Abstracts - posterkonkurrence DASAIMs Årsmøde 2014

Postersession III

Abstract 10

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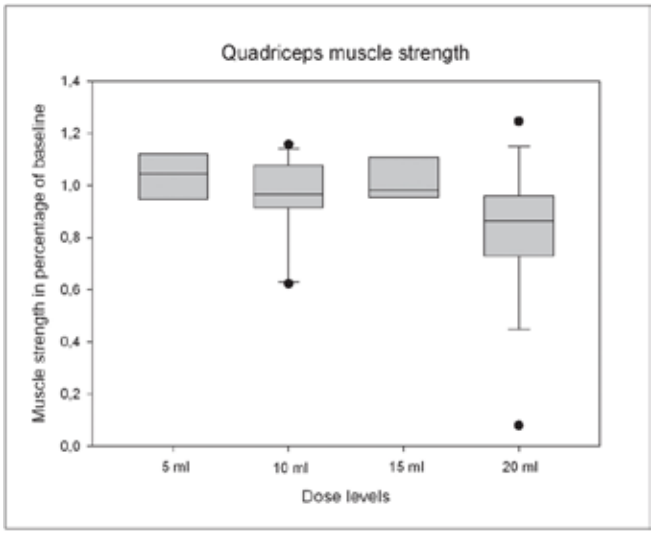
Titel Optimal volume of local anesthetics for the adductor canal block – using the continual reassessment method to estimate the ED95

Introduction
Theoretically, the optimal volume of local anesthetics for adductor canal block (ACB) would ensure sufficient spread throughout the canal as well as avoidance of proximal spread to the femoral triangle. In this dose-finding study we aimed to investigate the minimal effective volume needed to fill the adductor canal distally.

Methods
We performed a blinded, prospective trial, enrolling 40 healthy men. The continual reassessment method (CRM) was used to determine the ED95 for an ACB sufficient to fill the adductor canal distally as assessed by MRI (primary outcome). The adductor canal was considered to be filled if the injectate could be traced to the distal end of the canal in the MRI scans. Our a priori probabilities of distal spread corresponded to 0.5, 0.75, 0.90, 0.95, 0.98, and 0.99 for the respective dose levels of 5, 10, 15, 20, 25, and 30 ml of 1% lidocaine. Secondary endpoints were proximal spread into the femoral triangle and quadriceps muscle weakness (decrease by more than 25% from baseline). Clinicaltrials.gov identifier: NCT02033356.

Results
The ED95 ensuring distal spread was 20 ml, with a response probability of 95.1% (95% credibility interval: 0.91 to 0.98). Proximal spread to the femoral triangle was seen in: 0/4 (0%), 7/12 (58%), 4/8 (50%) and 8/16 (50%) of subjects, at the 5, 10, 15 and 20 ml dose levels, respectively. Seven subjects had a decrease in muscle strength, but there was no difference between the groups (P=0.85). However, figure 1 indicates that impairment may be more pronounced for 20 ml.

Conclusion
The dose closest to the ED95 of 1% lidocaine needed to fill the adductor canal distally with an ACB is 20 ml. The effect of volume on analgesia and muscle strength needs to be investigated in future studies.



Data are expressed as median (horizontal bar) with 25th to 75th (box) and 10th to 90th (error bars) percentiles.

Abstract 13

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Medforfattere	Joachim Knop, Merte Nordentoft and Henrik Kehlet on behalf of the Lundbeck Foundation Centre for Fast-track hip and knee replacement collaboration
Titel	Psychiatric disorders and psychopharmacologic treatment are risk factors in elective fast-track total hip and knee arthroplasty.

Introduction
A recent study found increased bleeding and postoperative morbidity in patients with perioperative use of selective serotonin inhibitors (SSRI) (1). However, patients with psychiatric disorder (PsD) have increased comorbidity and lower quality of health care (2), potentially influencing results. Furthermore, there are no studies on PsD in fast-track arthroplasty, which has reduced LOS without increasing postoperative morbidity (3).

