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A systematic review of local anesthetic systemic absorption after regional anesthesia: Truncal blocks

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Introduction

Regional anesthesia practice has significantly transformed in the last two decades ever since the initial description of abdominal field block by Rafi in 2001. Subsequently, a plethora of ultrasound guided blocks have been employed as an alternative to thoracic epidural analgesia for truncal analgesia and includes thoracic paravertebral blocks, intercostal blocks and a wide variety of interfascial plane blocks. The truncal blocks often employ large volumes of local anesthetic (LA) to establish and maintain analgesia and while several studies have measured of plasma local anesthetic level to evaluate the safety of administering large volumes of LA in these blocks and the time to peaking of plasma levels, the safety profile of administering such large volumes of LA in these blocks need critical appraisal from the perspective of plasma LA levels. With this background, we performed a systematic review of plasma local anesthetic levels following peripheral nerve and interfascial plane blocks and are reporting here on the plasma pharmacokinetic profile and safety of local anesthetics following truncal blocks.

Materials and Methods

As the study is devoid of patient identifiers and participation of human subjects and this a systematic review of published literature, this study is exempt from IRB review requirements as per the University of Iowa IRB policy. The systematic review protocol was registered before the beginning of the study searches (PROSPERO CRD42023450675). Literature searches were performed in OVID MEDLINE, OVID Embase, PubMed, the Database of Abstracts of Reviews and Effects (DARE), the Cochrane database of systematic reviews (CDSR) and library, and all the databases and indices of Web of Science. The full systemic review will include all single shot and continuous peripheral and interfascial nerve blocks in different patient populations, however for the purpose of this abstract, only results from single shot interfascial truncal blocks in adult population are being reported. Primary articles measuring systemic concentrations of LA after single-shot truncal blocks were included. Blocks of interest included paravertebral (PVB), erector spinae plane (ESP), transversus abdominis plane (TAP), quadratus lumborum (QL), rectus sheath (RS), Pectointercostal fascial (PIFB) and intercostal blocks. Time to maximal serum concentrations (Tmax) and highest plasma concentrations (Cmax) in arterial and venous samples and the proportion of patients who breached safe margin of plasma levels of individual LA were collected. Two reviewers independently performed study screening and data extraction. When there was more than 1 study present for a particular block, LA and measurement method (arterial vs venous), data was pooled using Der-Simonian Laird inverse variance method of random effects model

using OpenMeta Analyst

Results/Case Report

A total of 4752 references were screened and after various exclusions, 35 studies met the inclusion criteria and were included for data extraction. Pooled data for individual nerve blocks with corresponding local anesthetic level measured as arterial or venous level is summarized in table 1 and show a great variability in Cmax and Tmax between individual truncal blocks. The block with the highest mean Cmax in our review was the intercostal block followed by TAP and PVB. Our review of literature also showed that most of the blocks exhibited a safe profile following single shot blocks with peak plasma levels within a safe margin. Of a total of 1009 patients, mean peak concentrations of LA exceeded toxic thresholds in 52 patients (n=52/ 972 blocks), however only 2 patients reported mild symptoms of local anesthetic systemic toxicity (LAST), and none of the patients in included studies had overt LAST (seizures or cardiac instability). Thus the pooled data seems to indicate that the proportion of patients breaching the acceptable range of plasma LA levels is around 4% following single shot truncal blocks (Figure 1). Tmax varies greatly between different blocks with PVB demonstrating the fastest Tmax at a range of 18-21 min while most blocks average around 30 to 44 (Figure 2). An effect of adding epinephrine was seen on both Cmax and Tmax whereby adding epinephrine in TAP blocks delayed the time to peaking from 31.1 to 65.5 min. A similar effect was observed in other blocks except in PVB. The impact of epinephrine on Cmax was also observed with lower Cmax levels seen with the addition of epinephrine.

Discussion

Our review of literature showed that the plasma levels of local anesthetics after single shot truncal blocks often exceed the accepted safe limits, yet this does not necessarily correlate with the occurrence of overt LAST. We also summarized the peak plasma concentrations and time to peaking with various local anesthetics following a variety of single shot truncal blocks. While we did not observe a higher incidence of LAST in any reports, is important to bear in mind that none of these studies were primarily powered to assess for subclinical or overt LAST. Further studies on the safety of prolonged infusions of large volumes of LA in truncal blocks are needed as subclinical LAST is often unrecognized. Epinephrine has been used as an additive to LA to improve their safety profile by decreasing Cmax and prolonging Tmax as supported by some studies in neuraxial anesthesia and based on our review findings, a similar trend of the effect of epinephrine on Cmax and Tmax in truncal blocks may be present. The fact that T max shows a wide variability among different blocks should be correlated with clinical practice pertaining to patient observation after a regional block. Rather than setting a standardized time for block recovery, monitoring time should be tailored to each block. Tmax and Cmax associated with individual blocks may serve as a guide to ensure adequate monitoring periods following single shot truncal blocks.

