/ml ($p = 0.013$).There was no difference in number of patients requiring any analgesia with respect to surgery, diagnostic procedure, meniscus resection, shaving of synovia or a combined meniscus resection and shaving. The VAS pain score at 24 hours was also lower in the levobupivacaine groups as compared to the lidocaine group ($p=0.019$; median values 2 (0-8), 3 (0-8) and 5 (0-10); mean values 2.8 (SD 2.3), 4.5 (SD 3.4), and 3.1 (SD 1.9) respectively).

Study III

All surgery and anaesthesia was uneventful and all patients were discharged in accordance to the routines of the department. In the recovery area pain was overall low, pain rating at 30 minutes median 0 (0-6).

The need for rescue analgesics was highest the evening after surgery when 42 % of patients required one or more oral rescue analgesics. The need for rescue analgesics decrease thereafter with time, and 30%, 25%, 16% and 11% of the patients required rescue analgesics for day 1 to 4 respectively.
Sixty-one patients (50%) needed at some point one or more rescue analgesics. There was, however, no difference found in the primary study variable, the need for rescue medication between the two groups studied; 30 NSAID and 31 coxib patients had not taken any further analgesics than the prescribed anti-inflammatory drug during the first 4 postoperative days (ns.)

Used rescue analgesics	Dosage
Paracetamol 1 g (first choice)	1 x 1-4
Dextropropoxipene 100 mg (second choice)	1 x 1-4

Used rescue analgesics in study III

Overall pain ratings were low, and showed similar pattern with a rapid decrease over time. A pain rating of more than 4 was recalled by 20 % of patients during the first evening after surgery and 16, 6, 4 and 2 % during the first 4 postoperative days. Accumulated, 4-day VAS, of more than 10/40 was reported from 25 (21%) patients.
Pain assessed by VAS was also similar between the groups. Accumulated pain-rating day 1 through 4, did not differ between the NSAID patients median 7 (0 – 39) and the coxib patients 7 (0 – 33) respectively (ns).

Side -effects were reported in 20 patients of all, 10 patients in each group. Most commonly recalled side-effect was gastrointestinal symptoms, second most common fatigue and third general dizziness.

Patients overall satisfaction with their pain management after discharge was high and did not differ between the groups, 8,9 (0-10) and 9,0 (5-10) for NSAID and coxib patients respectively.

Study IV

Three-hundred-and-twenty-four (95%) of the 342 enrolled and included patients returned the questionnaire, some after several reminders.

No repeat arthroscopies occurred in the SA or GA groups, three occurred in the LA group. (n.s.)

The reason for the recurrent surgery was persistent knee symptoms. No technical difficulties were described at first surgery in two cases. In the third case surgery was accelerated because of pain, and the diagnosis was chondral defects.

After control the clinical course was altered by the repeat arthroscopy in only one case. There was no difference in the satisfaction rate between the anaesthesia groups.

There were 20 patients (11 LA, 4 SA and 5 GA) that considered their knee problems worse 6 months after the arthroscopy.

	Study I	*Study II*	*Study III*
Pain during surgery (median)	*GA, SA 0 mm LA 6 mm*	*0 mm*	*0 mm*
No need for analgesics postop	*GA 56% SA 26 % LA 47 %*	*13 %*	*50 % (rescue analgesics)*
Observation period	*3 days*	*24 hours*	*4 days*

Pain during surgery/rescue analgesics.

Discussion

Knee arthroscopy is one of the most common orthopaedic procedures, and today a majority is performed in day-case surgery.
There are studies focusing on mapping the peri- and postoperative pain pattern in accordance to the chosen anaesthesia. General guidelines concerning the choice of anaesthesia and the postoperative pain management in outpatient knee arthroscopy are limited (Harris et al 2001, Mulroy et al 2000). The knee arthroscopies are today commonly performed under general anaesthesia and often a local anaesthetic is administered intra-articularly postoperatively. For pain medication after surgery and discharge various drugs, and drug combinations, are used; from paracetamol only, by combinations with dextroprophoxiphene or codeine, to morphine. In addition to, or as an alternative to these, an anti-inflammatory drug is frequently prescribed.