Methods
A registry study in 7 arthroplasty departments with similar fast-track protocols, prospective data on preoperative characteristics, and 90 days follow-up through the Danish National Patient Registry and patient records. Information on psychotropic treatment was acquired from the Danish National Database on Reimbursed Prescriptions. Patients were stratified as PsD, "potential" PsD and no PsD respectively. (Fig. 1) Multiple logistic regression was used to analyze association between PsD and LOS >4 days, 30 and 90 days readmissions. Stratified analysis was done on psychotropic treatment (SSRIs, other antidepressants (OA), combination of SSRI with OA, and antipsychotic treatment. Validation of the results was done in a propensity matched cohort.

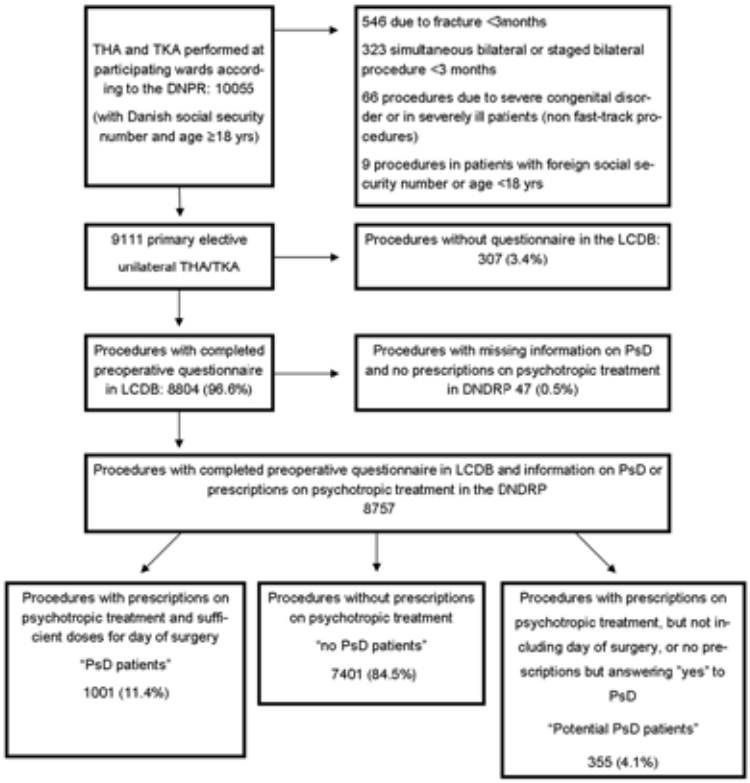
Results
Of PsD patients 43.4% used SSRIs, 31.6% used OA, 8.5% used a combination, and 16.5% used antipsychotics. Median LOS in all patients was 2 days, but PsD increased the risk of LOS >4 days (odds ratio: 2.00; 95% confidence interval 1.43-2.81), regardless of treatment with SSRIs, OA or antipsychotics.
90-days readmission rate was 8.3% with PsD being associated with both 30 and 90-days readmissions, significant for SSRIs and OA. The results were confirmed in the propensity matched cohort (table 1).
Pain (1.4%), postoperative anemia (1.1%) and pulmonary complications (1.1%) were the most common causes of LOS>4 days in PsD patients. Hip displacements (2.8%) and falls (1.9%) were the most common readmissions. 90-days surgically related mortality was 0.7% with and 0.2% without PsD.

Discussion
PsD has been found to impair postoperative outcomes. Whether this is due to drug-related side effects, increased burden of comorbidity or PsD per se is not well established. Our results found PsD to be associated with impaired postoperative outcomes, regardless of type of psychotropic treatment and despite adjusting for numerous preoperative characteristics.

Conclusion
PsD is an important independent risk factor for postoperative morbidity after fast-track THA and TKA. However, whether due to the underlying PsD or/and drug-related side-effects remains uncertain, calling for further studies of mechanisms and treatment strategies.

1. Perioperative use of selective serotonin reuptake inhibitors and risks of adverse outcomes after surgery Auerbach et al JAMA Int Med 2013;173:1075-81
2. Physical illness in patients with severe mental disorder I. De Hert et al. World Psychiatry 2011;10:52-77
3. Fast-track hip and knee arthroplasty Kehlet Lancet 2013 11;1600-2

Figure 1



DNPR; Danish National Patient Registry LCDB; Lundbeck Foundation Centre Database PsD; Psychiatric disorder
DNDRP; Danish National Database of Reimbursed Prescriptions

