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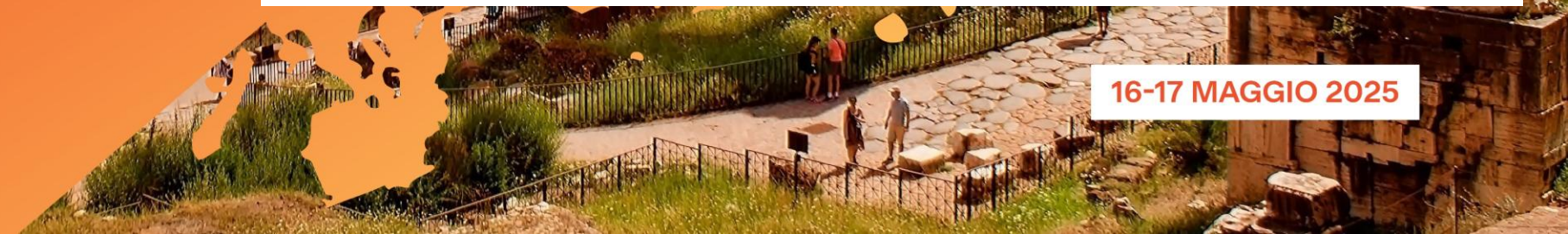
ROMA

2025

Ruolo dei farmaci adiuvanti durante l'allungamento

R. Perna



16-17 MAGGIO 2025

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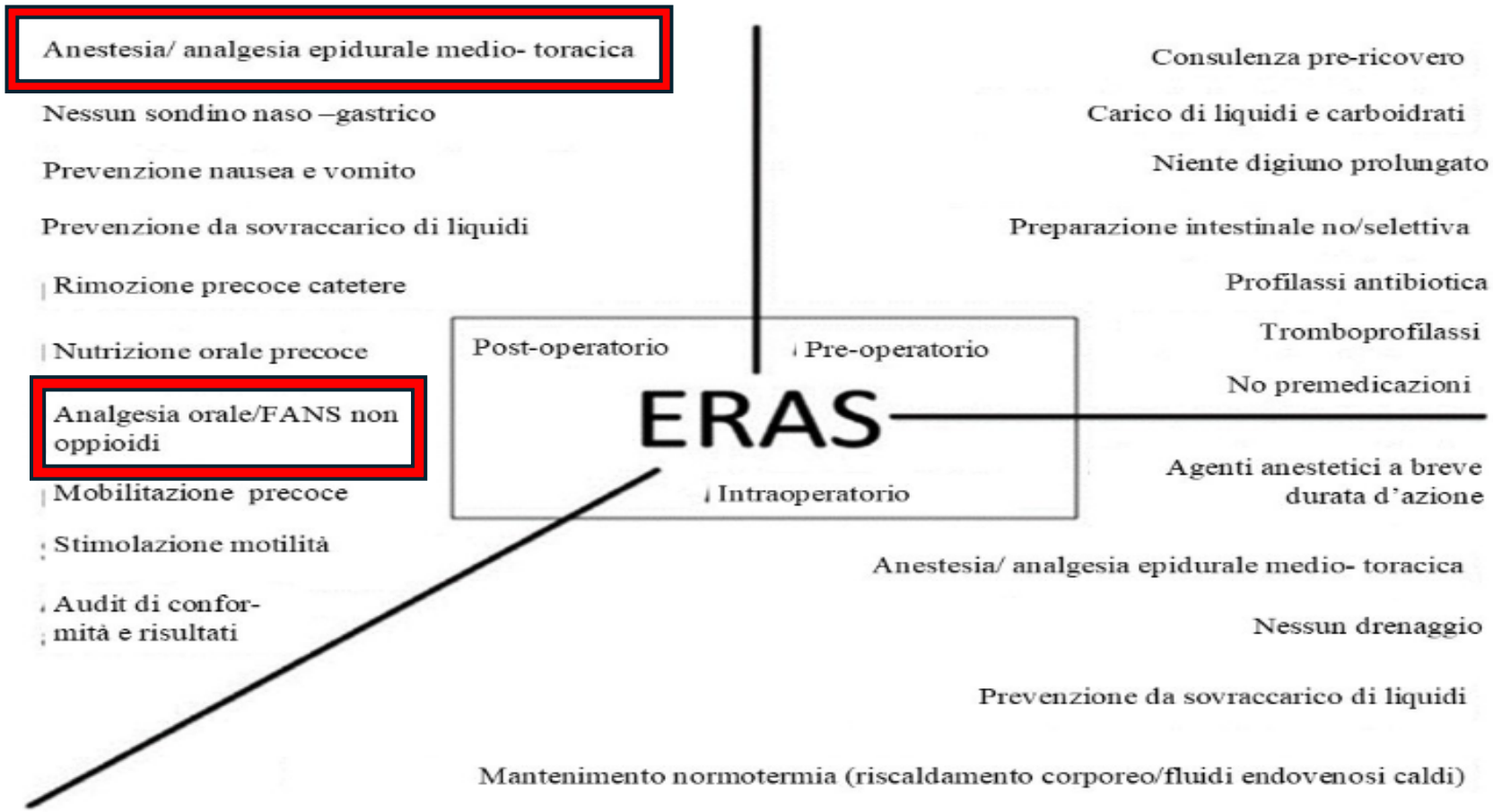
Anestesia/ analgesia epidurale medio- toracica
Nessun sondino naso –gastrico
Prevenzione nausea e vomito
Prevenzione da sovraccarico di liquidi
Rimozione precoce catetere
Nutrizione orale precoce
Analgesia orale/FANS non oppioidi
Mobilitazione precoce
Stimolazione motilità
Audit di conformità e risultati
Post-operatorio
Pre-operatorio
ERAS
Intraoperatorio
Consulenza pre-ricovero
Carico di liquidi e carboidrati
Niente digiuno prolungato
Preparazione intestinale no/selettiva
Profilassi antibiotica
Tromboprofilassi
No premedicazioni
Agenti anestetici a breve durata d'azione
Anestesia/ analgesia epidurale medio- toracica
Nessun drenaggio
Prevenzione da sovraccarico di liquidi
Mantenimento normotermia (riscaldamento corporeo/fluidi endovenosi caldi)

