Distribution Patterns, Dermatomal Anesthesia, and Ropivacaine Serum Concentrations After Bilateral Dual Transversus Abdominis Plane Block

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Background and Objectives: The ability of transversus abdominis plane (TAP) blocks to anesthetize the upper abdomen remains debatable. We aimed to describe the local anesthetic distribution following ultrasound-guided TAP blocks with repeated magnetic resonance imaging investigations and to relate this to the resulting dermatomal anesthesia.

Methods: Eight volunteers were included in a randomized, observer-blinded study. Sixty milliliters of ropivacaine 0.375% was administered: 1 injection of 30 mL as a lateral classic TAP block, followed by a sham upper intercostal TAP block, and on the contralateral side, 2 separate 15-mL injections at the upper intercostal and lateral classic TAP plexuses, respectively. The primary outcome measure was magnetic resonance imaging-assessed area expansion of all injectates over a 6-hr period. Dermatomal anesthesia and sequential serum ropivacaine levels were recorded at the same time intervals.

Results: All injectate areas expanded in a statistically significant manner in the anterior abdominal wall. Lateral classic TAP blocks with 30-mL injectates did not extend into the upper intercostal TAP plexus. The dual 15-mL injectates on the other hemiabdomen remained within the upper intercostal and lateral classic TAP compartments and resulted in significantly (P < 0.018) more widespread dermatomic anesthesia. Measured serum ropivacaine concentrations were below the potential level of toxicity.

Conclusions: Magnetic resonance imaging analysis revealed a significant time-dependent expansion of injectates. Magnetic resonance imaging and the degree of dermatomal anesthesia confirmed that the upper and lateral TAP compartments do not appear to communicate. Separate injections at the upper intercostal and lateral classic TAP plexuses are necessary to block the entire abdominal wall.

Methods

Ethics

The study was performed in accordance with the Helsinki II declaration, registered at ClinicalTrials.gov after the 2010 CONSORT guidelines (BBH-USG-PNB-1), and approved as an additional protocol by the Committees on Biomedical Research Ethics for the Capital Region of Denmark (H-3-2010-111).

Volunteers

Following written informed consent, 8 healthy male volunteers were included in the study. Phenotypic data of the volunteers were mean age of 31 (SD, 12) years; weight, 81 (SD, 11) kg; height, 1.85 (SD, 0.06) m; and body mass index, 23.6 (SD, 1.3) kg/m². Inclusion criteria were as follows: age older than 18 years, no medication, no history of abdominal trauma or
surgery, no coagulopathy, and no claustrophobia. The exclusion criteria consisted of allergy to the applied local anesthetic and inability to tolerate the administration of TAP blocks.

**Design**

The study was conducted as a randomized, placebo-controlled, observer-blind trial. On the day of investigation, the volunteers were randomized to receive a single injection of large-volume (30 mL) USG lateral classic TAP block above the iliac crest and beneath the thoracic cage on either the right or left side of the abdomen. An USG sham injection was subsequently performed on the same side at the upper intercostal TAP plexus to ensure patient blinding; however, no fluid was injected. On the contralateral side, 2 single-injection, low-volume TAP blocks (2 × 15 mL) were performed, that is, a USG lateral classic TAP block above the iliac crest and beneath the thoracic cage in the anterior axillary line, and a USG upper intercostal TAP block administered as cephalad and medially as possible beneath the posterior rectus sheath and above the transversus abdominis muscle.

Randomization was performed by the sealed envelope technique. The consultant radiologist and 2 radiographers involved in the study were kept unaware of the injection sequence. The same consultant radiologist examined all magnetic resonance images.

**Subject Preparation and Measurements**

The blocks were administered with the volunteers in the supine position and without sedatives or analgesics (Fig. 1). Pulse and respiration were monitored continuously in the preparation room. The TAP in the upper and lower abdomen was visualized using a SonoSite ultrasound apparatus (SonoSite S-ICU; SonoSite, Bothell, Washington) with a linear-array ultrasound transducer (6–15 MHz; HFL50x), on which a sterile plastic cover (SaferSonic Sterile sonography cover; SaferSonic Mediinprodukte Handels GmbH, Ybbs, Austria) was applied. Before the nerve block administration, the abdominal skin was disinfected with 2% chlorhexidine/70% isopropyl alcohol. All blocks were applied using an in-plane technique in a medial-to-lateral direction at all 4 sites of injection. A 21-gauge, 90-mm needle was used (Pompecide ultrasound needle, 30-degree bevel; te me na SAS, Carrières sur Seine, France). In all cases, the neurovascular and fascial planes between the muscles were identified.