Table 1. Multiple logistic regression analysis

	LOS>4		30-days readmissions		90-days readmissions	
Variable	OR (95%CI)	P-value	OR (95%CI)	P-value	OR (95%CI)	P-value
PsD overall (n:911)	2.00 (1.43-2.81)	<0.001	1.93 (1.49-2.49)	<0.001	1.68 (1.34-2.10)	<0.001
"potential" PsD (n:331)	1.90 (1.52-2.37)	<0.001	1.30 (0.84-2.02)	0.238	1.50 (1.05-2.14)	0.024
PsD stratified by psychotropic treatment						
SSRI (n:394)	2.19 (1.62-2.97)	<0.001	1.97 (1.38-2.82)	<0.001	1.77 (1.29-2.43)	<0.001
Other antidepressants (n:291)	1.81 (1.25-2.61)	0.002	2.23 (1.51-3.32)	<0.001	1.82 (1.27-2.61)	0.001
SSRI+other antidepressants (n:73)	1.05 (0.49-2.27)	0.893	0.88 (0.31-2.47)	0.803	0.91 (0.38-2.16)	0.829
Antipsychotics (n:153)	1.90 (1.62-3.16)	0.013	1.85 (1.03-3.31)	0.040	1.49 (0.88-2.55)	0.141
Propensity matched cohort n:1802						
PsD (901)	2.08 (1.52-2.84	<0.001	2.45 (1.53-3.30)	<0.001	1.81 (1.31-2.49)	<0.001
PsD stratified by psychotropic treatment						
SSRI (390)	2.39 (1.64-3.47)	<0.001	2.38 (1.50-3.76)	<0.001	1.97 (1.34-2.91)	0.001
other antidepressants (290)	1.93 (1.26-2.94)	0.002	2.55 (1.57-4.17)	<0.001	1.95 (1.28-2.99)	0.002
SSRI+other antidepressants (72)	1.30 (0.60-2.82)	0.505	1.08 (0.37-3.12)	0.894	1.02 (0.42-2.45)	0.968
antipsychotics (149)	2.02 (1.17-3.51)	0.012	1.97 (1.03-3.79)	0.041	1.54 (0.87-2.45)	0.142

Number of patients included in analysis differs from the total number of patients due to missing data. PsD: psychiatric disorder
Adjusted for age, gender, BMI, joint, living alone, use of walking aids, smoking, alcohol >2 units/day, pulmonary disease, cardiovascular disease, diabetes, preoperative anemia and place of surgery

Abstract 14

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Titel The Impact of Tourniquet Use During Ankle Surgery On Postoperative Opioid Use

Introduction
Ankle surgery is often done using a tourniquet. Ischaemia/reperfusion injury caused by the tourniquet may increase postoperative pain. The aim of our study was to investigate the amount of opioids given to patients after ankle surgery with and without tourniquet.

Methods
Data collection was conducted with approval from Danish Data Protection Agency (J-no: HEH-750.16-32, I-Suite nr: 01788). According to Danish legislation database studies do not require ethics committee consideration.
We did a cohorte study based on data from patient's records in a tertiary care university affiliated hospital between January 2008 and December 2011
We identified patients undergoing reconstructive ankle fracture surgery from hospital records. We excluded: multiple fractures of the same extremity, major trauma, reoperations, arthrodesis of the ankle joint and missing data on tourniquet use. We included 603 patients.
Main outcome measures: Main outcome was opioid consumption during first 24 hours postoperatively (in equipotent i.v. morphine doses). Secondary outcomes were time in post-anaesthetic care unit, and additional antiemetic medicine. We performed multiple regression to analyse the primary outcome.

Results
358 patients underwent surgery with tourniquet. There was a correlation between tourniquet time and postoperative opioid consumption (p-value 0.001) after controlling for confounders. The slope of the correlation was 0.04 mg/min (95% C.I. 0.02;0.07) which means there is an increase in postoperative opioid consumption by 0.43 mg for every 10 minutes of tourniquet time.

Conclusion
We found an increase in postoperative opioid consumption correlated to tourniquet use. Possible preventive measures with antioxidant treatment to prevent Ischaemia/reperfusion injury should be investigated.

Abstract 15

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Titel Danske anæstesiologers vurdering af egne kompetencer indenfor smertebehandling.