SJA Saudi Journal of Anaesthesia
Official Publicationn of Saudi Anaesthetic Association

Saudi J Anaesth. 2020 Jan-Mar; 14(1): 77–84.
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PMID: 31998024

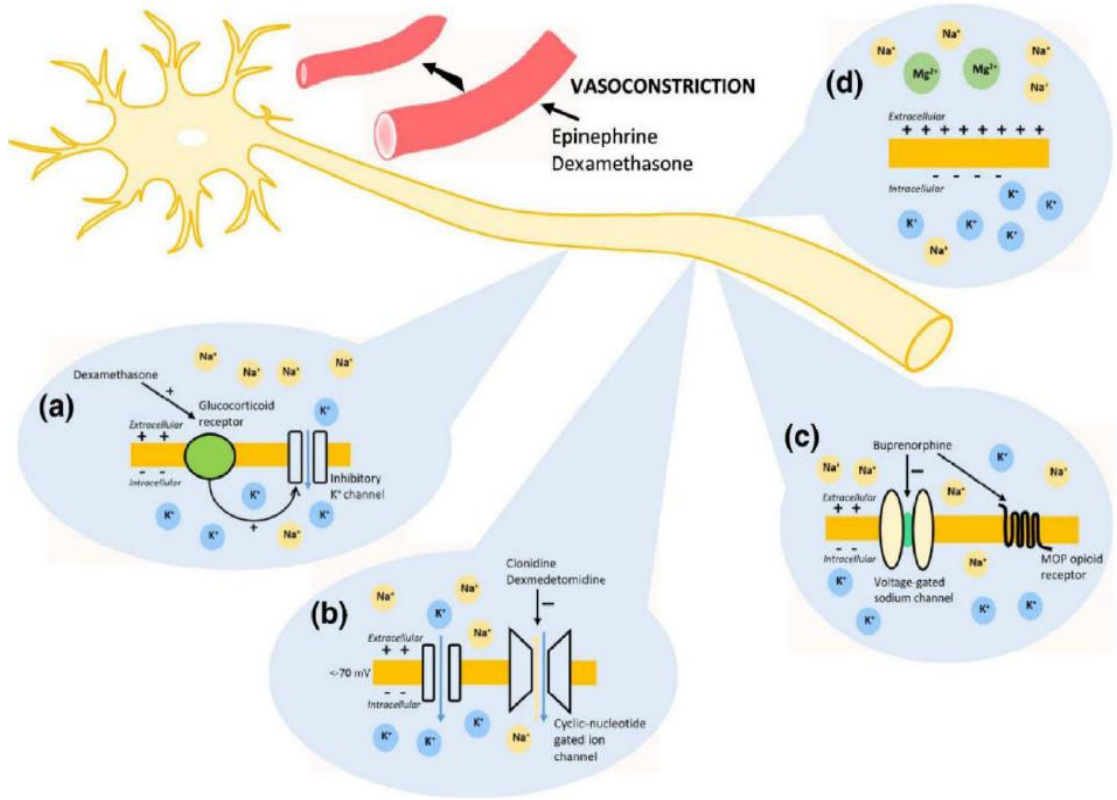
Review of adjuvants to local anesthetics in peripheral nerve blocks: Current and future trends

G V Krishna Prasad, Sangeeta Khanna, and Sharma Vipin Jaishree

little or no adverse event related to neurotoxicity and tissue damage. Although there is extensive use of such adjuvants in the clinical field, none of the molecules is approved by the FDA and is used as an off-label drug. The risk to benefit ratio must be assessed while using such an agent. This review will try to delineate the basic need of adjuvant in peripheral nerve block and will discuss the advantages and limitations of using different adjuvants and will discuss the future prospect of such application.

L'iniezione perineurale di anestetici locali (LA) fornisce analgesia o anestesia attraverso il blocco reversibile dei canali del sodio, con conseguente inibizione della conduzione nocicettiva.

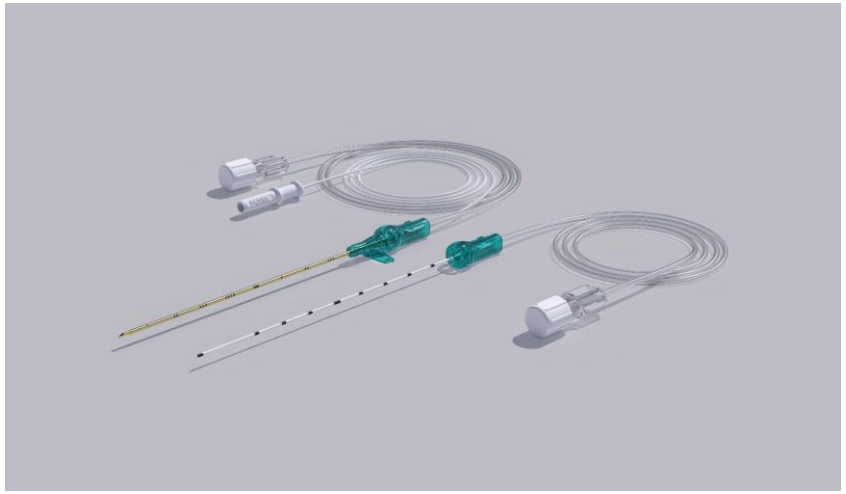
La durata massima di un blocco dei nervi periferici a dose singola dipende principalmente dalla sede o dal sito di iniezione e dal tipo, dal volume e ***dalla concentrazione di ANESTETICO LOCALE utilizzato***



