

An Experimental Study Comparing the Respiratory Effects of Tapentadol and Oxycodone in Healthy Volunteers

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Abstract

Background: There is a clinical need for potent opioids that produce little or no respiratory depression. In the current study we compared the respiratory effects of tapentadol, a mu-opioid receptor agonist and noradrenaline reuptake inhibitor, and oxycodone, a selective mu-opioid receptor agonist. We hypothesize that tapentadol 100 mg has a lesser effect on the control of breathing than oxycodone 20 mg.

Methods: Fifteen healthy volunteers were randomized to receive oral tapentadol (100 and 150 mg), oxycodone 20 mg or placebo immediate release tablets in a crossover double-blind randomized design. The main end-point of the study was the effect of treatment on the ventilatory response to hypercapnia and ventilation at an extrapolated end-tidal PCO₂ of 7.3 kPa (55 mmHg, VE55); VE55 was assessed prior and for 6-h following drug intake.

Results: All three treatments had typical opioid effects on the hypercapnic ventilatory response: a shift to the right coupled to a decrease of the response slope. Oxycodone 20 mg had a significantly larger respiratory depressant effect than tapentadol 100 mg (mean difference -5.0 L min⁻¹, 95% confidence interval: -7.1 to -2.9 L min⁻¹, P<0.01), but not larger than tapentadol 150 mg (oxycodone vs. tapentadol 150 mg: P>0.05).

Conclusions: In this exploratory study we observed that both tapentadol and oxycodone produce respiratory depression. Tapentadol 100 mg but not 150 mg had a modest respiratory advantage over oxycodone 20 mg. Further studies are needed to explore how these results translate to the clinical setting.

Keywords: breathing; hypercapnic ventilatory response; opioid-induced respiratory depression; opioids; respiratory depression.

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- [A randomised, placebo-controlled trial comparing the effects of tapentadol and oxycodone on gastrointestinal and colonic transit in healthy humans.](#) Jeong ID, Camilleri M, Shin A, Iturrino J, Boldingh A, Busciglio I, Burton D, Ryks M, Rhoten D, Zinsmeister AR. *Aliment Pharmacol Ther.* 2012 May;35(9):1088-96. doi: 10.1111/j.1365-2036.2012.05040.x. Epub 2012 Feb 21. PMID: 22348605 Clinical Trial.
- [Tapentadol for chronic musculoskeletal pain in adults.](#) Santos J, Alarcão J, Fareleira F, Vaz-Carneiro A, Costa J. *Cochrane Database Syst Rev.* 2015 May 27;(5):CD009923. doi: 10.1002/14651858.CD009923.pub2. PMID: 26017279 Review.
- [\[New Opioid Options in Japan - Methadone, Tapentadol and Hydromorphone\].](#) Takagi Y, Aruga E. *Gan To Kagaku Ryoho.* 2018 Feb;45(2):205-211. PMID: 29483406 Review. Japanese.
- [Tapentadol immediate release versus oxycodone immediate release for treatment of acute low back pain.](#) Biondi D, Xiang J, Benson C, Etropolski M, Moskovitz B, Rauschkolb C. *Pain Physician.* 2013 May-Jun;16(3):E237-46. PMID: 23703422 Clinical Trial.
- [Influence of Ethanol on Oxycodone-induced Respiratory Depression: A Dose-escalating Study in Young and Elderly Individuals.](#) van der Schrier R, Roozekrans M, Olofsen E, Aarts L, van Velzen M, de Jong M, Dahan A, Niesters M. *Anesthesiology.* 2017 Mar; 126(3):534-542. doi: 10.1097/ALN.0000000000001505. PMID: 28170358
- [Efficacy and tolerability of tapentadol immediate release and oxycodone HCl immediate release in patients awaiting primary joint replacement surgery for end-stage joint disease: a 10-day, phase III, randomized, double-blind, active- and placebo-controlled study.](#) Hartrick C, Van Hove I, Stegmann JU, Oh C, Upmalis D. *Clin Ther.* 2009 Feb;31(2):260-71. doi: 10.1016/j.clinthera.2009.02.009. PMID: 19302899 Clinical Trial.
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Afilalo M, Etropolski MS, Kuperwasser B, Kelly K, Okamoto A, Van Hove I, Steup A, Lange B, Rauschkolb C, Haeussler J. Clin Drug Investig. 2010;30(8):489-505. doi: 10.2165/11533440-00000000-00000. PMID: 20586515 Clinical Trial.