Choice of anaesthesia

This thesis demonstrates that LA is a valid *alternative* to GA, or SA for routine use in knee arthroscopy, both from the patient's and the surgeon's perspective, and is not associated with an increased need for recurrent surgery.
Patient's preference and expectations, besides the medical history, including the intra-articular pathology to address, are of course important factors for determining the anaesthesia used in outpatient knee arthroscopy. Basically GA, LA or SA are possible alternatives, as of today GA seem to be the most common used. In study I there were relatively more patients not accepting SA (both before and after randomization), even though acceptance of SA is relatively high in Sweden (Holmström et al 1997). Thorough information regarding the potential advantages of LA and careful selection of suitable patients might reduce the patients declining LA. There were also patients rejecting any anaesthesia but LA and accordingly were excluded before randomization.
When excessive synovitis is present LA might not be the first choice, since this was the case when patient and surgeon agreed on LA not being an optimal anaesthesia for the procedure. Another aspect of LA is that the vasovagal reaction is always at risk when the patient is wake. An intra-venous access is recommended in surgery

under LA, not only to administer atropine, but also to give additional anxiolytics and/or analgesics when needed.

The majority of the LA patients experienced no or mild intra-operative pain. Still their pain rating, and the technical difficulties reported during surgery were statistically more intense compared to the GA and SA patients. Some discomfort may be acceptable intraoperatively , but peri-operative pain is hardly acceptable from neither the patient's, nor the surgeon's points of view. Pain during surgery may not only be distressful but also result in a less complete and successfully performed surgery. Interestingly we found patients considering LA optimal, still reporting VAS pain scores above 30 mm. A pain score of more than 30 mm is generally not acceptable (Collins et al 1997). This indicates that pain and nausea are not the only variables involved in assessing satisfaction with procedure.

The performing surgeons in these studies were all specialists in orthopaedic surgery (no teaching was at the time performed at the clinics involved in the studies), however the least experienced seemed to have caused more pain intraoperatively, which may also have influenced outcome (surgery not completed ?). Ten of the 20 patients reporting their knee problems as worse six-months after surgery had had the same performing surgeon (n.s.). This can be an implication that knee arthroscopy under LA may be reserved for surgeons with a vast arthroscopic experience for best results.

Eighty-one percent of the SA patients were satisfied with the procedure, still it should be remembered that the eventually operated patients in SA were strictly selected. GA was highly accepted by both patients (97 %) and surgeons, and there were few complications with this technique, in accordance with other studies (Cardosa et al 1994). GA does however carry inherent risks, such as aspiration (Wetchler ed 1988).

Postoperative period

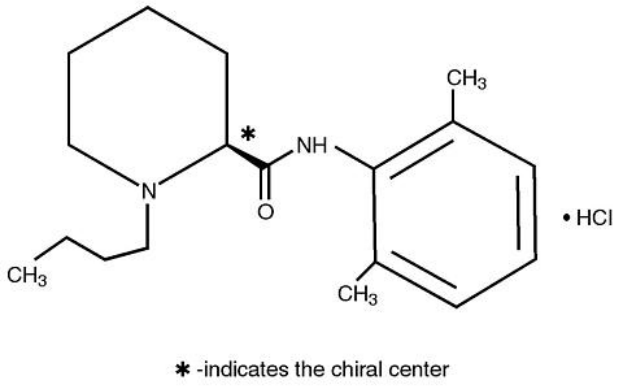
The postoperative course can, as mentioned in the introduction, be divided in different parts. Important factors for all the phases of recovery are avoidance of pain and side-effects related to anaesthesia and surgery.

We studied the early recovery, the period in hospital, but perhaps even more important, the first 24 hours, as well as the first four days following the procedure. We did choose intake of any analgesics during the first 24 hours following surgery as a primary study endpoint. This is a primary efficacy variable maybe even more important than VAS grading only. It is important to notice that not only the use of analgesics was studied, the secondary study objective was the pain experienced as described by VAS.