Desai N, Kirkham KR, Albrecht E. Local anaesthetic adjuncts for peripheral regional anaesthesia: a narrative review. Anaesthesia. 2021;76(S1):100-109. doi:10.1111/anae.15245

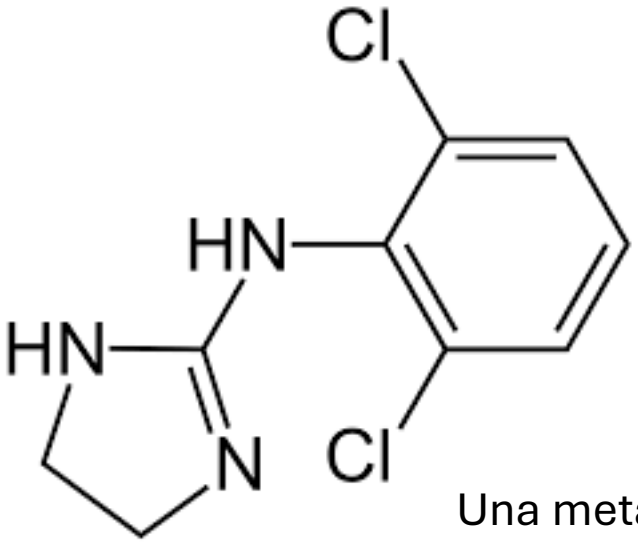
<u>L'analgesia può essere prolungata con</u>:

1. l'inserimento di cateteri perineurali per l'infusione continua o intermittente di AL,
2. l'uso di oppioidi sistemici
3. ***farmaci adiuvanti per prolungare l'effetto dell'effetto clinico dell'AL***.



Tutti questi metodi, tuttavia, presentano delle limitazioni

Medication	Meta-Analysis of RCTs	No. of Trials and Patients	Dose	Analgesia Duration Mean Difference and Range[a]	Duration of Sensory Block Mean Difference and Range	Duration of Motor Block Mean Difference and Range[b]	Side Effects
Epinephrine	Tschopp et al 2018[3]	6 trials; 203 participants	2.5-5 μg/mL	1 hour (32-100 min)[c]	Increased or no difference	Increased or no difference	Hypertension Tachycardia
Buprenorphine	Schnabel et al 2017[4]	13 RCTs; 685 participants	100-300 μg	8.64 h (6.44-10.85)	Not reported	Not reported	PONV (RR 5 [1.12-22.27]) Pruritis (RR 6 [0.75-47.88])
Clonidine	Pöpping et al 2009[6]	20 RCTs, 573 participants received clonidine	150 μg	2.03 h (74-169 min)	1.23 h (37-111 min)[d]	2.35 h (83-199 min)	Bradycardia (OR 3.09 [1.10-8.64]) Hypotension (OR 3.61 [1.52-8.55]) Orthostatic hypotension (OR 5.07 [1.20-21.4]) Sedation (OR 2.28 [1.15-4.51])
Dexmedetomidine	Schnabel et al 2018[7]	46 trials, 3149 participants	30-60 μg	4.87 h (4.02-5.73)[e]	Not reported	3.92 h (3.17-4.67)	Hypotension (OR 3.42[1.24-9.48])
	Sun et al 2019[8]; TAP blocks	20 RCTs, 1212 participants	0.5-1 μg/kg	3.33 h (2.85-3.82) (weighted mean difference)[f]	Not reported	Not reported	Bradycardia (OR 2.83 [1.5-5.33]) Sedation
	Hussain et al 2021[9]; IV versus perineural	10 studies, 359 participants IV, 358 participants perineural	50 μg or 0.5-1 μg/kg[g]	4.94-8.67	1.98-7.75 h[h]	1.55-8.06 h	
Magnesium	Zeng et al 2021[10]	21 RCTs, 1323 participants	150-600 mg	Not reported[i]	1.9 h (89.31-139.88 min)[j]	Not reported	None
Dexamethasone	Pehora et al 2017[11]; perineural or IV dexamethasone	35 RCTs, 2702 participants	4-10 mg	Not reported[k]	6.7 h (5.54-7.85)[l]	5.87 h (4.44-7.30)	Mild increase in glucose concentration with intravenous dose 0.7 mmol/L (0.3-1.2)[11]
	Teshome et al 2020[13]; IV dexamethasone + regional block	11 RCT, 709 participants	4-10 mg	10 mg IV: 5.04 h (2.65-7.44)[m]	8-10 mg IV: 2.74 h (1.65-3.84)	No change	