Our study highlights that single shot truncal blocks with a wide variety of local anesthetics are relatively safe regarding LA systemic toxicity. Local anesthetic injection following truncal blocks can lead to detectable systemic concentrations and while most blocks do not breach safe plasma levels, some blocks have a higher propensity to reach toxic levels.

There are multiple limitations to our review due to variation in study methodology such as dosing of LA, the timing of blood withdrawals, arterial or venous sampling, effect of additives, as well as block technique.

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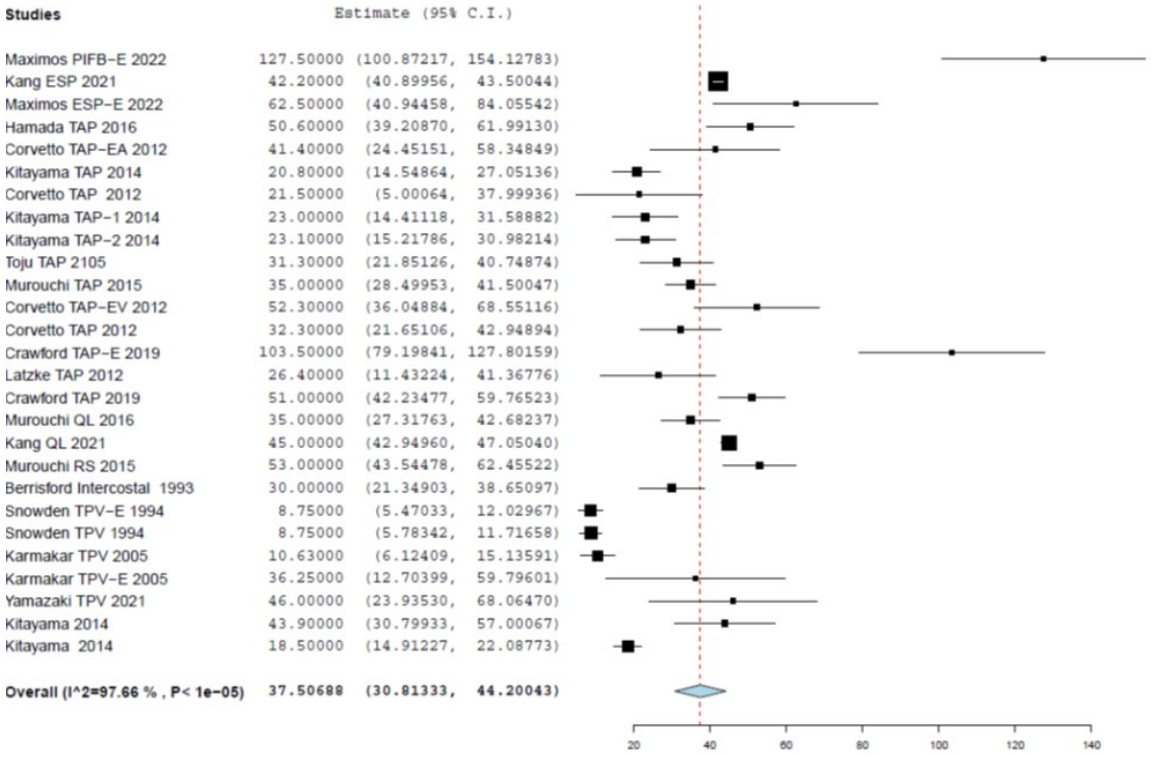
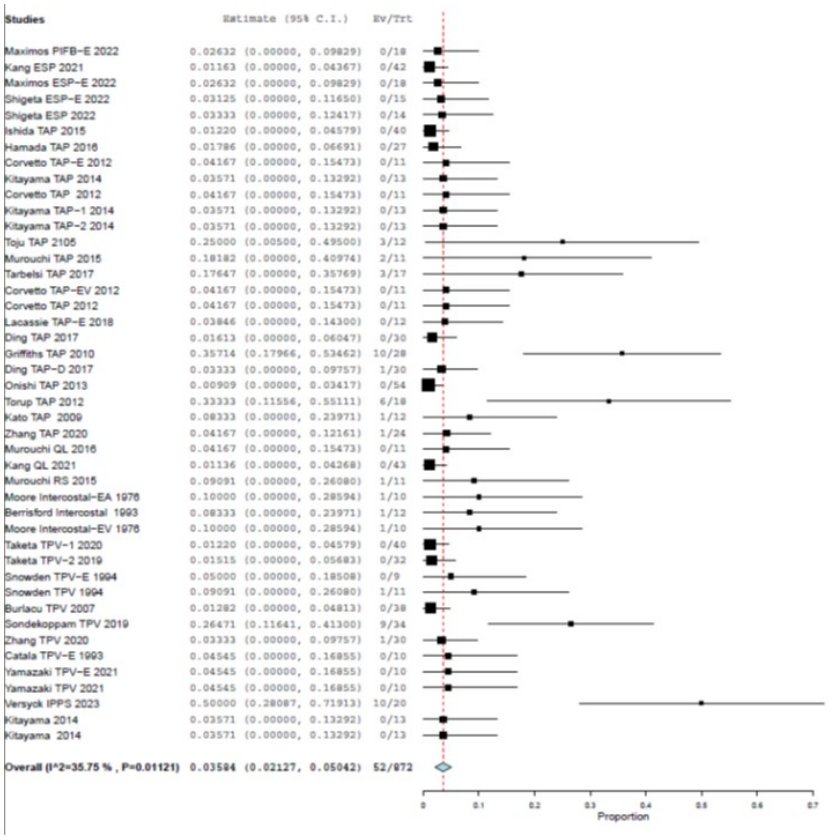
Disclosures