Local anaesthetic

In surgery under LA each of the portals are infiltrated with about 7 ml local anaesthetic with adrenaline and the rest is injected into the joint; to a total of 40-60 ml. In surgery under GA or SA the portals in the skin are likewise most often injected with LA to avoid skin bleeding intraoperatively.
In recent years it has become more or less praxis to immediately after surgery inject another 10-20 ml of local anaesthetic in the joint for postoperative pain management, regardless of used anaesthetic technique
Intra-articular bupivacaine was shown as early as 1989 to be an effective and safe analgesic after arthroscopic meniscus resection (Chirwa et al 1989). Today intra-articular injection of local anaesthetics and other adjuvants has become normal practice during arthroscopy to reduce postoperative pain. The optimal choice of postoperative local anaesthetic to be used in day surgical arthroscopy of the knee is, however, not well-defined. While levobupivacaine 5 mg/ml was found to be superior to both 2.5 mg/ml levobupivacaine, and lidocaine-adrenaline when evaluating the entire first 24 hours following surgery. The positive findings regarding the higher levobupivacaine group, a threefold increase in the number of patients not needing any further pain medication after surgery, may not be so unexpected as compared to lidocaine, having a far shorter duration of action than the bupivacaine analogues. However, it is important to notice that we also found a clinically relevant dose/concentration effect: 20 ml of 2.5 mg/ml did not provide adequate analgesia during either the early postoperative or the entire 24-hour postoperative period. This finding is to some extent contradictory to a recent study that found the same analgesic effect with different concentrations of

levobupivacaine, however the total amount of levobupivacaine in that study was the same in both groups (Dernedde et al 2003).
When studying the time in the hospital regarding need for rescue analgesics, lidocaine-adrenaline was as effective as levobupivacaine.



Levobupivacaine.

Levobupivacaine

Levobupivacaine, the levo form of the racemic mixture bupivacaine, is a long-acting local anaesthetic with a clinical profile very closely resembling that of bupivacaine but with a far safer cardiotoxicity profile (Foster et al 2002, Gristwood et al 2002). Its use as an analgesic has not been clinically compared to lidocaine, nor has it earlier been studied in conjunction with arthroscopy.
In general levobupivacaine has been shown to be more or less equally effective as bupivacaine, when used for caudal blocks in children and is effective for scalenic blockade (Ivani et al 2002, Sinardi et al 2002). It has also been shown to be comparable to ropivacaine (Casati et al 2003). We did not include any bupivacaine groups in the study and are therefore not able to confirm levobupivacaine's similarities to racemate bupivacaine.

One double-blind placebo-controlled comparison of bupivacaine and prilocaine showed no major differences in the need for postoperative analgesics between active drug and placebo (Ates et al 1994). Also a more recent double-blind placebo-controlled study failed to demonstrate any decrease in VAS scores at eight hours and later postoperatively when 20 ml of ropivacaine 0.5% was injected intra-articularly after day-case knee arthroscopy performed under spinal anaesthesia (Santanen 2001). Furthermore, these authors found no significant difference in the need for postoperative pain medication between the study groups. A systematic review of the literature on local anaesthetics injected intra-articularly from 1999 concluded that the effect of intra-articular local anesthesia indeed is relatively weak and short lasting (Moiniche et al 1999).

Our results should of course be put into perspective. The pain recordings at 24-hour were sufficiently intense to distinguish the analgesic effects of the local anaesthetics (Kalso et al 2002).

The volume of injected local anesthetic, has not been examined here. The volume effect, dilution per se, should not be entirely neglected. Pure saline (10 ml) has been shown to be equally effective to intra-articular morphine when administered at pain intensity of 50 on a scale from 0 to 100 (Rosseland et al 2003).

Oral analgesics

There were only small differences between the groups with respect to postoperative pain in study I. However, significantly more patients in the LA and GA groups did not use analgesics postoperatively compared with patients in the SA group. It is interesting that the only postoperative analgesic used in this first study was paracetamol, and in a modest dose: a vast majority of patients used no more than 6 tablets (3 g). In study III more patients requested postoperative analgesics. This difference is beyond the scoop of this thesis to explain; but maybe the preoperative information and the access to analgesics, play a role.

