Quotations from Articles on Propranolol for Aggression – Compiled by Strayhorn

"The best evidence of effectiveness in the management of agitation and/or aggression following ABI [acquired brain injury] was for beta-blockers. Two RCTs found propranolol to be effective." Fleminger S et al., 2006 Pharmacological management for agitation and aggression in people with acquired brain injury. Cochrane Database of Systematic Reviews. https://doi.org/10.1002/14651858.CD003299.pub2

"Case report. Mr A, a 20-year-old man diagnosed as having moderate intellectual disability and generalized epilepsy, presented to our clinic with severe aggression, both verbal and physical, occurring with little or no provocation over the past 3 years. These episodes would last up to several hours….He had already received trials of olanzapine (up to 15 mg/d for 6 weeks) and chlorpromazine (up to 400 mg/d for 3 months) without significant improvement and was currently on olanzapine 10 mg/d and chlorpromazine 300 mg/d in addition to his medications for epilepsy. As his mother reported features of autonomic arousal—such as increased perspiration, motor agitation, and rapid breathing—during each episode, he was given a trial of propranolol, starting at 20 mg/d and increased by 20 mg every week. At 40 mg/d, there was a significant reduction in his aggression, and his food intake was better. On further increasing the dose to 60 mg/d, his mother reported that he was essentially "normal," with no significant episodes of aggression. Over the next year, olanzapine and chlorpromazine were tapered and stopped, and he remained stable. He has been well on carbamazepine 1,000 mg/d, propranolol 60 mg/d, and diazepam 10 mg/d for the past 3 months with no recurrence of either seizures or aggression, and it is now possible to engage him in household tasks and speech therapy." Rajkumar RP 2012. Successful Management of Difficult-to-Treat Aggression With Low-Dose Propranolol in a Patient With Intellectual Disability: A Case Report. Prim Care Companion CNS Disord. 2012; 14(5): PCC.12l01373. doi: 10.4088/PCC.12l01373

"Of eight Mayo Clinic patients with intermittent explosive disorder who had been treated with propranolol between 1983 and 1985, five had substantial diminution or complete remission of symptoms. This response confirms the previously published reports of the effectiveness of propranolol in the treatment of intermittent explosive disorder." Mayo Clin Proc 1987 Mar;62(3):204-14. doi: 10.1016/s0025-6196(12)62444-6.Therapeutic use of propranolol for intermittent explosive disorder. S C Jenkins, T Maruta. PMID: 3546964 DOI: 10.1016/s0025-6196(12)62444-6

"Beta-blockers appear to be effective in decreasing the frequency and intensity of aggressive outbursts associated with a wide variety of conditions, such as dementias, attention-deficit disorder, personality disorders, Korsakoff's psychosis, posttraumatic stress disorder,

schizophrenia, profound mental retardation, autism, and brain injury." Haspel T. Beta-blockers and the treatment of aggression. Harv Rev Psychiatry. 1995;2(5):274-281. doi:10.3109/10673229509017146

"Although a neurochemical basis for aggression in these cases is unclear, a hyperadrenergic state is considered to be one possibility. This has led to the hypothesis that beta blockers may be useful in the control of aggression. The original assumption was that the site of antiaggressive action of beta blockers is in the brain. However, the antiaggressive efficacy of nadolol, which does not cross the blood-brain barrier to any great extent, suggests a peripheral site or sites. A review of several studies in which both old and young aggressive patients with various organic brain disorders received propranolol showed that aggressive behavior was reduced in 75 (86%) of 87. These results are encouraging because none of the patients had responded to earlier drug treatment. However, with the exception of one study of nine patients, none of the studies were controlled for placebo effects and most were retrospective. Preliminary results suggest tentative guidelines for treatment of aggressive behavior with beta blockers. Further studies are needed, and these should use a prospective, longitudinal double-blind design; large enough patient samples to permit testing hypotheses about disease-specific or symptom-specific responses to beta blockers; and improved instruments for measuring and classifying aggression." Volavka J. Can aggressive behavior in humans be modified by beta blockers?. Postgrad Med. 1988;Spec No:163-168.

"The authors successfully treated four patients who had irreversible CNS lesions and socially disabling aggressiveness and outbursts of rage, which had not been affected by high doses of major tranquilizers or anticonvulsants, with 320-520 mg/day of propranolol. Disorientation, memory impairment, and psychotic thought processes associated with the CNS lesions were not altered by the propranolol." Yudofsky S, Williams D, Gorman J. Propranolol in the treatment of rage and violent behavior in patients with chronic brain syndromes. Am J Psychiatry. 1981;138(2):218-220. doi:10.1176/ajp.138.2.218

"Trends identified in the literature reviewed suggested that amantadine, propranolol, and anti-epileptics were the best supported medications to consider." Nash RP, Weinberg MS, Laughon SL, McCall RC, Bateman JR, Rosenstein DL. Acute Pharmacological Management of Behavioral and Emotional Dysregulation Following a Traumatic Brain Injury: A Systematic Review of the Literature. Psychosomatics. 2019 Mar-Apr;60(2):139-152. doi: 10.1016/j.psym.2018.11.009. Epub 2018 Dec 18. PMID: 30665668; PMCID: PMC8609889.