Introduktion
Diagnostik og behandling af smerter udgør en af de fire søjler i det anæstesiologiske speciale. Uddannelsessøgende læger modtager under hoveduddannelsen formaliseret uddannelse i basal smertebehandling, mens speciallæger har mulighed for videreuddannelse på eget initiativ (fx SSAI diplom uddannelse i avanceret smertebehandling). Tidligere undersøgelser af lægers selv-evaluering inden for smertebehandling har vist en oplevet utilstrækkelighed og behov for videreuddannelse (1,2). Der er dog ikke tidligere foretaget undersøgelser blandt anæstesiologier. DASAIMs Smerteudvalg mener derfor at der mangler viden om danske anæstesiologers selvevaluering af egne kompetencer inden for smertebehandling og har derfor taget initiativ til denne undersøgelse.

Metoder
En internet baseret spørgeskemaundersøgelse blev udsendt til alle medlemmer af DASAIM omfattede selvvurdering af kompetencer og omfang af videreuddannelse indenfor behandling af akutte og kroniske smerter. Speciallægers undervisning af uddannelsessøgende læger i smertebehandling indgik i undersøgelsen.

Resultater
Spørgeskemaet blev besvaret af 662 læger besvarede spørgeskemaet (44%) heraf var 63% mænd. 73% af besvarelserne kom fra speciallæger. Smertebehandling blev angivet som et af deres faste arbejdsområder af 14%. Besvarelser fra anæstesiologer med hovedfunktion på operationsafsnit eller intensiv terapi afsnit er angivet i tabel 1 og 2. Blandt speciallæger havde 24 (4%) gennemført den nordiske diplomuddannelse

i avanceret smertebehandling, mens 64% af samtlige læger har aldrig fået videreuddannelse inden for behandling af kroniske smerter. Blandt speciallægerne underviste 66% aldrig eller kun sjældent uddannelsessøgende læger i smertebehandling.

Diskussion
Resultaterne af denne spørgeskemaundersøgelse ligger på linje med tidligere undersøgelser (1,2). Selv-vurderingen af egne kompetencer viser en tydelig tendens af oplevet utilstrækkelighed og behov for videreuddannelse indenfor smertebehandling. Tendenserne i besvarelserne kan dog være påvirket af den lave svarprocent. Resultatet af undersøgelsen er bekymrende, især hvad angår behandlingen af patienter med kroniske smerter og de mangelfulde muligheder for rådgivning til behandling.
Konklusion
Flertallet af danske anæstesiologer vurderer sig selv som ude af stand til at yde smertebehandling på et højt fagligt niveau, især hvad angår patienter med kroniske opioidkrævende smerter. Om dette kan afhjælpes ved øget fokus på videreuddannelse kræver yderligere undersøgelser.

Referencer

1. Silvoniemi et al. Physicians' self-assessment of cancer pain treatment skills--more training required. Support Care Cancer 2012;20:2747-53.
2. Douglass et al. Physicians' pain management confidence versus competence. J Opioid Manag 2009;5:169-74.

Tabel 1. Hovedfunktion ved operationsafsnit: 391 besvarelserne (59%)

	I høj grad	I nogen grad	I begrænset grad	Nej/ved ikke
Ansvar for planlægning af postoperativ smertebehandling	45%	51%	4%	0%
Kompetencer til behandling af postoperative smerter	47%	47%	6%	1%
Kompetencer til behandling af patienter med kroniske opioidkrævende smerter	19%	63%	16%	2%
Har du adgang til rådgivning/tilsyn hos disse patienter?	31%	45%	18%	5%

Tabel 2: Hovedfunktion på Intensiv Terapi Afsnit: 159 besvarelser (24%)

	I høj grad	I nogen grad	I begrænset grad	Nej/ved ikke
Oplever du smertebehandling af intensiv patienter som et klinisk problem?	25%	53%	22%	0%
Føler du dig fagligt kompetent til at varetage disse patienters smertebehandling?	39%	57%	3%	1%
Har du adgang til rådgivning/tilsyn hos disse patienter?	32%	35%	19%	13%

Abstract 19

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Titel Choice of anesthesia affects postoperative opioid consumption in ankle fracture surgery.

Intro
There is very little research on the effects of various anaesthetic options on the postoperative care after reconstructive surgery of ankle fractures. This despite the fact that 20-25 % of patients suffer functional impairment for up to 5 years. [Winters].
Despite the obvious need for improved treatment, the effects of anaesthetic techniques on the post-operative phase has not been explored sufficiently [Jordan et al.].
With this study, we aimed to investigate the impact of anaesthesiological teqhnique, on the postoperative pain-management in anklefractures.