The introduction of the more selective COX-II-inhibitors (coxibs) was for some years heavily promoted because of their potentially lower side-effect profile. One of the most popular, rofecoxib, has been shown more effective than diclofenac,

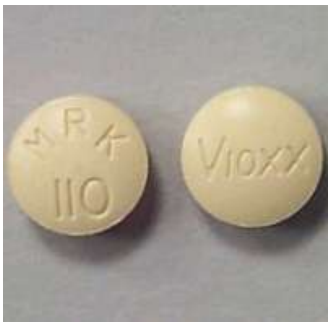
traditional oxycontin/paracetamol as well as codeine for the treatment of acute pain and with a better side-effect profile (Chang et al 2001, 2002, Korn et al 2004). Further studies have, however, been requested in order to prove more accurately the cost-benefit of these new, more expensive anti-inflammatory agents in postoperative pain management (Cicconetti et al 2004). Even more important, recently major concerns have been raised as to the unselective use of the coxibes also in the perioperative period (Okie 2005).Our study was however initiated while the coxibs had no restrictions for use.

Oral diclofenac has been shown to be more effective than intra-articular ropivacaine in reducing VAS scores beyond eight hours postoperatively (Rautoma et al 2002). An NSAID is often prescribed for reducing postoperative synovitis.
The potential risk for side effects associated with NSAID's should not be entirely neglected. In a survey of drug related side effects, NSAID's were found to be the third most common drug with reported adverse events in ambulatory care (Gandhi et al 2003).

Choice of anti-inflammatory agent

There are two main findings in study III. First it acknowledges the fact that also minor surgical procedures, such, as elective outpatient knee arthroscopy is associated with postoperative discomfort requiring medication for pain during several days after surgery. Looking at the entire study period more than every other patient used at least one paracetamol additional to the basic prescribed anti-inflammatory drug. This finding is somewhat contradictory to study I, but one must remember the difference in patient population between the studies. Second there is, indeed, no further benefit in using the new more costly and potentially risky coxibs for regular medication against pain and inflammation, following outpatient knee arthroscopy.
We did choose an anti-inflammatory agent as the first line medication in order to give both pain relief and to limit postoperative synovitis. The aim of our study was to compare the effect of a traditional NSAID to a more selective coxib during the first four days following surgery, in seemingly equipotent doses (Romsing et al 2004). Rofecoxib is known to have a long duration of action and is used in one dose

a day only, whereas the conventional NSAIDs have shorter duration of action and is usually prescribed twice, or even three times a day, as for diclofenac. The present study was started with the hypothesis coxibs being more effective with respect to 24-hour pain relief, and therefore reduced need for rescue analgesia, as compared to standard NSAIDs, with known shorter duration of action, as suggested by some (Chang et al 2001, 2002). Our results with regard to the pain alleviating effects may indeed not be that surprising. We studied what is considered equipotent daily doses. Also others have shown similar analgesic efficacy for traditional NSAIDs and coxibs, and there are also others suggesting that the conventional NSAIDs are the rational choice for short-term acute pain management before the coxibs (Chen et al 2004, Jeske et al 2002).



Vioxx tablets.

Rofecoxib (Vioxx©) was released on the Swedish market year 2000 indicated for pain management in arthritis, and the year after it was a top-selling product. During the first years of the new millennium rofecoxib as well as other coxibs were also strongly promoted for acute postoperative pain management. This study was started before the alert on adverse cardiovascular events related to the coxibs (Bresalier et al 2005, Nussmeier et al 2005). We still find it of importance to report our overall results both from an ethical point of view, as well as some of the results can be seen and used from a more general pain management perspective, especially as the coxibs still is in common use.

The coxibs – other effects

A recent article questions the use of coxibs as an alternative to traditional NSAIDs in another respect (Warden et al 2005); coxibs are detrimental to tissue-level repair in animal models of acute injury. Specifically they have been shown to impair the return of mechanical strength following acute injury to bone, joint and tendon. However, the coxibs do not appear to categorically affect ligament healing (Hanson et al 2005).

