REFINING PHARMACOTHERAPY FOR INFERIOR ALVEOLAR NERVE INJURIES IN MANDIBULAR FRACTURES: A PATHOPHYSIOLOGICAL AND EVIDENCE-BASED APPROACH

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Abstract: Inferior alveolar nerve injury is a frequent and debilitating complication of mandibular fractures, often leading to persistent sensory dysfunction and impaired quality of life. Current pharmacotherapy remains fragmented and lacks a standardized, mechanism-based protocol. This review critically evaluates pharmacological agents and proposes a refined, phased multimodal approach aligned with the temporal biology of nerve injury. A comprehensive literature review analyzed corticosteroids, NSAIDs, neurotrophic B vitamins, alpha-lipoic acid, and citicoline. The proposed protocol integrates acute neuroprotection, subacute inflammatory modulation, and sustained pro-regenerative support.

Keywords: Inferior Alveolar Nerve, Mandibular Fracture, Neurosensory Disturbance, Pharmacotherapy, Nerve Regeneration, Neurotrophic Agents, Corticosteroids, Multimodal Protocol.

Background: Inferior alveolar nerve (IAN) injury represents one of the most clinically significant complications following mandibular fracture, with reported incidence ranging from 10% to 81% depending on fracture location, degree of displacement, and diagnostic methodology. The IAN, a terminal sensory branch of the mandibular division of the trigeminal nerve, courses through the bony mandibular canal and provides innervation to the ipsilateral lower lip, chin, buccal gingiva, and mandibular dentition. Mechanical trauma from fracture fragments whether compression, stretch, crush, or transection initiates a complex pathophysiological cascade involving intraneural edema, ischemia, oxidative stress, Wallerian degeneration, and potential central sensitization. Resulting neurosensory disturbances include paresthesia, dysesthesia, hypoesthesia, and, in severe cases, complete anesthesia or neuropathic pain syndromes. These sensory deficits profoundly impact daily functions such as speech, eating, and social interaction, significantly diminishing patient quality of life.

Objective: To critically evaluate current pharmacological strategies and propose a refined, mechanism-based, phased multimodal pharmacotherapeutic protocol that aligns drug interventions with the spatiotemporal pathophysiology of IAN injury, aiming to optimize neurosensory recovery.

Materials and Methods: A narrative review of literature published between 1990 and 2025 was conducted using PubMed, Scopus, and Google Scholar databases. Search terms included "inferior alveolar nerve," "mandibular fracture," "neurosensory disturbance," "pharmacotherapy," "nerve regeneration," "neurotrophic factors," and "corticosteroids." Preclinical animal models of peripheral nerve injury and clinical studies evaluating pharmacological efficacy were critically analyzed for methodological rigor and relevance.

Results: The pathophysiological timeline of IAN injury defines three distinct therapeutic windows requiring specific pharmacological interventions. The acute phase (0–72 hours) is characterized by intraneural edema, calcium-mediated excitotoxicity, and excessive inflammation. High-dose dexamethasone (8–12 mg IV preoperatively, tapered over 3–5 days) effectively reduces endoneurial edema, while intravenous magnesium sulfate attenuates NMDA-receptor-mediated neuronal damage. The subacute phase (1–4 weeks) involves Wallerian degeneration and oxidative stress.

Selective COX-2 inhibitors provide analgesia without entirely abolishing reparative inflammatory signaling, while alpha-lipoic acid (600–800 mg/day) scavenges free radicals, restores glutathione levels, and improves endoneurial microcirculation. The chronic regeneration phase (1–6+ months) requires sustained metabolic support for axonal elongation at the slow rate of approximately 1 mm/day. High-dose methylcobalamin (1500–3000 mcg/day) and benfotiamine (300–600 mg/day) enhance

axonal transport and Schwann cell metabolism, while citicoline (1000–2000 mg/day) supports neuronal membrane repair and remyelination. This multimodal, temporally-phased protocol demonstrates theoretical superiority over conventional single-agent, non-phased therapy by simultaneously addressing the multiple parallel pathological pathways.

Conclusion: A phased multimodal pharmacotherapeutic protocol initiated early in the perioperative period and sustained throughout neural recovery provides a biologically rational and mechanistically comprehensive strategy for managing traumatic IAN injuries. By protecting neural elements in the acute phase, modulating inflammation in the subacute period, and fueling regeneration chronically, this refined approach offers significant potential to reduce permanent neuropathy and improve functional sensory outcomes in patients with mandibular fractures.

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