When administering the USG upper intercostal TAP blocks for the upper abdomen (T6–T9), the transducer was placed as cephalad and as medial as possible (Fig. 1A). In all cases, the transversus abdominis muscle reached medially below the posterior rectus sheath. At this point, the blocks were administered between the posterior rectus sheath and the transversus abdominis muscles (Fig. 1A). When administering the lateral classic TAP block bilaterally for the lower abdomen (T10–T12), the insertion point on the skin was in the anterior axillary line beneath the costal margin and above the iliac crest (Fig. 1B). The needle was then advanced laterally and posterior through the external and internal oblique muscles, with the end point in the neurovascular plane between the transversus abdominis and internal oblique muscles. Depending on randomization, 1 of the upper intercostal TAP blocks was performed as a sham block, with the needle penetrating the skin and entering the level of the upper intercostal TAP plexus but avoiding the injection of fluid. All volunteers were administered a total of 60 mL of ropivacaine 0.375% (225 mg). The same consultant anesthetist performed administration of all the TAP blocks (J.B.). All injections were recorded using the storage system of the ultrasound apparatus. Following completion of the blocks, the volunteers remained resting in the supine position on a magnetic resonance–compatible stretcher for 30 mins; they were then subjected to MRI.

**Sensory Dermatome Testing**

The number of dermatomes anesthetized by the various injections was initially recorded by using a cold test with ethanol.
A consultant anesthetist blinded to the injection sequence performed the sensory dermatome testing with this method at 30, 120, 240, and 360 mins after injection, and the number of anesthetized dermatomes was then recorded on a specific chart that depicted all dermatomes, from T6 to T12. Testing was also performed cephalad to T6 and caudad to T12. A consultant neurologist blinded to the injection sequence used another well-known procedure to examine the degree of dermatomes anesthetized. This standard procedure tests sharp sensation with the broken wooden stick of a cotton swab. The same recording procedure with a specific chart was conducted. For both testing methods, the measure was dichotomous (yes/no).

### Ropivacaine Assay and Pharmacokinetics

Quantitative analysis of serum ropivacaine was performed using ultraperformance liquid chromatography tandem mass spectrometry, and noncompartmental analysis was performed subsequently for determination of pharmacokinetic parameters. Details of the procedures and ultraperformance liquid chromatography conditions (Table 1) are shown in the appendix.

### Magnetic Resonance Imaging

The magnetic resonance scanning was conducted at 30, 120, 240, and 360 mins after injection. Magnetic resonance imaging was performed using a GE HDX 1.5-T scanner (GE Healthcare, Waukesha, Wisconsin) and a body array with a field of view (FOV) of 48 cm. T2 spin-echo fat-saturated sequences were performed in 3 planes: coronal, sagittal, and axial, from above the diaphragm to below the iliac crest. The scan parameters are presented in Table 2 in the appendix. Figure 2 illustrates how distances were measured between specific measurement points and how the injected local anesthetic on skin.
solutions were distributed in the various TAP compartments. Sagittal and axial MRI scans were used for measuring maximal values for cephalad-caudal (Fig. 2A), lateral-medial, and anterior-posterior (Figs. 2B, C) spread of the injected local anesthetic solutions. Axial MRI was also used for (i) measurements of the minimal distances between linea semilunaris and the most anterior expansion point of the injectate of a large-volume lateral classic TAP block and the most cephalad expansion point of the injectate of a low-volume lateral classic TAP block (Fig. 2D). Coronal MRI was used for measurements of the minimal distances between the most caudad expansion point of the injectate of an upper intercostal TAP block (Fig. 2E) and the most cephalad expansion point of the injectate of a low-volume lateral classic TAP block (Fig. 2F). Thus, the time-dependent area expansions of the injected anesthetic solutions in the various TAP compartments were measured systematically. Areas in each of the TAP compartments were calculated by the formula \( \pi ab \), where \( a \) and \( b \) are one-half of the ellipse’s major and minor axes, respectively.

