Chapter 8

Summary and General discussion

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Summary

In this thesis we investigated risk / benefit issues of a combined psoas compartment sciatic nerve block (PCSNB) for patients undergoing prosthetic hip surgery. In chapters 2-4, we explored the clinical benefits of a PCSNB for prosthetic hip surgery. In chapters 2, 5-7 we evaluated undesirable side effects and complications of a PCSNB. Results of our studies should help improve on existing knowledge with regard to risks and benefits of a PCSNB for anesthetic and analgesic strategies in patients undergoing prosthetic hip surgery (main objective).

In chapter 2 we concluded that for postoperative analgesia, PCSNB is an alternative to neuraxial block and is superior to both IV opiates and the anterior approach of the lumbar plexus block (femoral nerve block, ‘3-in-1 block’). For intra-operative anesthesia, there is, however, insufficient evidence to support the use of PCSNB combined with sedation as an alternative to general anesthesia or neuraxial anesthesia. With respect to undesirable side effects or complications, this review of the literature reported a low incidence of complications. Most frequent undesirable side effect was epidural diffusion of local anesthetics (incidence 3 – 27 %) and pharmacokinetic studies reported that bolus and continuous administration of local anesthetics into the psoas compartment is safe.

In chapter 3 we reported that a single injection PCSNB resulted in sufficient postoperative pain relief for patients undergoing a total hip arthroplasty under general anesthesia. A low consumption of rescue opioids provided support for the adequate analgesic potency of a PCSNB for patients undergoing a THA. The non-racemic levobupivacaine and ropivacaine, showed, in equipotential doses, the same analgesic potency compared to reacemic bupivacaine. We described a lack of sensory block in dermatome L1 which could be the
reason for some residual pain located at the upper part of the incision, regardless of the local anesthetic used. To counter this problem and to optimize a PCSNB for prosthetic hip surgery, a modification of this technique such as a continuous PCSNB or an additional subcostal or paravertbral block, should be considered. The duration and intensity of the motor impairment was more pronounced after a PCSNB with bupivacaine, making this local anesthetic less suitable.

In chapter 4 we concluded that a continuous PCSNB resulted in low pain scores. However, the hypothesis that a continuous PCSNB using a stimulating catheter through a cephalad directed Tuohy needle, infusing large volumes of local anesthetics, should lead to a more extended psoas compartment block, could not be supported. The height of the sensory block was comparable with data from single injection PCSNB – studies. The continuous PCSNB described in this study was characterized by a slow onset, which could be the result of a relatively low dose of local anesthetics in the initial bolus. A stimulating catheter used in this study was of limited benefit because in most cases, motor response disappeared during advancement of the catheter while stimulating.

In chapter 5-7 we described our investigations concerning possible undesirable side effects or complications associated with a PCSNB. There were two areas of interest: at first we analyzed the total plasma concentrations of used local anesthetics in a PCSNB to assess the risk of toxicity. At second, undesirable hemodynamic side effects and cardio - electrophysiologic consequences of a PCSNB were reported.

In chapter 5 we presented low local anesthetic total plasma concentrations after a PCSNB with maximum recommended doses bupivacaine, ropivacaine and levobupivacaine. Total plasma concentrations remained far below described threshold-values to produce central
nervous system- or cardiac toxicity, suggesting a wider margin of safety with regard to administrable volumes and doses. Initial systemic absorption of levobupivacaine was slower than bupivacaine and ropivacaine, although total absorption of three local anesthetics during the first 4 hours post block did not differ. This could be explained by a more vasoconstrictor effect of levobupivacaine making this local anesthetic more favourable when using large doses of local anesthetics in a PCSNB.

In chapter 6 we reported no overall changes in cardiac index in patients undergoing a PCSNB. We described a small, but significant, reduction of the stroke volume index after the PCSNB, which was probably the result of a reduction of preload and afterload due to vasodilatation in the anesthetized limb (hemisympathectomy). This was in accordance with the observation of a decrease in mean arterial blood pressure and diastolic blood pressure after a PCSNB. The changes in arterial blood pressure, although statistically significant, remained within a clinically acceptable range. The clinical relevance of observed hemodynamic changes after a PCSNB might be questioned.