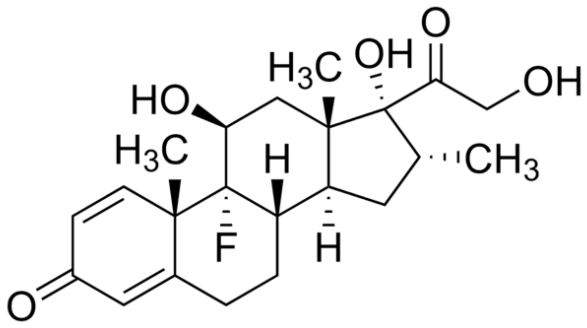


CLONIDINA

La **clonidina** è un agonista parziale dei recettori alfa 2 presenti in abbondanza nel corno dorsale del midollo spinale e nel locus coeruleus. L'iniezione di clonidina attorno ai nervi sensoriali provoca molto probabilmente un'iperpolarizzazione delle fibre A e C

Una meta-analisi del 2009 di 20 RCT che valutavano gli effetti della clonidina perineurale (30-300 µg, più comunemente 150 µg) nei blocchi dei nervi periferici degli arti superiori e inferiori o nei blocchi del plesso ***ha mostrato che i blocchi sensoriali e motori erano prolungati di circa 1,5-2 ore***

Popping DM, Elia N, Marret E, et al. Clonidine as an adjuvant to local anesthetics for peripheral nerve and plexus blocks. Anesthesiology. 2009;111(2):406-415.



DESAMETASONE

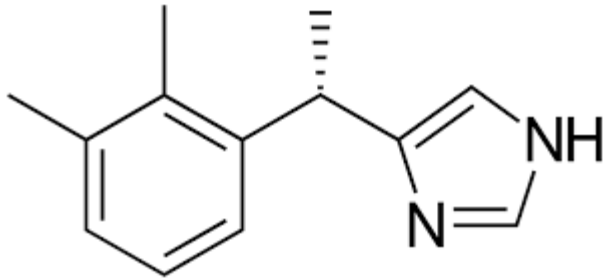
Il ***desametasone*** è un potente farmaco glucocorticoide comunemente usato come adiuvante per ridurre il dolore postoperatorio.
I meccanismi del desametasone somministrato per via perineurale sono probabilmente attribuiti a interazioni complesse, tra cui ***l'inibizione diretta della trasmissione del segnale nelle fibre C nocicettive***, **vasocostrizione locale e riduzione dell'infiammazione locale**

De Oliveira et al. hanno dimostrato che la **somministrazione endovenosa** di 0,1-0,2 mg/kg di desametasone ha ridotto il dolore postoperatorio e il consumo di oppioidi senza effetti collaterali significativi.

De Oliveira GS, Almeida MD, Benzon HT, McCarthy RJ. perioperative single dose systemic dexamethasone for postoperative pain. Anesthesiology.

Analogamente, una meta-analisi che ha valutato il controllo del dolore con desametasone endovenoso in combinazione con blocco dei nervi periferici ha rilevato un miglioramento della durata dell'effetto analgesico nei pazienti trattati con 8-10 mg di desametasone.

Teshome D, Fenta E, Hunie M. Intravenous dexamethasone and peripheral nerve blocks: a systemic review and metaanalysis of randomized controlled trials. Int J Surg Open. 2020



DEXMETEDOMIDINA

La ***dexmedetomidina*** è un agonista selettivo del recettore adrenergico α2 che ha recentemente guadagnato una notevole popolarità in anestesia grazie alle sue ***proprietà sedative, analgesiche e ansiolitiche*** e sta guadagnando interesse come coadiuvante perineurale all'anestesia regionale

Similmente alla clonidina, la dexmedetomidina si lega ai canali attivati dai nucleotidi, ***inibisce il ritorno del neurone allo stato di riposo e previene l'ulteriore generazione di potenziale d'azione***

Diversi studi hanno esaminato il rischio di neurotossicità della dexmedetomidina somministrata per via perineurale. **Schnabel et al.**, ad esempio, hanno riassunto che l'iniezione di dexmedetomidina nei nervi sciatici di ratto in combinazione con ropivacaina o bupivacaina non ***ha mostrato alterazioni significative all'interno del nervo rispetto alla sola somministrazione locale di LA. Inoltre, l'aggiunta di dexmedetomidina ai LA potrebbe avere un effetto protettivo sulla riduzione degli effetti infiammatori dei LA.***

Local Anesthetic Peripheral Nerve Block Adjuvants for Prolongation of Analgesia: A Systematic Qualitative Review

Meghan A. Kirksey[1,2], Stephen C. Haskins[1,2], Jennifer Cheng[1], Spencer S. Liu[1,2]*

1 Department of Anesthesiology, Hospital for Special Surgery, New York, New York, United States of America, **2** Department of Anesthesiology, Weill College of Medicine at Cornell University, New York, New York, United States of America

Table 2. Clinical findings for most extensively studied agents not covered by recent meta-analyses.