"Metoprolol, a selective beta 1-adrenoreceptor blocker, was administered to two patients with intermittent explosive disorder who had not done well with previous medications, including propranolol and carbamazepine. Both patients improved dramatically, suggesting clinical and theoretical relevance." Mattes JA. Metoprolol for intermittent explosive disorder. Am J Psychiatry. 1985;142(9):1108-1109. doi:10.1176/ajp.142.9.1108

“All three patients responded to propranolol with a decrease or complete cessation of episodic aggressive outbursts and a trend toward less aggressiveness overall. Their symptoms had not been controlled with high doses of antipsychotics, anticonvulsants, and in one case, lithium. Numerous social, behavioral, and other psychotherapeutic measures were also unsuccessful in controlling the patients’ rage attacks. In two cases propranolol was used when all other therapies failed, and in the other case propranolol was used to control a gross tremor disorder and serendipitously controlled the rage episodes.” Ratey JJ, Morrill R, Oxenkrug G. Use of propranolol for provoked and unprovoked episodes of rage. Am J Psychiatry. 1983;140(10):1356-1357. doi:10.1176/ajp.140.10.1356

“Methods/Procedures: Here, we present 46 retrospective analyses of clinical cases that were followed by a psychiatrist. Propranolol was prescribed as an add-on to the patients' existing medications. The doses ranged from 120 to 960 mg per day (mean = 462 mg). Findings/Results: Thirty-nine (85%) of 46 patients were found to be much improved or very much improved on the physician-rated Clinical Global Impression Improvement scale. There were few side effects noted, with only 2 subjects unable to tolerate the propranolol. Implications/Conclusions: It appears that high-dose propranolol can be given safely with minimal adverse cardiovascular problems, provided that close clinical monitoring is maintained. A more rigorous clinical trial is needed to elucidate and verify its clinical utility, clinical practice parameters, and the effects of propranolol as a monotherapy versus as an add-on to the patient's existing medication regimen. London EB, Yoo JH, Fethke ED, Zimmerman-Bier B. The Safety and Effectiveness of High-Dose Propranolol as a Treatment for Challenging Behaviors in Individuals With Autism Spectrum Disorders. J Clin Psychopharmacol. 2020;40(2):122-129. doi:10.1097/JCP.0000000000001175

“The belligerence of 7 patients who had suffered an acute brain insult was effectively controlled by propranolol in doses of 60 to 320 mg per day. Of the 7 patients, 3 were treated in the acute stage after a stroke, a severe closed head injury, and a gunshot wound of the brain, respectively. A chronic postconcussion syndrome associated with chronic irritability was present in 2, and 2 were not chronically irritable but suffered from intermittent attacks of explosive rage in response to minor irritations. In all instances the belligerent behavior was controlled without inducing general sedation.”Elliott FA. Propranolol for the control of belligerent behavior following acute brain damage. Ann Neurol. 1977;1(5):489-491. doi:10.1002/ana.410010516

“Propranolol in doses up to 520 mg/day was administered to eight patients with organic brain disease characterized by violent and assaultive behavior refractory to conventional treatment. Improvement was demonstrated in the seven patients able to tolerate adequate drug dosages. Hypotension, bradycardia, and interactions with other medications constituted complications.” Greendyke RM, Schuster DB, Wooton JA. Propranolol in the treatment of assaultive patients with organic brain disease. J Clin Psychopharmacol. 1984;4(5):282-285.

“This review assesses the usefulness of beta-blockers in the treatment of aggression and describes the parameters for their clinical use. A Medline search using the terms "beta-blockers," "aggression," "propranolol," and "brain injury" identified relevant journal articles published in English between 1977 and 1993. Open, prospective and double-blind, placebo-controlled studies, as well as case reports, were included. Beta-blockers appear to be effective in decreasing the frequency and intensity of aggressive outbursts associated with a wide variety of conditions, such as dementias, attention-deficit disorder, personality disorders, Korsakoff's psychosis, posttraumatic stress disorder, schizophrenia, profound mental retardation, autism, and brain injury. A general discussion attempts to resolve some of the issues surrounding the possible mechanisms of beta-blocker effects, reviews the anatomic and neurochemical bases of aggression, and explores implications of the clinical use of beta-blockers.” Haspel T. Beta-blockers and the treatment of aggression. Harv Rev Psychiatry. 1995;2(5):274-281. doi:10.3109/10673229509017146

“In this population-wide study, we found no consistent links between β-blockers and psychiatric outcomes. However, β-blockers were associated with reductions in violence, which remained in sensitivity analyses. The use of β-blockers to manage aggression and violence could be investigated further.” Molero Y, Kaddoura S, Kuja-Halkola R, et al. Associations between β-blockers and psychiatric and behavioural outcomes: A population-based cohort study of 1.4 million individuals in Sweden. PLoS Med. 2023;20(1):e1004164. Published 2023 Jan 31. doi:10.1371/journal.pmed.1004164

“There is some evidence that propranolol may benefit individuals with behavioural and psychological symptoms of dementia (BPSD). A total of three case series, one randomized controlled trial and one case report were identified (from a literature search of three major databases: PubMed, Ovid, and Cochrane collaboration) that assessed the use of propranolol for the management of BPSD. From these studies, it appears that propranolol improves BPSD, including agitation and aggression. Propranolol is also well tolerated with no significant bradycardia or hypotension noted in these studies. Current data on the use of propranolol for the management of BPSD are limited in comparison to other pharmacological agents (atypical antipsychotics, antidepressants, acetylcholinesterase inhibitors, memantine, and cannabinoids) and treatment modalities (repetitive transcranial magnetic stimulation and electroconvulsive therapy).” Tampi RR, Tampi DJ, Farheen SA, Ochije SI, Joshi P. Propranolol for the management of behavioural and psychological symptoms of dementia. Drugs Context. 2022;11:2022-8-3. Published 2022 Dec 8. doi:10.7573/dic.2022-8-3