In chapter 7 we reported a significant postoperative QTc interval prolongation after a PCSNB with levobupivacaine, ropivacaine or bupivacaine, in combination with general anesthesia, with the following drugs: fentanyl, thiopental, succinylcholine and sevoflurane. We also described a more pronounced QTc interval prolongation just after the induction and PCSNB in a subgroup analysis. To exclude confounding factors such as above mentioned general anesthesia induction and maintenance drugs, which all could be of any influence of the QTc interval, we analyzed in five patients QTc dynamics after a PCSNB without general anesthesia. Although the QTc interval prolongation after this ‘stand alone’ PCSNB was statistically significant as well, it was significantly lower compared to the QTc interval prolongation of the combined group.
In chapter 8 we described the summary and general discussion of this thesis.
General discussion

Patients undergoing prosthetic hip surgery often report substantial early postoperative pain at rest, which is aggravated by movement $^{1-3}$. This substantial pain could result in a significant stress, associated with undesirable hemodynamic side effects such as tachycardia and hypertension, in a patient with often a low tolerance for these side effects (advanced age, cardiovascular co-morbidities, diabetes etc.). Furthermore, postoperative pain impedes wound healing, ambulation, physiotherapy and recovery, resulting in a prolonged hospital stay. Finally, significant postoperative pain could be a possible predisposing factor of the development of chronic pain $^4$. Therefore, adequate postoperative pain relief is instrumental to the rehabilitation process and the well being of the patient undergoing prosthetic hip surgery. Analgesia for prosthetic hip surgery is traditionally provided by intravenous analgesics (opioids) or epidural analgesia $^5, 6$. An alternative analgesic regimen is a posterior lumbar plexus block or psoas compartment block, with or without a sciatic nerve block, which could provide similar analgesic potency with regard to hip surgery $^5, 7-9$. Although this peripheral nerve block is not associated with the disadvantages of intravenous opioids (pruritus, nausea and vomiting) or epidural analgesia (hypotension, extended motor block, urinary retention, risk of epidural hematomas when using anticoagulants), it is used less frequent for prosthetic hip surgery $^6, 10$.

In this thesis, we outlined the clinical benefits (chapter 2-4) and a risk analysis (chapter 2,5-7) of a PCSNB for patients undergoing prosthetic hip surgery, in order to put this peripheral nerve block technique in a right perspective for this kind of surgery.
The clinical efficacy of a PCSNB for patients undergoing prosthetic hip surgery.

An overview of the literature showed that a single injection PCSNB result in low postoperative pain scores and a reduced consumption of postoperative rescue opioids in patients undergoing prosthetic hip surgery \(^7,11\) (chapter 2). This was in accordance with our results of the clinical efficacy analysis of a single injection PCSNB, presented in chapter 3. Maximum recommended doses of levobupivacaine, ropivacaine and bupivacaine resulted in equally low postoperative pain scores and a low consumption of rescue parenteral opioid consumption. However, a single injection technique has some limitations regarding the duration of this beneficial effect. Pooled data from Biboulet et al. and Stevens et al. indicated no significant differences in pain scores after 8 hours post block between posterior lumbar plexus block and IV opioids, although opioid consumption remained significantly lower in the posterior lumbar plexus group \(^7,11\) (chapter 2). In our clinical efficacy analysis of the single injection PCSNB, we concluded that some residual pain could be the result of a lack of analgesia in dermatome L1 and we hypothesized that a continuous PCSNB (with a more cephalad positioned catheter) could achieve a more extended block countering this problem (chapter 3). In a clinical observational study, we analyzed the clinical efficacy of a continuous PCSNB using a stimulating catheter (chapter 4). The outcome of this study could not support the above mentioned hypothesis; in general, the dermatome L1 remained unaffected and the (low) pain scores did not differ from the single injection PCSNB group during the first 24 hours post block. We concluded that a sensory block of L1 is difficult to achieve with either a single injection PCSNB nor a continuous PCSNB using the Chayen (L4-L5) approach with a nerve stimulator. A possible explanation for this is the anatomic location of the lumbosacral plexus. Kirchmair et al. reported that in the majority of cases, the lumbosacral plexus lies within the psoas major muscle, and not inside a sheath between the muscles \(^12\). The absence of a nerve
sheath between muscles could prevent a cephalad advancement of a stimulating catheter. The loss of motor response in 8 out of 10 cases during advancement of the catheter and the radiographic control of the catheter tip using contrast medium (contrast was found below L1 in the majority of the cases) supports the latter hypothesis (chapter 4).