Safety

The present study is, of course, far too small to evaluate safety. When considering side-effects the duration of therapy should of course be taken into account. The risk for gastrointestinal side-effects from short term postoperative use of NSAIDs have been questioned (LeParc et al 2002).The risk for a severe NSAID-induced gastrointestinal bleeding during a maximum four-day treatment in preferably young and otherwise healthy patients (ASA I-II) may be considered very low**.** The surgical stress of a knee arthroscopy is probably also low, not enhancing ulcer development. The coxibs are associated with serious and potentially fatal side effects, mainly from the cardiovascular system. The majority of cardiovascular events related to coxibs were reported in long term/chronic use. There are, however, reports on cardiovascular adverse events following postoperative treatment with coxibs (Hersh et al 2005). Although the negative cardiac vascular outcome was reported following heart surgery, the potential pro-coagulant effects has also been suggested just after one dose in ordinary patients undergoing minor surgery (Naesh et al 2005). As expected we could see no difference in side-side effects between the two groups studied. This should of course be seen in the perspective of the limited number of patients and days studied.

Rescue analgesics

Postoperative pain after knee arthroscopy does not seem to be so severe motivating the prescription of heavy analgesics. Probably is it sufficient with a

combination of paracetamol and a NSAID, maybe enhanced by raising the limb. It is, however, of importance to inform the patient that pain during the first two days after surgery usually requires medication to avoid false expectations.
We found rescue analgesia requiring pain in more than 25 % of the patients studied during the first 24 hours following surgery which is similar to findings by other authors (McGrath et al 2004, Rawal et al 1997). We considered a pain rating of 4 or more to be unacceptable and thus rescue requiring medication, according to our hospital routine. The chosen level for compulsory medication can be questioned as high (Collins et al 1997), but in the outpatient situation this may be tolerated if you have to consider the effects on heavy pain medication close to discharge. Naturally all patients got rescue medication on request, regardless of pain rating.

Outcome.

Outcome

Six months after surgery the patients satisfaction rate does not depend on the type of anaesthesia used. The patient's satisfaction with the knee arthroscopy reflects a variety of components; diagnosis, preoperative information, expectations, skill of performing surgeon, choice of anaesthesia, postoperative pain management, postoperative information and the confidence of staff involved in the procedure. The independent effect of the anaesthetic technique used intraoperatively on the satisfaction of the patient six months following elective

knee arthroscopy is limited, or even non-existing. Surgical indication in combination with patient's expectation, have a major impact on postoperative satisfaction. Pre- and postoperative information is of great importance for the patient's evaluation of the effects of the knee arthroscopy, especially in the case of osteoarthritis. A patient having just a partial meniscus resection is expected to have a high satisfaction rate at six months, more or less regardless of information. However, if osteoarthritis is present at the time of the meniscal resection, this may not benefit the patient; it can even accelerate the symptoms of the osteoarthritis (Englund M, 2004).

The incidence of recurrent surgery is technically the most important factor regarding outcome after surgery. There is a common opinion that surgery can be difficult and not complete under LA. Our results with respect to both patient satisfaction and need for re-intervention is overall low, which is in agreement with other authors (Forssblad et al 1999).

Health economics.

Economy

Health economics of ambulatory surgery have frequently been studied (Dolk et al 2002, Heidvall et al 2000, Rockborn et al 2000) and LA is proven to have advantages in cost and efficacy (Forssblad et al 2004, Linter et al 1996). However, in Forssblad's study an office-based setting for LA is compared to an outpatient GA

set-up. It is actually the presence of an anaesthesiologist that makes the difference in cost. This presence defines that the knee arthroscopy always can be performed completely, and without any discomfort for the patient, or the surgeon. All orthopaedics surgeons, no matter how experienced in knee arthroscopy under LA, occasionally are forced to work under stress, when LA suddenly does not provide sufficient anaesthesia during surgery. In such situation the office-based LA setting has a major draw-back since you cannot supplement the given anaesthesia to a full GA if necessary.
Patient safety also talks for the present anaesthesiologist – vasovagal reactions can be hazardous and difficult to deal with for the orthopaedic surgeon her-/himself.
The use of a NSAID postoperatively in combination with the least expensive paracetamol, is a valid choice in terms of cost-minimisation; in Sweden the 24-hour-cost for the coxibs is twice that of a regular NSAID (FASS 2005).
Levobupivacaine is today more expensive than bupivacaine, but less toxicity and flexibility in packing may be economically advantageous in the long run.

