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| TBI Pharmacological Regimen | Proposed Mechanism |
| Cholinesterase Inhibitors | Cholinesterase inhibitors including galantamine, donepezil, and rivastigmine, have been repurposed for TBI patients1. |
| NMDA receptor antagonists | NMDA receptor antagonist, amantadine, has been shown to improve cognition in moderate to severe TBI patients2. |
| SSRIs | Selective serotonin reuptake inhibitors (SSRIs) like sertraline and escitalopram have been utilized to mange behavioral symptoms in TBI patients3. |
| Guanfacine | Guanfacine has been reported to improve working memory deficits in mild TBI patients4. |
| Nutraceuticals | A number of nutraceuticals have been utilized in treatment of TBI preclinical and clinical studies, including N-acetylcysteine (NAC), flavonoids, resveratrol, alpha-tocopherol (vitamin E), coenzyme Q105. |
| NSAIDs | COX-2 selective drugs like carprofen, celecoxib, meloxicam, nimesulide, and rofecoxib have undergone testing in various preclinical TBI models, with no significant degree of established efficacy6. |
| Glucocorticoids | Despite several promising preclinical studies, clinical trials have resulted in limited success, likely due to a narrow therapeutic window7. |
| Phosphodiesterase Inhibitors | Phophodiesterase inhibitors have been utilized mostly in preclinical studies, and have not systematically studied in clinical trial setting8. |
| Minocycline | In prior preclinical studies, minocycline given between 5 min and 1 h after injury improved performance on a variety of neurobehavioral9. |
| Progesterone | A large, multi-center Phase III PROtect III trial, , as well as a second larger scale trial (SYNAPSE) examined progesterone did not establish clinical effiacy10. |
| Erythropoietin | Despite preclinical studies success, the evidence for the use of erythropoietin has not reached the threshold for its use in a phase III trial6. |
| Anakinra | A small phase II randomized controlled clinical trial reported anti-inflammatory benefits in Anakinra treated group, but the study size was too small to establish efficacy, but provided an intriguing potential future approach11. |
| Tau phosphorylation targets | The studies focusing on tau-phosphorylation targets have been mostly preclinical, with possible future clinical applications12. |
| Tau acetylation targets | Tau acetylation inhibitors including salsalate, as well as methylene blue, as well as histone deacetylase 6 and sirtuins have largely been examined in the preclinical setting13. |
| Immunotherapy | Specific antibodies targeting the pathogenic cis-P-tau post TBI have been reported to lead to improved structural and functional outcomes14, but yet to be examine in larger clinical trial setting. |

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