Adjuvant Analgesics: Dr. Ralph Laraiso

CLASS OF ADJUVANT ANALGESIC	EXAMPLES
Caffeine	Caffeine monotherapy; caffeine/paracetamol; caffeine/ibuprofen
Antidepressants	Amitriptyline; duloxetine; venlafaxine
Anticonvulsants	Gabapentin; pregabalin; carbamazepine; sodium valproate
Antipsychotics	Olanzapine
Glucocorticoids	Dexamethasone; methylprednisolone
Alpha-2 agonists	Dexmedetomidine; clonidine
NMDA-receptor antagonists	Ketamine; dextromethorphan; memantine; magnesium
Skeletal muscle relaxants	Tizanidine; methocarbamol; baclofen
Antiarrhythmic agents	Lidocaine; mexiletine; tocainide
Medicinal cannabis	CBD; THC

Table 1. Classes of Adjuvant Analgesics

Source: Indian Journal of Pain, Vol. 37, Issue 2 (2023).

Line	Class/Drug	Examples
First line	Tricyclic antidepressants	Amitriptyline; desipramine
First line	"Newer" antidepressants	Paroxetine
First line	Oral local anesthetics	Mexiletine; tocainide; flecainide
Refractory	Alpha-2 adrenergic agonists	Clonidine
Refractory	Anticonvulsants	Carbamazepine; phenytoin; valproate; clonazepam
Refractory	Topical agents	Capsaicin; local anesthetics
Refractory	Neuroleptics	Prochlorperazine; haloperidol
Refractory	NMDA receptor antagonists	Dextromethorphan; ketamine
Refractory	Calcitonin	—
Refractory	Baclofen	—

Adjuvant Analgesics for Neuropathic Pain (Predominating Continuous Dysesthesias)

NMDA = N-methyl-D-aspartic acid. Source: Indian Journal of Pain, Vol. 37, Issue 2 (2023).

Line	Class/Drug	Examples
First line	Anticonvulsants	Carbamazepine; phenytoin; valproate; clonazepam
First line	Baclofen	—
Refractory	Oral local anesthetics	Mexiletine; tocainide; flecainide
Refractory	Tricyclic antidepressants	Amitriptyline; desipramine
Refractory	"Newer" antidepressants	Paroxetine
Refractory	Pimozide	—
Refractory	Clonidine	—
Refractory	Topical agents	Capsaicin; local anesthetics
Refractory	NMDA receptor antagonists	Dextromethorphan; ketamine
Refractory	Calcitonin	—

Adjuvant Analgesics for Neuropathic Pain (Lancinating/Paroxysmal Dysesthesias)

NMDA = N-methyl-D-aspartic acid. Source: Indian Journal of Pain, Vol. 37, Issue 2 (2023).

Adjuvant	Study	Study type	Study population	Outcome	Comments
Caffeine	Schachtel et al. [21]	RCT	Patients with acute sore throat	Aspirin with caffeine provided significantly better pain relief than aspirin alone	
Dexmedetomidine	Cai et al. [33]	RCT	Patients undergoing thoracic surgery	Lower postoperative pain scores and opioid requirements; P<0.05	Systemic dexmedetomidine
Dexmedetomidine	Patro et al. [34]	RCT	Patients undergoing infra-umbilical surgeries	Early onset of analgesia; P<0.001, with lower pain scores 3 h postoperative; P<0.001, compared to bupivacaine alone	Intrathecal dexmedetomidine
Clonidine	Samantaray et al. [30]	RCT	Patients undergoing thoracic surgery	Less intraoperative opioid requirement; P=0.03, with longer time to first postoperative analgesic requirement; P=0.00001 compared to placebo	Premedication with single intravenous dose
Ketamine	Kundra et al. [57]	Randomized, double-blind cross-over study	In-patients undergoing wound dressing for major thermal burns. Oral ketamine versus oral dexmedetomidine	The mean pain score was significantly reduced in both the groups (P<0.05). More patients preferred ketamine than dexmedetomidine (P<0.05)	Delirium and excessive salivation were common side effects of the oral ketamine
Magnesium sulfate	Tsaousi et al. [62]	RCT	Systemic magnesium sulfate versus saline placebo	Lower intraoperative opioid consumption; P<0.01 and postoperative analgesics consumption; P=0.001, in the magnesium group	No significant differences in surgical site infection and wound healing
Methylprednisolone	Kurosaka et al. [26]	RCT; two-arm, parallel-group	Patients undergoing lumbar laminectomy / Total hip replacement. Periarticular injection cocktail with, versus without prednisolone	Lower postoperative pain in the corticosteroid group compared to the no-corticosteroid group; P=0.002	
Methocarbamol	Emrich et al. [55]	RCT	Patients with acute low back pain associated with spasms	19% discontinued treatment because it was considered ineffective (placebo 52%); P<0.0001)	Treatment was well tolerated
Tizanidine	Pareek et al. [49]	Randomized, controlled, parallel-group study	Patients with acute low back pain associated with degenerative spine disease	76% of the patients on the aceclofenac-tizanidine treatment versus 34% on aceclofenac alone rated their response as excellent-good	The incidence of adverse events in both treatment groups was comparable, and none was serious
Gabapentin	Mahoori et al. [45]	RCT	Premedication with gabapentin versus placebo in patients undergoing inguinal herniorrhaphy	Pain scores and total opioid consumption in the first 24 h after surgery were significantly lower in gabapentin group than in the placebo group (P<0.05 and P=0.003, respectively)	

Table 2: Studies of adjuvant analgesics for different types of pains (Part 1)

Adjuvant	Study	Study type	Study population	Outcome	Comments
Amitriptyline	Urquhart et al. [37]	RCT with active comparator (benztropine mesylate) control	Adults with chronic, nonspecific, low back pain	Clinically significant improvement in disability at 3 months in the low-dose amitriptyline group but not the control	Minimal adverse events reported with low-dose amitriptyline
Carbamazepine	Saeed et al. [42]	Open-label, uncontrolled trial	Adult diabetic neuropathy patients	The mean ± SD pain severity score decreased from 5.8 ± 2.0 at baseline to 3.6 ± 2.2 at week 12; P<0.001	None of the 452 enrolled patients discontinued the study due to adverse events
Dexamethasone, Methylprednisolone	Kim and Brown [29]	Comparative randomized clinical trial	Patients with chronic lumbar radiculopathy	87% of patients in the methylprednisolone group and 90% in the dexamethasone group had decreases in postoperative pain	Translaminar epidural injections
Medicinal cannabis	Abrams et al. [5]	Randomized controlled trial	In-patients with HIV-associated chronic neuropathic pain	Smoked cannabis reduced daily pain by 34% versus 17% with placebo; P=0.03	No serious adverse events were reported

Table 2: Studies of adjuvant analgesics for different types of pains (Part 2)

Drug/Class	Cardiotoxicity	Sedation	Anticholinergic
Tertiary amines – Amitriptyline	++	+++	+++
Secondary amines – Nortriptyline	+	++	+
Secondary amines – Desipramine	+	+	+
SSRIs – Paroxetine	-	+/-	-

Comparison of Antidepressant Side Effects

References

Nwosu AS, Chukwu LC, Onwuasoigwe O, et al. Redefining the role of analgesic adjuvants in pain management: A narrative review. Indian Journal of Pain. 2023;37(2):65–73.