This lack of blockade of dermatome L1 also could be the reason that this PCSNB seemed to be insufficient for as a stand-alone anesthetic technique for intra-operative anesthesia. In the meta-analysis we concluded that there is insufficient evidence to support the use of a PCSNB and sedation as an alternative to general anesthesia or spinal anesthesia for hip surgery 13, 14 (chapter 2). In addition, Mannion et al. described the psoas compartment block as an “unreliable method for anaesthesia for major hip surgery” due to the variable innervation of the surgical site from the T12 and L1 dermatomes 15.

Motor impairment is another important clinical efficacy issue because extended motor block also could impede early mobilisation. Early mobilisation is associated with a decreased risk of venous trombo-embolism and shorter hospital stay as well as improved quality-of-life outcomes 16. In the single injection PCSNB, most extended motor block was found during the first 8 hours post block, regardless of the local anesthetic used (levobupivacaine, ropivacaine or bupivacaine). The duration of the motor impairment was significantly longer in the bupivacaine group, compared to levobupivacaine and ropivacaine, making bupivacaine less favourable for a PCSNB (Chapter 3). However, after the first 8 hours, the extent of the motor block was reduced. Therefore, interference with physical therapy on postoperative day 1 was not an issue. The continuous PCSNB study showed less motor impairment during the first 8 hours post block, compared with the single injection PCSNB study, which could be explained by a lower initial dose of local anesthetics in the continuous PCSNB group. The duration of the motor block, although very mild, was significantly longer in the continuous
PCSNB group (Chapter 4). In general, motor impairment in both studies was mild and was not an impeding factor in the rehabilitation process.

The undesirable side effect profile or complications of a PCSNB.

In technically successful performed PCSNBs, i.e. without inadvertent intravenous or subarachnoidal administration of local anesthetics, toxicity remains a point of concern. As the lumbosacral plexus is located within highly vascularised muscle tissue, initial systemic absorption of local anesthetics after a PCSNB could be substantial, theoretically enhancing the risk of local anesthetic toxicity. In chapter 5 we described that total plasma concentrations of bupivacaine, ropivacaine and levobupivacaine, analyzed after a single injection PCSNB, remained far below described threshold values to produce central nervous system (CNS) - or cardiac toxicity 17-19. In addition, none of the 45 studied patients showed any clinical signs of CNS- or cardiac toxicity. Vanterpool et al. underscribed the prevalence of low plasma concentrations of local anesthetics after a PCSNB using 300 mg ropivacaine 20. Adding epinephrine to the local anesthetic solution resulting in a local vasoconstriction, as suggested by Odoom et al., has had a positive influence on reducing total plasma concentrations and should be the standard of care (unless there are contra indications) 21. Furthermore, manufacturers’ recommendation regarding maximum doses for a single injection peripheral nerve block could be questioned. The low plasma concentrations as measured in our study indicate that dosages exceeding the recommendations are required to reach plasma levels associated with systemic toxicity. However, incidental high plasma concentrations measured in this study, makes vigilance regarding toxicity signs obligatory. The pharmacokinetic profile of levobupivacaine (slower initial absorption compared to ropivacaine and bupivacaine) makes this local anesthetic more favourable for PCSNB, compared with bupivacaine and ropivacaine.
Cardiotoxicity can also be expressed by cardiac nerve conduction disorders. In chapter 7 we described a clinical observational safety assessment, evaluating QTc interval dynamics after a PCSNB with or without general anesthesia. We reported a significantly QTc interval prolongation after a PCSNB combined with general anesthesia. QTc interval prolongation after a PCSNB without general anesthesia was significantly lower in five consecutive patients, compared to the combined group. However, post block QTc intervals were significantly prolonged compared to baseline values. The QTc prolongation seemed to be more influenced by the used general anesthesia related drugs like thiopental, succinylcholine and sevoflurane, but a synergistic effect could not be ruled out and more randomized controlled studies are required to assess the contribution of each of these drugs to this phenomenon 22-24.