Agent	Local Anesthetic	Site/Dose	Prolongation of Analgesia or Sensory Block	Side Effects & Toxicity	Systemic Control (route)	Jadad Scale (I-V)
Buprenorphine	Bupivacaine 0.5% + epi [18]	Sciatic—0.3mg	6h*	PONV events: 7 in control group, 21 in IM buprenorphine group, 19 in PN buprenorphine group	No	V
Buprenorphine	Mepivacaine 1% + tetracaine 0.02% + epi [16]	Axillary—0.3mg	15h**	None	No	III+
Buprenorphine	Mepivacaine 1% + tetracaine 0.02% + epi [17]	SCB—0.3mg	12h?	PONV in 2/20 in PN buprenorphine group, 6/20 in IM buprenorphine group, 3/20 in control group	Yes	V
Buprenorphine	Levobupivacaine 0.75% [18]	ISB—0.15mg	6h***	PONV in 4/50 pts; hypotension in 1/50 pts	No	IV+
Buprenorphine	Lidocaine 1% + bupivacaine 0.5%[15]	SCB- 3mcg/kg	9h*	Pruritus in 4/20 pts; PONV in 10/20 pts	No	II
Buprenorphine	Bupivacaine 0.3%[20]	SCB- 3mcg/kg	6h**	PONV in 2/20 pts in PN buprenorphine group and 2/20 pts in IM buprenorphine group. No buprenorphine-free control group.	Yes (IM)	III
Morphine	Bupivacaine 0.5% + epi [25]	ISB- 5mg	None	1) PONV in 5/20 pts in placebo group and 10/20 pts in morphine group. Pruritus in 3/20 in placebo group and 0/20 in morphine group.	No	III
Morphine	Bupivacaine 0.5%[26]	Intercostal-4mg	None	None	No	III
Morphine	Lidocaine 1.5% + epi[24]	Axillary—0.1mg/kg	None (Note: decreased opiate consumption)	Pruritus in 1/20 PN morphine; nausea in 1/20 PN morphine and 2/20 IV morphine. No morphine-free control group.	Yes (IV)	III
Morphine	Lidocaine 1% + bupivacaine 0.5%[19]	SCB- 75mcg/kg	10h*	Pruritus in 1/20 pts. PONV in 2/20 in morphine group, 1/20 in control group	No	II
Morphine	Lidocaine 1% + bupivacaine 0.5%[27]	Axillary- 4mg	None	PONV in 2/19 PN morphine and 4/21 IV morphine. No morphine-free control group.	Yes (IM)	III
Morphine	Bupivacaine 0.125%[28]	Popliteal-10mg	3h*	Somnolence and nausea in 14/46 pts in morphine phase and 9/46 pts during bupivacaine-alone phase. Decreased BP and HR described in morphine phase without data.	No	IV
Fentanyl	Ropivacaine 0.75%[30]	Axillary- 20mcg	None	Not reported	No	V
Fentanyl	Lidocaine 1.5% + epi[29]	Axillary-100mcg	None	Not reported	No	V
Fentanyl	Lidocaine 1.5% + epi[31]	Axillary-100mcg	1h**,***	Not reported	Yes (IV)	V
Fentanyl	Ropivacaine 0.75%[33]	Sciatic/femoral-1mcg/kg	None	No difference in sedation or oxygen saturation	No	IV+
Fentanyl	Mepivacaine 1.5% + epi [32]	SCB- 75mcg	1h**	Not reported	Yes (IM)	III
Fentanyl	Lidocaine 1.5%[34]	ISB- 75mcg	None	Not reported	No	V
Fentanyl	Bupivacaine 0.25%[35]	Axillary-100mcg	3h***, 10h**	Nausea in 1/20 pts in each fentanyl group, 0/20 in control group. No sedation in any group.	No	III+

(Continued)

Table 2. (Continued)

Agent	Local Anesthetic	Site/Dose	Prolongation of Analgesia or Sensory Block	Side Effects & Toxicity	Systemic Control (route)	Jadad Scale (I-V)
Fentanyl	Articaine 2%[36]	Axillary-100mcg	2h*, 1h***	5/22 with sedation in fentanyl group, 2/22 with sedation in control group	No	V
Fentanyl	Bupivacaine 0.25% + epi[37]	Paravertebral—0.6mcg/kg	12h*	None	No	V
Fentanyl	Bupivacaine 0.5% + lidocaine 2%[38]	Cervical plexus- 50mcg	3h*	Bradycardia in 2/38 in fentanyl group, 1/39 in control group. Hypercapnia in 3/38 in fentanyl group, 1/38 in control group.	No	V
Epinephrine	Lidocaine 1.5%[42]	Axillary-200mcg/ml	45min**	Tachycardia and hypertension with 200mcg	No	IV
Epinephrine	Mepivacaine 1%[43]	Brachial plexus-200mcg	1h***	None	No	III+
Epinephrine	Ropivacaine 0.5% and 0.2%[44]	Femoral-5mcg/ml	None*	None	No	IV
Clonidine	Bupivacaine 0.375%[53]	Sciatic popliteal-100mcg	~3-4h**	None	Yes (IM)	V
Clonidine	Levobupivacaine 0.5% [54]	Sciatic popliteal-150mcg	None*	50% with clonidine experience. >20% decrease in systolic BP	No	V
Clonidine	Ropivacaine 0.5%[55]	Axillary-150mcg	None***	None	No	IV+
Clonidine	Bupivacaine 0.5%[56]	SCB- 1mcg/kg vs. 2mcg/kg	21h with 2mcg/kg, 15h with 1mcg/kg	Higher hypotension, bradycardia, and sedation in 2mcg/kg group	No	V
Clonidine	Bupivacaine 0.5%[57]	SCB- 30mcg	220min*	Sedation	No	V
Clonidine	Lidocaine 1.5% (note: comparison to epinephrine 5mcg/ml) [58]	Cervical plexus- 5mcg/ml	None**	Increased lidocaine plasma concentrations compared to epinephrine	No	V
Clonidine	Bupivacaine 0.5% and lidocaine 2% (note: comparison to 5mg midazolam)[59]	SCB- 150mcg	None**	None	No	I+
Dexmedetomidine	Bupivacaine 0.375%[64]	SCB- 100mcg	~8h*	Bradycardia in one patient	No	III+
Dexmedetomidine	Ropivacaine 0.5%[65]	ISB- 150mcg	~4h**	Lower HR with dexmedetomidine, no neurotoxicity	No	V
Dexmedetomidine	Ropivacaine 0.375%[66]	Cervical plexus- 1mcg/kg	~50min**	Sedation, bradycardia requiring atropine	No	III+
Dexmedetomidine	Mepivacaine 1%[43]	Brachial plexus- 1mcg/kg	~75min**	Bradycardia	No	III+
Dexmedetomidine	Ropivacaine 0.75%[67]	Ulnar nerve block- 20mcg	~200min***	None	Yes (IV)	IV
Dexmedetomidine	Ropivacaine 0.5%[68]	Posterior tibial-1mcg/kg	~4.5h**	Hypotension, bradycardia	No	V
Dexmedetomidine	Bupivacaine 0.25%[69]	SCB- 1mcg/kg	~180min*	Bradycardia	No	V
Dexamethasone	Lidocaine 1.5% + epi[73]	SCB- 8mg	3h**	None	No	V
Dexamethasone	Prilocaine 2%[76]	Axillary- 8mg	3h**	Not reported	No	IV+