Methods
We performed a retrospective cohort study on 622 patients, 9 to 99 years of age, by collecting data from the patient records at Herlev University Hospital.
The Patients were divided into the following anaesthetic groups: Pure General Anaesthesia (GA), GA + Peripheral Nerve Block (PNB), pure Spinal Anaesthesia (SA), and SA + PNB.

The four groups were analyzed for differences in postoperative opioid pain medication in the first 24 hours; secondary outcomes were Post Anaesthetic Care Unit (PACU) pain score, treatment for Post-Operative Nausea and Vomiting (PONV), time in the PACU and length of stay (LOS). Outcomes were corrected for a number of demographic and anamnestic parameters.

Results
Our results show that spinal anaesthesia in combination with femoro-popliteal block had a better pain-management profile than any other technique, with a 33.38 % lower opioid consumption than general anaesthesia alone.
PACU pain score also yielded significant differences between GA and the other groups, while the other secondary outcomes did not.
For detailed results, please refer to Table I.

Discussion
Our findings show that the different anaesthesiological techniques are not equivalent in terms of pain management in ankle fractures. While a reduction of 2 morphine tablets (-6.9 iv-equivalents) may not seem significant, it could represent a reduction of pain by up to 33.38 %. This knowledge may help improve the post-operative pain management, and thereby mediate earlier rehabilitation after injury.

Table 1 - Differences between groups

Anesthesia Group	Mean consumption [mg]	Statistically Corrected difference*	P-value
GA	21.87	REF	-
GA+PNB	16.31	-4.9 (-8.6;-1.3)	0.008
SA	17.08	-4.5 (-8.1;-0.9)	0.01
SA+PNB	14.55	-6.9 (-10.4;-3.3)	0.0002

Difference in opioid consumption over 24-hours post-op, converted to equipotent dose IV-morphine [mg], (range).
A difference of -3.33 is equivalent to one less 10 mg morphine tablet.

Abstract B

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Titel Sårkateter til laparotomi.

Introduktion
Epidural analgesi postoperativt har længe været anvendt som standardbehandling ved større laparotomier, men sårkateter kunne måske være et gyldigt alternativ.

Metode
En søgning på PubMed med MESH-søgeordene: ”Pain” AND ”Postoperative Period” OR ”Pain, Postoperative” AND ”Anesthetics, Local” OR ”Anesthesia, Local” blev kombineret med enkeltvis søgning på MESH-ordene: ”Analgesia, Epidural” OR ”Anesthesia, Epidural” AND ”Abdomen”; ”Catheters”; ”Infusions, Intralesional”; Laparotomy”; ”Abdomen” og suppleret med en fritekstsøgning. Søgningen sluttede 12. maj 2014.
Inklusionskriterier: Randomiserede kliniske forsøg på voksne, minimum 40 patienter, sårkateter placeret i abdominalvæggen, større laparotomier og engelsksprogede artikler fra de sidste ti år.

Resultater
Fire studier omhandlede epiduralkateter (EDK) versus sårkateter (Tabel 1). Elleve studier undersøgte sårkateter versus placebo (Tabel 2).

Diskussion
Sårkateter versus EDK:
Der fandtes ingen sikker forskel i VAS-score mellem grupperne. I sårkatetergrupperne var morfinforbruget højere, men indlæggelsestiden var ikke forlænget.
Anvendelse af sårkateter er forbundet med færre ressourcer og komplikationer end epidural analgesi (1).

Sårkateter versus placebo:
Der blev fundet seks studier med effekt og fem uden. Det er således vanskeligt at føre stærke argumenter for, at der er effekt af sårkateteret i den fundne litteratur. I sårkatetergrupperne var der reduceret opioidforbrug, indlæggelsestid og tid til tarmfunktion.
Anvendelse af sårkateter førte til generel lavere VAS-score eller lavere opioidforbrug og kortere indlæggelsestid (1).

Konklusion
På baggrund af studierne i dette materiale kan det ikke konkluderes, at sårkateter er mere effektivt end placebo. Dette medfører, at der heller ikke kan argumenteres for, at sårkateter er ligeværdig med epidural analgesi.