Hemodynamic changes after a PCSNB could theoretically be a reflection of a cardiotoxic reaction. Bardsley et al. reported a significant decline of stroke volume index after intravenous administration of local anesthetics in healthy human volunteers 17. Measured local anesthetic plasma concentrations related to this phenomenon were comparable with the values after a single injection PCSNB as we described in chapter 5. However, cardiovascular changes after a PCSNB remain understudied. In chapter 6, we described hemodynamic changes during a single injection PCSNB. We reported a minor decline in stroke volume index, probably caused by a hemisypathectomy due to the PCSNB. A concomitant minor decrease in invasive mean arterial blood pressure (-10%) supported this hypothesis. Although cardiac output remained stable and clinical relevance of these small changes should be questioned, one should be cautious for patients with a low tolerance for blood pressure drops (severe coronary artery disease, aortic valve stenosis). In general, hemodynamic changes remained within an acceptable clinical range.

The incidence of bilateral- or epidural spread of the injected local anesthetics after a PCSNB varies from 3-27% and has been reported to be the most frequently observed unwanted side
effect of this technique (Chapter 2). It was previously thought that the approach was the major determinate of the epidural spread. A more cephalad, and closer to the midline approach described by Dekrey et al., has an incidence of epidural spread of 16-27%. In contrast, the Chayen approach, more lateral and distal than any other approaches, has a reported incidence of 1.5-5% of bilateral spread. More recently, Gasden et al. suggested that the cause of bilateral spread is not related to the approach, but more to high injection pressure. In addition, Mannion et al. suggested that the use of high volumes of local anesthetics in a psoas compartment block increases the risk of bilateral spread. However, the latter hypothesis was not supported by the experimental findings. In this thesis, we used the Chayen approach with large volumes of local anesthetics (30-40 ml) in three different studies. In chapter 3, we reported bilateral spread in 1 out of 45 study patients. However, in this study we could not evaluate a possible bilateral spread during the first two hours post block because of the fact that patients were anesthetized; therefore reported occurrence of epidural spread in our study could be an underestimation. In chapter 4 we evaluated 10 patients with a continuous PCSNB. None of these patients showed any signs of a bilateral spread. In chapter 6, we evaluated 20 patients after a single injection PCSNB without any occurrence of bilateral spread. Avoidance of high pressure injection during the single injection PCSNB is the standard of care in our institution. Furthermore, it is impossible to generate high pressure using a small bore catheter we used in the continuous PCSNB (chapter 4). In our opinion, the incidence of bilateral spread after a PCSNB using the Chayen approach without high pressure injection of local anesthetics is low and in accordance with other reports using the same approach.

Major complications after a psoas compartment block were described by Auroy et al. Five serious complications (1 cardiac arrest, 2 respiratory failure, 1 seizures and 1 death) after 394 performed psoas compartment blocks were reported. In contrast, only 3 minor complications
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(neuropathies) were reported after 10,309 femoral blocks. These major complications were all associated with inadvertent intrathecal-, high epidural-, or intravascular administration of high volumes of local anesthetics. Although in this thesis we did not find any of these major complications, one should be cautious about the possibility of injecting large volumes of, potentially cardiotoxic, local anesthetics, resulting in potentially life threatening circumstances.