(Continued)

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Table 2. (Continued)

Agent	Local Anesthetic	Site/Dose	Prolongation of Analgesia or Sensory Block	Side Effects & Toxicity	Systemic Control (route)	Jadad Scale (I-V)
Dexamethasone	Bupivacaine 0.5%[77]	Sciatic/saph-8mg; ankle-8mg	Sciatic/saph—13% of patients with pain in first 24hrs vs. 47% in IM group; ankle—none	Not reported	Yes (IM)	V
Dexamethasone	Ropivacaine 0.5%[78]	ISB- 10mg	None	3.8- and 5.1-mg/dL increase in blood glucose with PN and IV administration	Yes (IV)	V
Dexamethasone	Bupivacaine 0.5% + epi [79]	Sciatic- 8mg	None	Statistically insignificant increase in incidence of numbness and paresthesia at 24 and 48hrs. No symptoms persisted at 8wks in any group.	Yes (IV)	V
Dexamethasone	Bupivacaine 0.25%[74]	TAP- 8mg	1h*	Decreased nausea and vomiting (6/30 with dexamethasone vs. 14/30 with control).	No	IV+
Dexamethasone	Bupivacaine 0.25%[81]	SCB- 1mg, 2mg, 4mg	10h*	One transient paresthesia noted in 2mg group	Yes (IV)	V
Tramadol	Levobupivacaine 0.5% [80]	ISB—1.5mg/kg	7h*	None	Yes (IM)	V
Tramadol	Lidocaine 1.5% + epi[90]	Axillary- 200mg	160min*, 65min***	None	No	V
Tramadol	Levobupivacaine 0.5% + lidocaine 2%[91]	Axillary- 100mg	None*	Sedation, nausea	No	IV+
Tramadol	Levobupivacaine 0.5% [92]	Psoas—1.5mg/kg	None*	None	Yes (IV)	V
Tramadol	Mepivacaine 1.5%[93]	Axillary- 40mg, 100mg, 200mg	60min, 40min, 40min*	Nausea/vomiting	No	IV
Tramadol	Mepivacaine 1%[94]	Axillary- 100mg	100min***	None	Yes (IV)	IV
Tramadol	Ropivacaine 0.75%[95]	Axillary- 100mg	None*	None	No	V
Tramadol	Bupivacaine 0.5%[96]	Paravertebral—1.5mg/kg	None*	None	No	V
Magnesium	Bupivacaine 0.25%[102]	Femoral-500mg	10h*, 2h***	Not reported	No	III
Magnesium	Bupivacaine 0.5%[103]	ISB- 200mg	2h*	Nausea 2-3x more frequently at 4, 8, and 12hrs postoperatively with magnesium	No	V
Magnesium	Prilocaine 2%[104]	Axillary-150mg, 100mg	2h***, 1h***	None	Yes (150mg IV)	II
Magnesium	Levobupivacaine 0.5% [102]	Axillary- 150mg	150min***	No thrombi or vasospasm in any group. Other side effects not reported.	No	III+
Magnesium	Levobupivacaine 0.25% [105]	Axillary- 150mg	100min***	No thrombi or vasospasm in any group. Other side effects not reported.	No	III+

A multitude of adjuvants for prolongation of peripheral nerve blocks have been investigated, but none have FDA approval for this purpose and because most are off-patent, they are unlikely to gain FDA approval in the absence of a vested-interest commercial sponsor. Moreover, few agents have been thoroughly investigated for potential neurotoxicity, and few published clinical trials have appropriate INDs or equivalent status. Based on our review, however, a few adjuvants that are widely utilized and broadly studied have been shown to be efficacious for prolongation of peripheral nerve blocks for postoperative analgesia with no clinical evidence of neurotoxicity. A summary of findings and recommendations is shown in Table 3, along with each agent's criteria for inclusion.

Table 3. Summary of findings and recommendations.