**Statistics**

Statistical analyses were performed using the statistical software program SPSS 17.0 (SPSS Inc, Chicago, Illinois). Variables and demographics that were presumed to follow a Gaussian distribution were expressed as mean (SD), whereas other variables were expressed as median and range. The Wilcoxon matched-pairs \( U \) test analyzed differences between dermatomal anesthesia on the 2 hemiabdomens for each volunteer. \( P < 0.05 \) was considered statistically significant. The sample size was estimated by a minimal relevant difference of a 9-cm\(^2\) area expansion between the calculated areas of the injectates at the individual times of MRI measurements. In a preliminary group of 3 volunteers, the mean
FIGURE 3. The mean MRI-calculated areas of injectates at the various time intervals. Unbroken line = 30-mL lateral classic TAP block. Dotted line = 15-mL upper intercostal TAP block. Dashed line = 15-mL lateral classic TAP block. TAP = transversus abdominis plane.

expansion of MRI-calculated areas of injectates from 30 to 120 mins following administration of low-volume TAP blocks was 18 (SD, 7) cm². We accepted a 1-sided level of significance at 5%, power of 80%, and SD of 7%; that is, a minimal relevant difference of 9 cm² would require 8 volunteers.

RESULTS

All 8 participants successfully completed the study according to the protocol. The time-dependent expansions of mean MRI-calculated areas of injectates after injection are graphically depicted in Figure 3. The MRI-calculated areas of injectates were all seen to increase during the observation period in a statistically significant manner (with 1 exception: upper intercostal TAP block at 240 vs 360 mins) (Table 3). At no point during the 360-min observation period was the large-volume injectate of 30 mL deposited at the lateral classic TAP plexus seen to extend into the compartment of the upper intercostal TAP plexus (Table 4). In 3 of 8 cases (37.5%), the injectate of 30 mL deposited in the lateral classic TAP compartments was found to extend to the linea semilunaris, but the local anesthetic did not enter the upper intercostal TAP compartment (Table 4). Regarding the dual TAP block performed on the other hemiabdomen, it was evident that the low-volume injectate of 15 mL deposited both at the lateral classic TAP plexus and at the upper intercostal TAP plexus did not merge (Table 4).

The results from the sensory dermatome testing showed significantly (P < 0.018) more widespread dermatome anesthesia on the hemiabdomens where the dual injections were performed. Thus, dermatomal anesthesia was evident from T6 to T12 (7 dermatomes), where the dual TAP blocks were administered. In contrast to this, dermatomal anesthesia was registered from only T10 to T12 (3 dermatomes), on the hemiabdomens where the single large volume was injected at the lateral classic TAP compartment. Dermatomal anesthesia, as described, did not change over time. Thus, testing results were similar at 30, 120, 240, and 360 mins after injection. Sensory dermatome testing did not reveal anesthetized dermatomes cephalad to T6 or caudal to T12. On the hemiabdomens where the dual blocks were administered, dermatomal anesthesia was present only on the lower medial quadrants of the anterior abdominal wall. In contrast, on the hemiabdomens where the single blocks were administered, dermatomal anesthesia was present only on the lower medial quadrants of the anterior abdominal wall. No dermatomal anesthesia was recorded on the upper or lower lateral quadrant of the anterior abdominal wall on either hemiabdomen. Both testing methods showed exact matching results.