The risk / benefit evaluation of a PCSNB with regard to analgesic management for patients undergoing prosthetic hip surgery.

A PCSNB provides sufficient postoperative analgesic potency with regard to prosthetic hip surgery. There is evidence that a PCSNB resulted in low postoperative pain scores (at rest and movement) and a low consumption of rescue opioids in patients undergoing a total hip arthroplasty (this thesis). Compared to alternative pain relief regimens, like epidural analgesia and IV opioids, PCSNB is not associated with unwanted side effects of former techniques. The risk profile of a PCSNB is very mild. Toxicity remain a point of concern when large volumes of cardiotoxic local anesthetics are administered to highly vascularised tissues, but this thesis showed that total plasma concentrations after PCSNB remain far below described toxicity thresholds and cardiac nerve conduction minimally influenced by the PCSNB as a stand alone anesthetic technique. This thesis also provided evidence for the cardiovascular stability of the PCSNB. Cardiac output remain stable and minor hemodynamic changes were considered to be within acceptable clinical ranges whereby clinical relevance should be questioned. Finally, this thesis confirmed the low incidence of epidural spread using the Chayen approach for a PCSNB. Given the risks and benefits, described in this thesis, we concluded that a PCSNB can be recommended for patients undergoing prosthetic hip surgery.
However, some remarks regarding above mentioned conclusion have to be made. Firstly, the risk / benefit evaluation has been performed for the clinical efficacy of the PCSNB as postoperative analgesic regimen. In our opinion, there is no place for a PCSNB as stand alone intra-operative anesthetic regimen (i.e. without general anesthesia or central neuraxial block) for prosthetic hip surgery. Secondly, some disadvantages of this technique have been reported in this thesis in cases were a PCSNB was performed in anesthetized patients. In Chapter 3, the inability to evaluate the block or the unwanted side effects (epidural spread) in patients during the period of general anesthesia is described, and in chapter 7 more pronounced cardiac nerve conduction delays in the same patient group were reported. Although there is no evidence that performing PCSNB in anesthetized patients is less safe than in awake patients, the standard of care in our hospital nowadays is to perform PCSNBs in awake patients. Finally, the technical aspects of a PCSNB deserve some attention. As a part of the safety management for PCSNBs in our studies, we added epinephrine to the local anesthetic solution as intravascular marker. Furthermore, prior to injecting the local anesthetics and repeated every 5 ml, we performed an aspiration test. Injection of local anesthetics under high pressure was avoided. These technical aspects should be considered as preconditions for the risk – benefit evaluation.

Limitations of the different studies.

Some limitations have to be mentioned with regard to the studies performed in this thesis. In the meta-analysis (chapter 2), most of the comparative studies were of low quality, frequently caused by methodological shortcomings (failure to describe the method of randomization or blinding). This had minor consequences for the evidence synthesis, resulting in lower levels of evidence, leading to lower strength of recommendations. In chapter 3, we analyzed the
clinical efficacy of a PCSNB using three long acting local anesthetics in a randomized trial. We did not introduce a placebo group in order to compare the clinical benefits of this PCSNB (with regard to prosthetic hip surgery) with a sham procedure. In chapter 4, we analyzed the clinical efficacy of a continuous PCSNB in an observational pilot study and compared the outcomes with an archival dataset (clinical efficacy study single injection PCSNB – chapter 3). The limitations of this study were the small number of patients and the absence of a prospectively gathered control group with a sham procedure.