Tabel 1. Sårkateter versus epidural.

	VAS	Opioidforbrug	Tarmfunktion	PONV	Indlæggelsestid
Niraj, 2011, Anaesthesia	0	÷		0	
Revie, 2012, HPB	÷				+
Bertoglio, 2012, Pain Medicine	+	÷	+	+	(+)
Renghi, 2013, J Cardiothoracic and Vasc Anesthesia	0	÷	0		0

Effekt af sårkateter. +: Signifikant effekt. (+): Ikke signifikant kortere indlæggelsestid. 0: Ingen forskel mellem grupperne. ÷: Signifikant højere VAS-score eller signifikant højere morfinforbrug.
Et blankt felt betyder at parameteren ikke blev vurderet i undersøgelsen.

Tabel 2. Sårkateter versus placebo. Kun de seks studier hvor sårkateteret var effektivt er vist i tabellen.

	VAS	Opioidforbrug	Tarmfunktion	Mobilisering	Indlæggelsestid
Forastiere, 2008, Br J Anaesth	+	+	+		+
Baig, 2006, J Am Coll Surg	0	+	0	+	0
Wang, 2010, ANZ J Surg	0	+	+	+	0
Chan, 2010, Anaesthesia	+	+			
Beaussier, 2007, Anesthesiology	+	+	+		+
Ozturk, 2011, Tech Coloproctol	0	+			

+: Signifikant mindre VAS-score ved sårkateter end placebo, mindre opioidindgift ved sårkateter, hurtigere etablering af tarmfunktion postoperativt, kortere tid til mobilisering og kortere indlæggelsestid.
0: Ingen forskel i grupperne. Et blankt felt betyder at parameteren ikke blev vurderet i undersøgelsen.

Abstract C

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Titel Effect of adductor canal block with 10 ml versus 30 ml local anesthetics on quadriceps strength: a randomized study in healthy volunteers

Introduction
Adductor canal block (ACB) is predominately a sensory nerve block, but excess volume may spread to the femoral triangle, potentially affecting motor branches of the common femoral nerve. The optimal volume for the ACB should reduce overflow to the femoral triangle while preserving adequate analgesia. We hypothesized that ACB with 10 ml would lead to fewer subjects with impaired quadriceps strength than ACB with 30 ml.

Methods
We performed a blinded, randomized, controlled, crossover trial, including healthy men aged 18–30 years. All subjects received bilateral ACBs with 0.1% ropivacaine; 10 ml in one leg and 30 ml in the other leg. Quadriceps strength was assessed as maximum voluntary isometric contraction, pre-block, at 0.5, 1, 2, 3, 4, 5 and 6 hours post block. The primary outcome was the difference between volumes in number of limbs with decreased quadriceps strength by more than 25% from baseline, at two consecutive time-points. Secondary endpoints were quadriceps strength at 2, 3 and 4 h and when calculated as area under the curve (0.5–6 h), functional outcome assessed with a modified 30-second Chair Stand test performed on one leg at a time, sensory block and pain during a 30-second thermal stimulation in the saphenous innervation area. Clinicaltrial.gov identifier: NCT01981746.

Results
We included 26 subjects, who all completed the study. For each volume, two subjects had decreased quadriceps strength by more than 25% from baseline (RR 1.00, 95% CI: 0.07 to 13.8, P>0.99). Furthermore, there were no differences in quadriceps strength at any of the predefined time points (P>0.05, figure 1) or in sensory block (P>0.05).

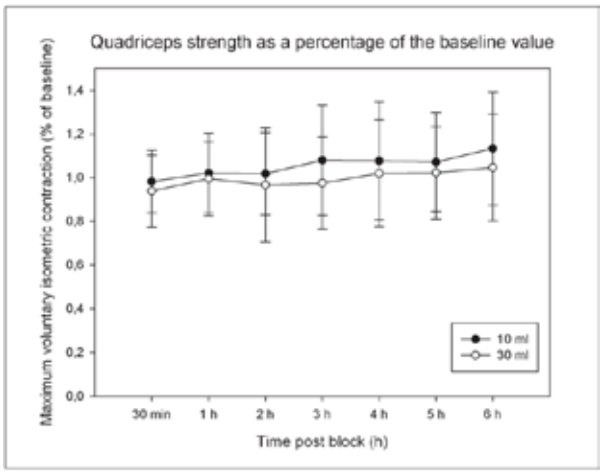
The only statistically significant difference between volumes was found in the 30-second Chair Stand test at 2 h: the mean decreases in the number of sits and rises from the pre-block value was 3 in the 10 ml group and 6 in the 30 ml group (P=0.015). This difference was no longer statistically significant at 4h: -1 and -4, 10 ml and 30 ml group, respectively (P=0.06).