DISCUSSION

This randomized, observer-blinded trial compares a single-injection versus a dual-injection TAP block on the distribution patterns of injected local anesthetic and the resulting dermatomal anesthesia. We have demonstrated that a dual-injection TAP block (2 × 15 mL) is required to anesthetize the entire anterior abdominal (T6–T12) and that a single injection with the same total volume (30 mL) is insufficient to anesthetize the entire anterior abdominal wall. Both large- and low-volume lateral classic TAP injectates, as well as low-volume upper intercostal TAP injectates, were seen to expand within their respective TAP compartments in a statistically significant manner during the observation period. Despite showing continuous significant area expansion of the injected local anesthetic during a 6-hr observation period, the low-volume lateral classic and upper intercostal TAP injectates did not merge. The large-volume lateral classic TAP injectates never extended into the upper intercostal TAP compartments, even though injectates in 37.5% of cases extended to the linea semilunaris. We also found that the resulting dermatomal anesthesia was significantly more widespread on the anterior abdominal wall with the dual-injection TAP block technique compared with the single-injection technique. In addition, following the administration of a total dose of 225 mg of ropivacaine, there was a significant increase in serum concentrations of ropivacaine compared with the single-injection technique.

TABLE 3. Temporal MRI Calculations of Injectate Area Expansion Over Time

<table>
<thead>
<tr>
<th>Comparisons Across Timeline</th>
<th>30-mL Classic TAP</th>
<th>15-mL Classic TAP</th>
<th>15-mL Intercostal TAP</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 vs 120 mins</td>
<td>Increase, P &lt; 0.001</td>
<td>Increase, P &lt; 0.001</td>
<td>Increase, P &lt; 0.001</td>
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<tr>
<td>30 vs 240 mins</td>
<td>Increase, P &lt; 0.001</td>
<td>Increase, P &lt; 0.001</td>
<td>Increase, P &lt; 0.001</td>
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<tr>
<td>30 vs 360 mins</td>
<td>Increase, P &lt; 0.001</td>
<td>Increase, P &lt; 0.001</td>
<td>Increase, P &lt; 0.001</td>
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<tr>
<td>120 vs 240 mins</td>
<td>Increase, P &lt; 0.001</td>
<td>Increase, P &lt; 0.02</td>
<td>Increase, P &lt; 0.001</td>
</tr>
<tr>
<td>120 vs 360 mins</td>
<td>Increase, P &lt; 0.001</td>
<td>Increase, P &lt; 0.001</td>
<td>Increase, P &lt; 0.001</td>
</tr>
<tr>
<td>240 vs 360 mins</td>
<td>Increase, P &lt; 0.05</td>
<td>Increase, P &lt; 0.001</td>
<td>Stationary, NS</td>
</tr>
</tbody>
</table>

MRI indicates magnetic resonance imaging; TAP, transversus abdominis plane; NS, not significant.
Based on the anatomic findings of Rozen et al,11 we recently proposed the BD-TAP block, involving separate injections of both the upper intercostal and the lateral classic TAP compartments. This new BD-TAP technique is based on the assumption that upper intercostal and lateral classic TAP injections will be confined to separate interfascial and neurovascular compartments that do not intercommunicate and that individual injections at all 4 locations are necessary to reliably anesthetize the entire anterior abdominal wall (T6–T12). Given this assumption, we agree with Hebbard et al16 that applying the oblique subcostal TAP block will achieve a similar result and provide for continuous blockade. Recently, Latzke et al11 tried to elucidate the mechanism of the somatic analgesic effect of the TAP block, testing the previously held belief that the anesthetic permeates from the depot at the site of injection along the abdominal muscles to the target nerves. In addition, Carney et al12 showed that the pattern of local anesthetic solution spread differs, depending on the site of injection into the TAP. Thus, the present study was mainly undertaken to further investigate the anatomic characteristics and to study the mechanism of the analgesic effect of various TAP blocks as well as the accuracy of our new BD-TAP block technique.

**TABLE 4. Measurements From MRI—Temporal Area Expansion Between the Regional Deposited Injectates**

<table>
<thead>
<tr>
<th>Distances, cm</th>
<th>30 mins</th>
<th>120 mins</th>
<th>240 mins</th>
<th>360 mins</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper border (cephalad extent) of 30-mL lateral classic TAP block to linea semilunaris (median and range)</td>
<td>2.4 (2.0–5.0)</td>
<td>1.9 (0.0–3.4)</td>
<td>1.8 (0.0–3.4)</td>
<td>0.7 (0.0–3.2)</td>
</tr>
<tr>
<td>Upper border (cephalad extent) of 15-mL lateral classic TAP block to lower border (caudal extent) of 15-mL upper intercostal TAP block (median and range)</td>
<td>4.9 (3.3–13.1)</td>
<td>4.5 (2.6–11.8)</td>
<td>3.9 (2.1–10.6)</td>
<td>3.7 (1.7–10.4)</td>
</tr>
</tbody>
</table>

MRI indicates magnetic resonance imaging; TAP, transversus abdominis plane.