Agent	Criteria for Inclusion[1]	Strength of Study Evidence[2]: a-Quality/Quantity; b-Consistency; c-Significance	Summary/Recommendations	Grade of Recommendation (level of evidence)[3]
Buprenorphine	Attestation	a- 4/6; b- 100%; c- high (all ≥ 6h)	Buprenorphine can significantly prolong PNB. Concern for PONV merits multimodal antinausea prophylaxis.	A (1b)
Morphine	FDA	a- 1/6; b- 33%; c- moderate (3h and 10h)	Not recommended due to lack of quality studies and lack of consistently positive results.	A (1b)
Fentanyl	Attestation	a- 9/10; b- 60%; c- moderate (3–12h for bupivacaine blocks)	May prolong bupivacaine PNB. Not recommended due to inconsistent results and concern for increased rates of sedation, bradycardia, and hypercapnia.	A (1b)
Epinephrine	Attestation	a- 3/3; b- 66%; c- low (no more than 1h)	May prolong blockade by a minimal amount (45–60min). High doses can result in systemic absorption, tachycardia, and hypertension. Avoid use in patients with preexisting neurovascular compromise, such as diabetic neuropathy.	A (1b)
Clonidine	Attestation	a- 6/7; b- 43%; c- moderate (3–6h for bupivacaine blocks)	Prolongs blockade with bupivacaine but does not appear to be effective with ropivacaine or levobupivacaine. *Meta-analysis of 20 other papers shows ~2-h prolongation of nerve block. High doses (2mcg/kg) can cause hypotension, bradycardia, and sedation via systemic absorption.	A (1a, 1b)
Dexmedetomidine	IND; Attestation	a- 7/7; b- 100%; c- moderate (1–8h)	Evidence supports block prolongation from 1–8h depending on the block and local anesthetic. *Meta-analysis of 4 other papers shows prolongation, but was not statistically significant. May increase bradycardia and sedation intraoperatively.	A (1a, 1b)
Dexamethasone	IND; Attestation	a- 6/6; b- 50% (100% with placebo control, 0% with systemic control); c- moderate (1–3h)	Perineural dexamethasone likely prolongs nerve blockade; however, analgesic effect is similar with systemic dexamethasone. Its use may decrease rates of PONV in procedures with high incidence. *Meta-analysis of 9 other papers supports prolongation of brachial plexus blocks compared to dexamethasone-free controls.	A (1a, 1b)
Tramadol	Attestation	a- 8/8; b- 50%; c- low with axillary (40–160min, 3 studies); high with ISB (7h, 1 study).	7/8 studies showed minimal to no prolongation of analgesia or nerve blockade. Not recommended due to lack of evidence of clinically significant efficacy and potential to increase sedation and PONV.	A (1b)
Magnesium	Attestation	a- 3/5; b- 100%; c- low for brachial plexus (1–2.5h, 4 studies); high for FNB (10h for analgesic request, 1 study)	Consistently shown to prolong PNB but likely not clinically significant for brachial plexus blocks. One study of moderate quality (Jadad III) suggests significantly increased duration of analgesia for FNB. Further high-quality studies needed to determine toxicity profile and minimal effective dose. Concern for PONV at 200mg dose. Not recommended at this time.	A (1b)
Ketamine	Harm	a- 2/2; b- 0%; c- N/A	Not recommended due to lack of evidence of efficacy and significant side effect profile (hallucinations, drowsiness, and nausea).	A (1b)
Neostigmine	Harm	a- 3/4; b- 25%; c- low (<1h)	Not recommended due to lack of evidence of efficacy, significant neurotoxicity in rabbit model, and high rate of GI distress.	A (1b)

Based on our review, however, a few adjuvants that are widely utilized and broadly studied have been shown to be efficacious for prolongation of peripheral nerve blocks for postoperative analgesia with no clinical evidence of neurotoxicity. A summary of findings and recommendations is shown in Table 3,along with each agent's criteria for inclusion

Table 3. (*Continued*)

Agent	Criteria for Inclusion[1]	Strength of Study Evidence[2]: a-Quality/Quantity; b-Consistency; c-Significance	Summary/Recommendations	Grade of Recommendation (level of evidence)[3]
Midazolam	Harm	a- 0/2; b- 100%; c- moderate (3h)	Not recommended due to established neurotoxicity when administered with local anesthetics in animal models, high incidence of sedation, and lack of quality clinical studies.	A (1b)

[1]Attestation: Referenced in textbooks and/or multiple (>5) peer-reviewed research publications; Harm: Not Food and Drug Administration (FDA)-approved and balance of evidence suggests harm with perineural use; FDA: FDA-approved for regional anesthesia; IND: Investigational New Drug status (or international equivalent) granted or waived for in at least one reviewed study.

[2]a: Studies with Jadad score III+ or higher/total number of studies; b: % of studies with positive results; c: clinical significance of positive results (extent of prolongation of analgesia or sensory block).

[3]Agency for HealthCare Research and Quality Levels of Evidence and Grades of Recommendations: Grade A: based directly on Level 1 evidence; Level 1a: evidence from meta-analysis of clinical trials; Level 1b: evidence from at least 1 randomized controlled trial.

Abbreviations: PNB = peripheral nerve block; PONV = postoperative nausea and vomiting; ISB = interscalene block; FNB = femoral nerve block; GI = gastrointestinal.

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Crystallization of ropivacaine and bupivacaine when mixed with different adjuvants: a semiquantitative light microscopy analysis

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CONCLUSION

Our study revealed that crystallization is present in pure, commercially available versions of long-acting LAs, and show a variable, unpredictable change pattern when these substances are mixed with adjuvants. A relationship between pH and grade of crystallization could only be observed in 1:1 mixtures and mixtures in clinically relevant concentrations, where higher pH, was weakly associated with more crystallization. Further research is necessary to translate these findings into clinical practice.