Yes

Tables / Images





Block	LA	Cmax Pooled estimate (95% CI)	Tmax Pooled estimate (95% CI)	Toxic level (mcg/ml)
TPV	Lidocaine	-	Without epi: 21.803 (-2.104, 45.710) (3 studies) With epi: 18.985 (2.069, 35.901) (3 studies)	>6.0 (1-5 has caused CNS toxicity)
	Bupivacaine	**A: 1.12 (0.73; 1.51) 1 study**		Arterial: 4.0 (1.4) (1.1–6.2) Venous: 2.1 (1.2) (0.8–4.5)
	Bupivacaine with epi	A: 0.74 (0.60, 0.87) 1 study		Arterial: 4.0 (1.4) (1.1–6.2) Venous: 2.1 (1.2) (0.8–4.5)
	Levobupivacaine	A: 0.57 (0.35, 0.79) 2 studies V: 0.51 (0.43; 0.58) 1 study		Venous: 2.6 mcg/ml
	Ropivacaine	A: 2.47 (2.16; 2.78): 1 study With EPI A: 1.85 (1.41; 2.28)		Arterial: 4.3 (0.6) (3.4–5.3) Venous: 2.2 (0.8) (0.5–3.2)
TAP	Lidocaine	V: 3.60 (3.20; 3.99) 1 study	**Without epi: 31.05 (25.21, 36.89) 8 studies** **With epi: 65.60 (32.09, 99.11) (3 studies)**	>6.0 (1-5 has caused CNS toxicity)
	Bupivacaine	**V: 0.80 (0.37; 1.23) 1 study**		Arterial: 4.0 (1.4) (1.1–6.2) Venous: 2.1 (1.2) (0.8–4.5)
	Levobupivacaine	A: 0.84 (0.31, 1.37) 3 studies V: 0.39 (0.22, 0.55) 1 study		Venous: 2.6 mcg/ml
	Ropivacaine	A: 1.30 (0.58, 2.01) 3 studies **V: 1.77 (1.48, 2.05) 4 studies**		Arterial: 4.3 (0.6) (3.4–5.3) Venous: 2.2 (0.8) (0.5–3.2)
ESP	Bupivacaine with epi	V: 0.37 (0.31; 0.42) (One study)	Without Epi: 42.20 (29.49; 54.90) (1 study) With Epi: 62.50 (51.18; 70.81) (1 study)	Arterial: 4.0 (1.4) (1.1–6.2) Venous: 2.1 (1.2) (0.8–4.5)
	Levobupivacaine	V: 0.93 (0.36, 1.50) (One study)		Venous: 2.6 mcg/ml
	Ropivacaine	A: 1.50 (1.41; 1.59) (One study only)		Arterial: 4.3 (0.6) (3.4–5.3) Venous: 2.2 (0.8) (0.5–3.2)
Intercostal	Bupivacaine	**V: 1.450 (1.26; 1.63) 1 study**	Without epi: 30.00 (23.21; 36.79) (1 study)	Arterial: 4.0 (1.4) (1.1–6.2) Venous: 2.1 (1.2) (0.8–4.5)
	Bupivacaine with epi	**A: 3.29 (2.83; 3.74) 1 study** **V: 2.52 (2.11; 2.92) 1 study**		Arterial: 4.0 (1.4) (1.1–6.2) Venous: 2.1 (1.2) (0.8–4.5)
QLB	Ropivacaine	A: 1.17 (0.88, 1.46) 2 studies	Without epi: 38.40 (29.11, 47.68) (2 studies)	Arterial: 4.3 (0.6) (3.4–5.3) Venous: 2.2 (0.8) (0.5–3.2)
Rectus sheath	Ropivacaine	A: 1.79 (1.59; 1.98) One study	Without epi: 53.00 (46.50; 59.50) (1 study)	Arterial: 4.3 (0.6) (3.4–5.3) Venous: 2.2 (0.8) (0.5–3.2)
PFIB	Bupivacaine	A: 0.32 (0.22; 0.41) 1 study	With epi: 127.50 (119.18; 135.81) (1 study)	Arterial: 4.0 (1.4) (1.1–6.2) Venous: 2.1 (1.2) (0.8–4.5)