**Somatic Analgesic Efficacy of the TAP Block**

Despite a rapidly expanding literature, it is still debatable how effective different TAP block techniques are in anesthetizing the nerves of both the upper (T6–T9) and lower (T10–T12) abdomen, and thus, it remains unclear whether the upper intercostal and the lateral classic TAP compartments, in fact, intercommunicate.4–10 Based on the anatomic findings of Rozen et al,11 we recently proposed the BD-TAP block, involving separate injections of both the upper intercostal TAP and the lateral classic TAP compartments.14 This new BD-TAP technique is based on the assumption that upper intercostal and lateral classic TAP injections will be confined to separate interfascial and neurovascular compartments that do not intercommunicate and that individual injections at all 4 locations are necessary to reliably anesthetize the entire anterior abdominal wall (T6–T12). Given this assumption, we agree with Hebbard et al16 that applying the oblique subcostal TAP block will achieve a similar result and provide for continuous blockade. Recently, Latzke et al11 tried to elucidate the mechanism of the somatic analgesic effect of the TAP block, testing the previously held belief that the anesthetic permeates from the depot at the site of injection along the abdominal muscles to the target nerves. In addition, Carney et al12 showed that the pattern of local anesthetic solution spread differs, depending on the site of injection into the TAP. Thus, the present study was mainly undertaken to further investigate the anatomic characteristics and to study the mechanism of the analgesic effect of various TAP blocks as well as the accuracy of our new BD-TAP block technique.

**The Influence of Time on the Spread of TAP Injections**

It has previously been suggested that local anesthetics injected into the TAP at the lateral position above the iliac crest and below the thoracic cage would eventually reach the final destination, thereby providing analgesia of the entire abdominal wall.5,7 Using repeated high-performance MRI, we were able to verify that the injected volume of local anesthetics continuously spreads within the neurovascular plane in the anterior abdominal wall and that there is a significant increase in areas covered by the local anesthetic as time progresses. However, despite this continuous spread of local anesthetic solution during the 6-hr observation period, a single lateral classic TAP injection of 30 mL resulted in dermatomal anesthesia only on the anterior abdominal wall, from T10 to T12. Interestingly, sensory dermatome testing was similar at 30 mins until 360 mins after injection. Thus, even allowing significant onset time for a lateral classic TAP block, it does not appear reasonable to expect clinically useful postoperative somatic analgesia of more than the lower part of the abdomen from such an approach.

**Potential Communication Between the Upper Intercostal and the Lower Classic TAP Compartments**

Despite the observation that some of the 30-mL lateral classic TAP injections extended to the linea semilunaris, no further expansion into the upper intercostal TAP compartment could be identified. Similarly, no intercommunication could be observed between the two 15-mL injectates deposited at the upper intercostal and the lateral classic TAP compartments, respectively. Based on these MRI findings and the resulting dermatomal anesthesia, we conclude that there is no communication between the upper intercostal and the lateral classic TAP compartments and that, to provide somatic analgesic coverage of both the upper and lower anterior abdominal walls, separate TAP injections are necessary.