Different perspectives

There are other ways of categorizing all our collected information. One perspective would have been *quality* measured in different pain parameters (on VAS, need for rescue medication or influence on daily life activity, street-fit or work-fit). Another view could have been on the surgical outcome, which can be related to the disease itself, to the performed surgery or to the patient her/himself. In the presented studies we concentrated on the latter opinions of the patient, which reflects both personal experiences and expectations.

General population.

Study sites – demographics

The present thesis is based on studies performed at two different clinics.
In study I and IV at the Artro clinic we studied a selected group of patients, in study II and III the inclusion criteria was not as strict (only ASA I-II). The Artro clinic is well-known for being specialized in sports trauma, the Sabbatsberg's hospital is considered a general orthopaedic clinic, which might influence patient selection and maybe also expectations. The clinics are similar in that respect that they are elective, non-university clinics with no teaching responsibility where the orthopaedic surgeons perform a lot of arthroscopic surgery, which has the probable effect that the duration and trauma of surgery are minimized. At the time of the studies both clinics used three portals as routine for surgery, this had probably influence on pain rating.
Comparing demographics and patient motivation for study participation in all the four studies, do not reveal any major differences between the two clinics. To further analyze if there are differences between the two clinics, we are currently performing an outcome study also at the Sabbatsberg's hospital. This is executed by a questionnaire like the one used in study IV. The preliminary results from this present study are similar.

Conclusions

The present thesis addresses the anaesthetic technique, the postoperative pain management and the outcome. It does not deal with the initial preoperative phase, including the information given to the patient before, or after surgery. The motivation and opinion of the patient determines the choice of anaesthesia for outpatient knee arthroscopy. It is definitely an advantage for every clinic to be able to offer general and local anaesthesia since both have obvious advantages, but from different perspectives. Spinal anaesthesia does not seem to have a place in outpatient knee arthroscopy, since it is not an anaesthetic favoured by the patients, and it also does not make immediate discharge after surgery possible.
The choice of anaesthetic technique did not show any impact on late patient satisfaction and risk for recurrent surgery.
Long-acting LA in a higher concentration given at the end of surgery in the joint accomplishes effective analgesia, and reduces the need for rescue analgesics during the first, most painful, 24 hours postoperatively.
A combination of paracetamol with a traditional NSAID is a valid recommendation following outpatient knee arthroscopy as a baseline pain medication. The more costly coxibs have no advantage to the traditional NSAIDs in the initial postoperative pain management.
Studies from two different orthopaedic clinics have showed similar results regarding patient satisfaction, pain management and outcome.

Suggested guidelines

Summarizing the performed prospective, randomized studies might result in guidelines for outpatient knee arthroscopy; surgery is best performed under general or local anaesthesia and immediately after surgery a local anaesthetic with a long duration should be applied in the joint. Analgesic requiring pain is frequent also after minor procedures as outpatient knee arthroscopy. Providing a "booster dose" of a long-acting local anaesthetic in a higher concentration, e.g. levobupivacaine 5 mg/ml intra-articularly, at end of surgery, seem to be an effective way of reducing discomfort and severe pain during at least the first 24 postoperative hours. Nonetheless, patients should have access to pain-killers after surgery in order to avoid pain. Paracetamol and/or a conventional NSAID, like ibuprofen, are sufficient for postoperative pain management in a vast majority of patients. Still one should have in mind that there is a small group of patients experiencing a not tolerable pain regardless of this baseline medication.

Summary of conclusions of thesis

- Local anaesthesia is a valid alternative in a selected group of motivated patients in outpatient knee arthroscopy
- Long-acting local anaesthesia in higher concentration given immediately postoperatively in the joint, reduces the need for rescue analgesics during the first 24 postoperative hours in outpatient knee arthroscopy
- Analgesia requiring pain is frequent and patient undergoing outpatient knee arthroscopy must have access to analgesics for up to four days after surgery
- There are no obvious advantages with the more costly coxibs compared to conventional NSAIDs as postoperative analgesic in outpatient knee arthroscopy
- The anaesthetic technique has not proved to have any impact on the overall surgical outcome following elective knee arthroscopy

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