In addition, limitations should be pointed out in the studies regarding the side effect profile of a PCSNB. In chapter 6, we analyzed the hemodynamic changes after a PCSNB in an observational study. We did not introduce a placebo control group with a sham procedure, which could be of additional value. In chapter 7, we analyzed the QTc interval dynamics after a PCSNB with or without general anesthesia. In both the “combined” group and the PCSNB without general anesthesia the number of analyzed patients was limited, therefore caution is warranted with regards to the results. Furthermore, we did not analyze the QTc interval dynamics of a PCSNB in a randomized, placebo controlled, study set up (with and without general anesthesia).

**Future Research**

In our opinion, several directions for future research regarding both clinical efficacy and side effect profile of a PCSNB, can be distilled from this thesis. With regard to the anesthetic potency, the lack of a sensory block in dermatome L1 remains the limiting factor for the use of a PCSNB as stand alone anesthetic technique (i.e. without general anesthesia, neuraxial blockade or sedation) for prosthetic hip surgery. Furthermore, analgesic potency of a PCSNB for prosthetic hip surgery could be improved by a more proximal blockade of the lumbar
plexus. Future studies will have to show whether a more proximal block could be achieved by using different approaches or additional nerve blocks. A more proximal needle insertion point (L2-L3) is less attractive due to the enhanced risk of kidney puncture. Nowadays, more proximal approaches could be investigated with the help of ultrasound guidance, therewith reducing the risk of inadvertent kidney puncture. Whether this more proximal approach under ultrasound guidance is sufficient to block higher lumbar dermatomes, should be investigated. Furthermore, to counter the above mentioned lack of anesthesia / analgesia in the L1 dermatome by the current PCSNB, an additionally applied nerve block, for instance a paravertebral L1/Th12 block may be of clinical benefit regarding this kind of surgery. Future studies will be necessary to evaluate the role of an additional block for prosthetic hip surgery.

Additional research is needed to evaluate the side effect profile of a PCSNB. In chapter 5 we analyzed total plasma concentrations of local anesthetics after a PCSNB and in chapter 6 we analyzed the hemodynamic changes after a PCSNB. A next step would be to couple both studies, i.e. to analyze plasma concentrations of local anesthetics after a PCSNB and to analyze the effect on cardiac performance. Incidentally, we measured high plasma concentrations and it would be very interesting to analyze cardiac output dynamics of these specific patients. In chapter 7 we described stable cardiac nerve conduction (QTc interval) after a PCSNB without general anesthesia. However, a PCSNB combined with general anesthesia resulted in a significant QTc interval prolongation. It would be of clinical relevance to evaluate the QTc interval dynamics after a PCSNB in combination with different general anesthesia related drugs, in a study with a larger sample size, in order to assess the safety of this combined technique.

Traditionally, a PCSNB is a high volume block. With regard to undesired side effects (toxicity, neuraxial spread) this high volume could be detrimental and clinical experience in recent years showed that lower volumes of local anesthetics would be sufficient for a PCSNB.
Nowadays, an increasing number of dose reduction studies of other peripheral nerve block can be found. However, this "dose reduction hypothesis" in a PCSNB remains understudied. In our opinion, a dose reduction study, with the assistance of ultrasound for PCSNB would be of clinical relevance with regard to the undesired side effect profile of this block.

Furthermore, national- and international prospective standardization with regard to data concerning side effect and complications of peripheral nerve blocks is warranted to further evaluate the risks of these interventions. The Auroy study in 2002 is a large scale study regarding complications of peripheral nerve blocks, which has frequently been cited in studies concerning clinical efficacy and risks of a PCSNB. In our opinion, this study deserves a follow up for adequate positioning of the PCSNB within the therapeutic spectrum.

Finally, it would be of clinical benefit to evaluate rehabilitation benefits, hospital stay, and short-term morbidity and mortality, as well as long term functional outcome, morbidity and mortality following PCSNB. Although in hip fractures studies the anesthetic technique is in general of minor influence with regard to morbidity and mortality, patient characteristics of this group differ from those undergoing elective total hip arthroplasty surgery. Therefore outcome studies focussing on the latter group would still be of great value.
References