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**FIGURE 4.** Ropivacaine serum concentrations. A, Represents mean (SD) semilogarithmic scale. B, The individual curves. Included is mean maximum tolerated ropivacaine concentration: 2.2 mg/L (broken line).15
Anatomic Characteristics Determined by MRI

At this point, it is relevant to highlight the potential difference between a USG lateral classic TAP block and the original landmark-based blind technique, an issue recently raised by Carney et al. Ultrasound-guided lateral classic TAP blocks are often performed with a needle insertion point at the anterior axillary line (with needle advancement in a posterior-lateral direction ending in the midaxillary line) because the muscle layers of the external and internal oblique and transversus abdominis muscle are clearly defined at this location. However, the original landmark-based TAP blocks at the triangle of Petit are more lateral and posterior to the anterior axillary line, and at this location, the transversus abdominis muscle is often aperoneural, thus representing a distinctly different anatomic environment. Hence, it could be argued that the spread of the injected local anesthetic, using the original blind, double-pop technique at the triangle of Petit, may result in an entirely different distribution pattern (evaluated by MRI) as well as a different dermatomal anesthetic. McDonnell et al previously showed, using MRI, that the injected solution administered with the landmark-based blind technique at the triangle of Petit will spread within the TAP from the superior margin of the iliac crest to the level of the costal margin and as far posteriorly as the quadratus lumborum muscles. In their effort to further elucidate these findings, Carney et al compared various USG approaches with their original landmark-based blind technique at the triangle of Petit. Their MRI studies revealed that the so-called anterior subcostal and midaxillary USG techniques resulted in a predominantly anterior spread of the injected solution within the TAP. In contrast, more posterior approaches that use both the landmark-based blind technique at the triangle of Petit and the novel USG block technique as far posterior as the lateral border of the quadratus lumborum muscle resulted in predominantly posterior spread of the injected solution around the quadratus lumborum muscle extending to the paravertebral space. The resulting dermatomal anesthesia was described only for the original blind technique, and further clinical studies must address the implications of these findings. Although these novel findings by Carney et al were demonstrated in healthy volunteers, it now seems apparent that the spread of injected local anesthetic and resulting dermatomal anesthesia depend very much on the chosen site of injection. With the more posterior approaches, extensive spread to the paravertebral space should result in more widespread anesthesia even with single-shot injections, and these techniques may provide for blocks that last for a longer period.

The more anterior USG techniques such as the continuous subcostal TAP block and our own 4-point BD-TAP block seem to result in dermatomal anesthesia restricted to T6–T12, and the somatic analgesic efficacy may last for shorter periods.

Serum Concentrations of Ropivacaine Associated With TAP Blocks

Three previous studies have examined serum local anesthetic concentrations following TAP blocks. Most physicians normally inject a total of 30 to 60 mL of local anesthetic at varying concentrations when performing TAP blocks, and thus large-dose TAP blocks may constitute a potential risk of toxicity. A recent publication found TAP blocks that used 3 mg/kg ropivacaine exhibited venous plasma concentrations that were potentially toxic. Another recent study examined both local tissue and plasma ropivacaine levels following TAP blocks, using the in vivo microdialysis perfusion technique. We also found it worthwhile to study the serum concentrations of ropivacaine postinjection associated with our new technique. In our current study, serum concentrations of ropivacaine were measured to be well below the threshold of potential toxicity as reported by Knudsen et al (Fig. 4).

Limitations to This Study

There are several limitations to our current study. First, our study used volunteers and not patients undergoing abdominal surgery. Tissue swelling and surgical incisions might have resulted in a different pattern of spread of the injected local anesthetic. Other recent studies have also used volunteers or conducted cadaveric studies, but general conclusions should be avoided from such research. Studies and results from our current study can only serve to emphasize a hypothesis. Second, as demonstrated by Copeland et al, general anesthesia will change whole-body and regional pharmacokinetics of injected local anesthetics, as well as the systemic effects. The study by Griffiths et al reported potentially toxic ropivacaine concentrations following the use of TAP blocks in gynecologic surgery, even though they used a very similar total dose of ropivacaine (3 mg/kg) compared with the mean 2.82 (SD, 0.36) mg/kg used in our current study. Actually, Copeland et al also demonstrated significantly higher concentrations during anesthesia compared with consciousness in their animal model, and this could explain the difference between Griffiths et al and our current study. Third, our pharmacokinetic analysis should be regarded primarily as a pilot study. Adhering to the results from Griffiths et al, reporting mean peak total unbound ropivacaine concentrations at 30 mins, we began measurements at the same time. This poses the risk that we missed the peak total unbound ropivacaine concentrations and that data should have been measured at earlier time points. Latzke et al have since published their pharmacokinetic analysis in healthy volunteers, measuring at earlier time points postinjection, calculating a mean concentration of 0.44 hrs, which is quite similar to the result from Griffiths et al and our current study. However, future studies must begin measurements at earlier time points than reported in this study. In addition, future studies should also measure unbound ropivacaine levels whenever possible. In the study by Griffiths et al, unbound ropivacaine was directly measured, whereas Latzke et al calculated the free fraction of ropivacaine in the plasma using a protein-binding value of 94%, as described in the summary of the product characteristics. But we have not incorporated the latter method in our current study.