Moreover, there was no significant difference in VAS pain scores during thermal stimulation: 8 ±10 vs. 7 ±11 mm, 10 ml and 30 ml, respectively (95% CI: -5 to 6, P=0.82). All subjects except one (10 ml treatment) had a sensory block at 1 h post block, but at 6 h, the ACB had resolved in

7/26 of limbs receiving 10 ml and in 2/26 of limbs receiving 30 ml (P=0.07).

Discussion and conclusion

Varying the local anesthetic volume used for ACB between 10 and 30 ml did not have a statistically significant or clinically relevant impact on quadriceps strength. Other factors, such as distal spread of local anesthetics in the adductor canal (to reach the posterior branches of the obturator nerve), analgesia and toxicity, may be more important when determining the appropriate volume for the ACB.



Data are presented as mean (SD)

Abstract A

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Overskrift Analgesic Effect of an Oral Fixed-Dose Combination of Netupitant and Palonosetron (NEPA) in an Acute Pain Model: A Phase I, Randomised, Double-Blind, Placebo-Controlled, Cross-over Study

Background
NEPA is a fixed-dose combination of netupitant (NETU), a new, highly selective NK1 receptor antagonist (RA), and palonosetron (PALO), a pharmacologically distinct 5-hydroxytryptamine 3 (5-HT3) RA. Both substance P (endogenous ligand for NK1 receptor, released after noxious stimuli) and serotonin (5-HT) are involved in nociceptive responses. This Phase I, randomised, double-blind, placebo-controlled, cross-over study (EudraCT No: 2010-020052-56), was designed to assess the efficacy, safety, and tolerability of NEPA in an acute pain model.

Methods
Healthy non-smoker male subjects aged 18–35 years, with a BMI of 18–30kg/m2 received either NEPA (NETU 300mg + PALO 0.5mg), followed by a washout period of ≥3 weeks, and then placebo, or vice versa. In both treatment sessions subjects underwent the heat-capsaicin sensitisation test on the dominant forearm. The primary efficacy variable was the percentage change in the area of secondary hyperalgesia to von Frey hair stimulation after heat-capsaicin sensitisation on the dominant forearm, from baseline to 285 min post-treatment. Secondary efficacy variables included: evaluations of the same parameter at 185 and 235 min post-treatment; percentage change from baseline in the area of secondary hyperalgesia after brief thermal sensitisation of the dominant thigh and evaluation of the heat pain detection threshold, at 190, 240, and 290 min; and area under the VAS-pain curve after long thermal stimulation (45°C for 1 min). Differences between groups were an alysed with the Wilcoxon rank-sum test. Adverse events (AEs) were monitored throughout the study.

Results
Overall, 28 subjects were enrolled. The median change from baseline in the area of secondary hyperalgesia on the dominant forearm after heat-capsaicin sensitisation at 285 min post-treatment was 41% for the NEPA group and 55% for the placebo group, with no statistically significant difference (P=0.094). The other secondary variables also failed to show any significant difference in the analgesic activity of NEPA compared with placebo.
A total of 22 treatment-emergent AEs (TEAEs) were reported; 12 subjects reported 15 TEAEs during NEPA treatment, and 7 subjects reported 7 TEAEs during placebo treatment. Most TEAEs were of mild intensity. No severe TEAEs, serious AEs, or AEs leading to study discontinuation were reported. Fatigue was the most frequent TEAE, reported by 10 NEPA-treated subjects and 6 placebo-treated subjects. All of the reported TEAEs were resolved during the study.

Conclusions
No statistically significant analgesic effect was observed for NEPA treatment compared with placebo in the area of secondary hyperalgesia. This study confirmed the good safety and tolerability profile of NEPA. These results suggest further studies of NEPA in heat-capsaicin sensitisation models may not be meaningful, nevertheless, they do not exclude the possibility of a potential analgesic effect of NEPA in other pain models or clinical pain scenarios.