- [A randomized, double-blind, placebo-controlled phase 3 study of the relative efficacy and tolerability of tapentadol IR and oxycodone IR for acute pain.](#) Daniels S, Casson E, Stegmann JU, Oh C, Okamoto A, Rauschkolb C, Upmalis D. Curr Med Res Opin. 2009 Jun;25(6):1551-61. doi: 10.1185/03007990902952825. PMID: 19445652 Clinical Trial.
- [Effects of the NK1 antagonist, aprepitant, on response to oral and intranasal oxycodone in prescription opioid abusers.](#) Walsh SL, Heilig M, Nuzzo PA, Henderson P, Lofwall MR. Addict Biol. 2013 Mar;18(2):332-43. doi: 10.1111/j.1369-1600.2011.00419.x. Epub 2012 Jan 19. PMID: 22260216 Free PMC article. Clinical Trial.
- [A Randomized Controlled Trial on the Effect of Tapentadol and Morphine on Conditioned Pain Modulation in Healthy Volunteers.](#) Martini C, van Velzen M, Drewes A, Aarts L, Dahan A, Niesters M. PLoS One. 2015 Jun 15;10(6):e0128997. doi: 10.1371/journal.pone.0128997. eCollection 2015. PMID: 26076171 Free PMC article. Clinical Trial.
- [Combatting pain after orthopedic/trauma surgery- perioperative oral extended-release tapentadol vs. extended-release oxycodone/naloxone.](#) Haeseler G, Schaefers D, Prison N, Ahrens J, Liu X, Karch A. BMC Anesthesiol. 2017 Jul 11;17(1):91. doi: 10.1186/s12871-017-0383-6. PMID: 28693439 Free PMC article. Clinical Trial.
- [\[Undesired side effects of tapentadol in comparison to oxycodone. A meta-analysis of randomized controlled comparative studies\].](#) Merker M, Dinges G, Koch T, Kranke P, Morin AM. Schmerz. 2012 Feb;26(1):16-26. doi: 10.1007/s00482-011-1132-2. PMID: 22366930 German.
- [Comparison of the risks of opioid abuse or dependence between tapentadol and oxycodone: results from a cohort study.](#) Cepeda MS, Fife D, Ma Q, Ryan PB. J Pain. 2013 Oct;14(10):1227-41. doi: 10.1016/j.jpain.2013.05.010. Epub 2013 Jul 10. PMID: 23850177

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- [Cornea nerve fibre state determines analgesic response to tapentadol in fibromyalgia patients without effective endogenous pain modulation.](#) van de Donk T, van Velzen M, Dahan A, Niesters M. Eur J Pain. 2019 Oct;23(9):1586-1595. doi: 10.1002/ejp.1435. Epub 2019 Jun 24. PMID: 31162787 Free PMC article.
- [Desmetramadol Has the Safety and Analgesic Profile of Tramadol Without Its Metabolic Liabilities: Consecutive Randomized, Double-Blind, Placebo- and Active Comparator-Controlled Trials.](#) Zebala JA, Searle SL, Webster LR, Johnson MS, Schuler AD, Maeda DY, Kahn SJ. J Pain. 2019 Oct;20(10):1218-1235. doi: 10.1016/j.jpain.2019.04.005. Epub 2019 Apr 18. PMID: 31005596
- [Does 'Strong Analgesic' Equal 'Strong Opioid'? Tapentadol and the Concept of ' \$\mu\$ -Load'.](#) Raffa RB, Elling C, Tzschentke TM. Adv Ther. 2018 Oct;35(10):1471-1484. doi: 10.1007/s12325-018-0778-x. Epub 2018 Sep 11. PMID: 30206823 Free PMC article.
- [Review of Post-Marketing Safety Data on Tapentadol, a Centrally Acting Analgesic.](#) Stollenwerk A, Sohns M, Heisig F, Elling C, von Zabern D. Adv Ther. 2018 Jan;35(1): 12-30. doi: 10.1007/s12325-017-0654-0. Epub 2017 Dec 21. PMID: 29270779 Free PMC article. Review.