In conclusion, repeated MRI investigations and sensory dermatome testing confirmed that the upper intercostal and lower classic TAP compartments do not communicate. We have also found that, to anesthetize the entire anterior abdominal wall (T6–T12), separate bilateral injections of the upper and lower TAP compartments are necessary. The relatively large dose of ropivacaine administered to accomplish this (60 mL ropivacaine 0.375%) resulted in serum concentrations of ropivacaine that were measured to be below the threshold of potential toxicity.

ACKNOWLEDGMENTS

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REFERENCES

Bilateral Dual TAP Block

APPENDIX

Ropivacaine Assay and Pharmacokinetics: Blood samples were collected via an indwelling Teflon catheter inserted into a forearm vein at the beginning of every examination. Five milliliters of blood samples was collected in plain glass tubes at 0, 30, 120, 240, and 360 mins or as close to these specific time sets as was logistically possible. Following centrifugation (3000 rounds/min for 10 mins), serum was collected and stored at −20°C until final analysis.

Chemicals and Materials: Reference substances of ropivacaine (ropivacaine hydrochloride monohydrate, purity 100%; AstraZeneca A/S, Copenhagen, Denmark) and dibenzepin (ropivacaine hydrochloride, purity 99.8%; Novartis Healthcare A/S, Copenhagen, Denmark) were obtained from the pharmaceutical industry. Methanol and acetonitrile of analytical grade were obtained from Fisher Scientific UK Limited (Leicestershire, United Kingdom), and formic acid (98%–100% GR) came from Fluka (Buchs, Switzerland); butyl acetate for analysis and sodium hydroxide were supplied by Merck (Darmstadt, Germany). Purified water was obtained from Millipore Synergy UV water purification system (Millipore A/S, Copenhagen, Denmark). Acidic water (0.05% formic acid in water) and acidic acetonitrile (0.05% formic acid in acetonitrile) were prepared and used as mobile phases. Stock solution (1000 mg/L in methanol) of ropivacaine was prepared and stored at −20°C. A working solution of ropivacaine was prepared in methanol at 50 mg/L, and an aqueous internal standard (IS) solution of dibenzepin was made up at 0.25 mg/L. The working solution was diluted in water, and spiking serum with 20 μL aqueous dilutions corresponded to these serum levels produced 6 calibrators from 0.002 to 1.0 mg/kg.

Sample Preparation: Serum 0.100 g was mixed with 150 μL water and 20 μL IS solution. Then, 50 μL 2 M NaOH was added, and extraction with 250 μL butyl acetate was carried out. After the mixture has been centrifuged for 10 mins at 2000 g and 5°C, the organic fraction was collected in plain glass tubes at 0, 30, 120, 240, and 360 mins or as close to these specific time sets as was logistically possible. Following centrifugation (3000 rounds/min for 10 mins), serum was collected and stored at −20°C until final analysis.

Measuring Range: The absolute recoveries of ropivacaine and IS were 65% and 57%, respectively. There was a linear range for ropivacaine from 0.002 to 1.0 mg/kg with acceptable residuals (~20%). The precision (CV) of serum controls was less than 20% and with a bias below ±20%. Ropivacaine eluted at 3.60 mins and had an ion ratio of 3.2% ± 10% within measuring range. Some of the authentic human samples were diluted 10 times with solvent before analysis because of limitations in linear range.

Pharmacokinetics: The pharmacokinetic parameters for ropivacaine following extravascular dosing were calculated using the noncompartmental analysis model in WinNonLin Professional version 5.3 software (Pharsight Corp, Mountain View, California).