Table 2 pH and grade of crystallization of LAs, adjuvants and mixtures for three analytic steps

Step 1: Substances (pure)	pH t_0	GoC t_0	Step 3: Clinically relevant mixture over time (ratio in mL)	pH t_0	GoC t_0	GoC t_{15}	GoC t_{30}	GoC t_{60}
Reference			Ropivacaine 0.2%					
Sterile water	6.3	0	+Clonidine (30:1)	4.75	3	2	3	3
Triamcinolone	6.56	5	+Dexamethasone (30:2)	6.6	3	3	2	2
Local anesthetics			+Dexmedetomidine (30:1)	4.75	3	3	3	4
Ropivacaine 0.2%	4.34	2	+Fentanyl (4.8:0.2)	4.48	3	3	3	3
Ropivacaine 0.75%	4.14	3	+Sodium chloride 0.9% (1:1)	6.12	3	3	3	4
Ropivacaine 1%	4.11	3	+Sodium bicarbonate 8.4% (10:1)	7.60	4	4	5	5
Bupivacaine 0.25%	6.23	4	Ropivacaine 0.75%					
Bupivacaine 0.5%	5.85	4	+Clonidine (30:1)	4.18	1	2	4	4
Adjuvants			+Dexamethasone (30:2)	6.99	5	5	5	5
Clonidine	4.62	2	+Dexmedetomidine (30:1)	4.21	4	3	4	3
Dexamethasone	8.55	1	+Fentanyl (4.8:0.2)	4.20	3	3	4	4
Dexmedetomidine	5.87	2	+Sodium chloride 0.9% (1:1)	5.17	3	4	3	3
Fentanyl	5.73	2	+Sodium bicarbonate 8.4% (10:1)	6.93	5	5	5	5
Sodium chloride 0.9%	5.57	2	Bupivacaine 0.25%					
Sodium bicarbonate 8.4%	8.32	1	+Clonidine (30:1)	6.14	3	3	2	2
			+Dexamethasone (30:2)	6.74	3	3	3	4
Step 2: mixtures 1:1	pH	GoC	+Dexmedetomidine (30:1)	6.14	3	2	3	3
	t_0	t_0	+Fentanyl (4.8:0.2)	5.26	4	2	2	2
Ropivacaine 0.2%			+Sodium chloride 0.9% (1:1)	5.04	3	3	3	2
+Clonidine	4.75	3	+Sodium bicarbonate 8.4% (10:1)	7.75	4	4	5	5
+Dexamethasone	7.24	3	Bupivacaine 0.5%					
+Dexmedetomidine	4.81	2	+Clonidine (30:1)	5.95	3	3	3	3
+Fentanyl	5.41	2	+Dexamethasone (30:2)	6.55	4	3	3	3
+Sodium chloride 0.9%	6.12	3	+Dexmedetomidine (30:1)	5.91	4	3	3	3
+Sodium bicarbonate 8.4%	7.77	5	+Fentanyl (4.8:0.2)	6.07	2	3	3	3
Ropivacaine 1%			+Sodium chloride 0.9% (1:1)	6.10	2	4	3	3
+Clonidine	4.33	4	+Sodium bicarbonate 8.4% (10:1)	7.43	5	5	5	5
+Dexamethasone	6.83	4						
+Dexmedetomidine	4.62	4						
+Fentanyl	5	3						
+Sodium chloride 0.9%	4.37	3						
+Sodium bicarbonate 8.4%	8.51	5						
Bupivacaine 0.25%								
+Clonidine	5.7	3						
+Dexamethasone	7.28	3						
+Dexmedetomidine	6.15	3						
+Fentanyl	5.88	2						
+Sodium chloride 0.9%	5.04	3						
+Sodium bicarbonate 8.4%	8.20	4						
Bupivacaine 0.5%								
+Clonidine	5.85	2						
+Dexamethasone	7.05	2						
+Dexmedetomidine	5.93	3						
+Fentanyl	5.95	2						
+Sodium chloride 0.9%	6.10	2						
+Sodium bicarbonate 8.4%	8.91	5						

GoC, grade of crystallization; LA, local anesthetic; t_0, directly after mixing; t_{15}, 15 min after mixing; t_{30}, 30 min after mixing; t_{60}, 60 min after mixing.

Conclusione:

L'impiego degli adiuvanti in anestesia locoregionale rappresenta una strategia sempre più diffusa ed efficace per ***potenziare la qualità del blocco anestetico, prolungare la durata dell'analgesia e ridurre il consumo di anestetici locali***.

Molecole come gli oppioidi, gli α2-agonisti (es. clonidina e dexmedetomidina), i corticosteroidi, il magnesio e altri farmaci ***hanno dimostrato benefici significativi in diversi contesti clin***ici, sebbene la scelta dell'adiuvante debba sempre essere guidata dal profilo del paziente, dal tipo di procedura e dalla valutazione rischio-beneficio.

Tuttavia, nonostante i numerosi vantaggi, è fondamentale ***tenere conto delle possibili complicanze e degli effetti collaterali associati all'uso di tali sostanze***, sottolineando l'importanza di una corretta selezione dei farmaci, di un dosaggio appropriato e di un attento monitoraggio intra- e post-operatorio.

Ulteriori studi clinici controllati e linee guida aggiornate saranno essenziali per ottimizzare l'uso degli adiuvanti e per garantire la massima sicurezza ed efficacia nell'ambito dell'anestesia locoregionale.


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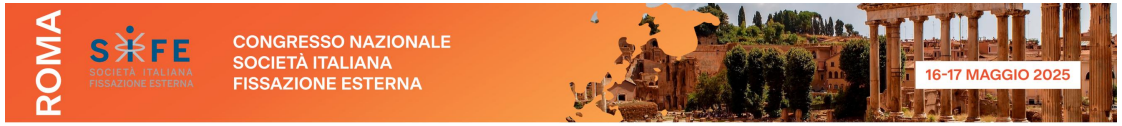
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