

SUPPLEMENTAL MATERIAL

Direct oral anticoagulants in treatment of cerebral venous thrombosis: systematic review

Gauruv Bose¹, Justin Graveline¹, Vignan Yogendrakumar¹, Risa Shorr¹, Dean Fergusson¹, Gregoire Le Gal¹, Jonathan M. Coutinho², Marcelo Mendonça³, Miguel Viana-Baptista³, Simon Nagel⁴, and Dar Dowlatshahi¹

1. Department of Medicine, University of Ottawa and The Ottawa Hospital Research Institute, Ottawa, Canada
2. Department of Neurology, University Medical Center, Amsterdam, Netherlands
3. Department of Neurology, Centro Hospitalar de Lisboa Ocidental, Lisbon, Portugal
4. Department of Neurology, University Hospital, University of Heidelberg, Heidelberg, Germany

Appendix I: Search Strategy

The complete protocol is previously published[1] and is hosted on PROSPERO (ID: CRD42017078398).[2]

Ovid MEDLINE(R) ALL Strategy:

1. apixaban.mp.
2. edoxaban.mp.
3. Dabigatran.mp.
4. Rivaroxaban.mp.
5. (doac* or noac*).tw,kw.
6. ((direct oral or novel) adj3 (anticoagul* or anti coagulat*)).tw.
7. exp Factor Xa Inhibitors/
8. Factor Xa Inhibit*.mp.
9. Antithrombins/ or thrombin inhibit*.mp.
10. or/1-9
11. "intracranial embolism and thrombosis"/ or intracranial thrombosis/ or exp sinus thrombosis, intracranial/
12. cvt.tw,kw.
13. (cerebral veins/ or exp cranial sinuses/) and (thrombosis/ or venous thrombosis/)
14. ((sinus* or sinovenous or cerebral or cavernous or sagittal venous or sagittal vein* or cerebrovenous or cerebro-venous or sigmoid) and thrombo*).tw,kw.
15. intracran* thrombo*.kw. or (intracran* adj3 thrombo*).tw.
16. 11 or 12 or 13 or 14 or 15
17. 10 and 16

Database: Embase Classic+Embase Strategy:

1. apixaban.mp.
2. edoxaban.mp.
3. Dabigatran.mp.
4. Rivaroxaban.mp.
5. (doac* or noac*).tw.
6. ((direct oral or novel) adj3 (anticoagul* or anti coagulat*)).tw.
7. exp *Factor Xa Inhibitors/

14. cvt.tw.
15. or/11-14
16. 10 and 15

Database: EBM Reviews - Cochrane Central Register of Controlled Trials
Search Strategy:

1. apixaban.mp.
2. edoxaban.mp.
3. Dabigatran.mp.
4. Rivaroxaban.mp.
5. (doac* or noac*).tw,kw.
6. ((direct oral or novel) adj3 (anticoagul* or anti coagulat*)).tw.
7. exp Factor Xa Inhibitors/
8. Factor Xa Inhibit*.mp.
9. Antithrombins/ or thrombin inhibit*.mp.
10. or/1-9
11. "intracranial embolism and thrombosis"/ or intracranial thrombosis/ or exp sinus thrombosis, intracranial/
12. cvt.tw,kw.
13. (cerebral veins/ or exp cranial sinuses/) and (thrombosis/ or venous thrombosis/)
14. ((sinus* or sinovenous or cerebral or cavernous or sagittal venous or sagittal vein* or cerebrovenous or cerebro-venous or sigmoid) and thrombo*).tw,kw.
15. intracran* thrombo*.kw. or (intracran* adj3 thrombo*).tw.
16. 11 or 12 or 13 or 14 or 15
17. 10 and 16

Supplemental references

- 1 Bose G, Graveline J, Yogendrakumar V, et al Direct oral anticoagulants in treatment of cerebral venous thrombosis: a systematic review protocol. *Syst Rev* 2019;**8**:99. doi:10.1186/s13643-019-1022-8
- 2 Bose G, Graveline J, Dowlatshahi D. Systematic review of direct oral anticoagulants in treatment of cerebral venous thrombosis. *PROSPERO* 2017.
- 3 Ferro JM, Coutinho JM, Dentali F, et al Safety and Efficacy of Dabigatran Etxilate vs Dose-Adjusted Warfarin in Patients With Cerebral Venous Thrombosis. *JAMA Neurol* Published Online First: 3 September 2019. doi:10.1001/jamaneurol.2019.2764
- 4 Hsu A, Mistry H, Lala N, et al Preliminary findings regarding the use of direct oral anticoagulants in cerebral venous thrombosis. *Clin Neurol Neurosurg* 2020;**198**:106204. doi:10.1016/j.clineuro.2020.106204
- 5 Powell M, Tremolet de Villers K, Schwarz K, et al A Single-Center Retrospective Evaluation of the Use of Oral Factor Xa Inhibitors in Patients With Cerebral Venous Thrombosis. *Ann Pharmacother* 2020;:106002802095274. doi:10.1177/1060028020952749
- 6 Lurkin A, Derex L, Fambrini A, et al Direct Oral Anticoagulants for the Treatment of Cerebral Venous Thrombosis. *Cerebrovasc Dis* 2019;**48**:32–7. doi:10.1159/000502454
- 7 Wasay M, Khan M, Rajput HM, et al New Oral Anticoagulants versus Warfarin for Cerebral Venous Thrombosis: A Multi-Center, Observational Study. *J Stroke* 2019;**21**:220–3. doi:10.5853/jos.2019.00150
- 8 Herweh C, Griebe M, Geisbüsch C, et al Frequency and temporal profile of recanalization after cerebral vein and sinus thrombosis. *Eur J Neurol* 2016;**23**:681–7. doi:10.1111/ene.12901
- 9 Covut F, Kewan T, Perez O, et al Apixaban and rivaroxaban in patients with cerebral venous thrombosis. *Thromb Res* 2018;**173**:7–8. doi:10.1016/j.thromres.2018.11.018
- 10 Rusin G, Wypasek E, Papuga-Szela E, et al Direct oral anticoagulants in the treatment of cerebral venous sinus thrombosis: a single institution's experience. *Neurol Neurochir* 2019;**53**:384–387. doi:10.5603/PJNNS.a2019.0037
- 11 Shankar Iyer R, TCR R, Akhtar S, et al Is it safe to treat cerebral venous thrombosis with oral rivaroxaban without heparin? A preliminary study from 20 patients. *Clin Neurol Neurosurg* 2018;**175**:108–11. doi:10.1016/j.clineuro.2018.10.015
- 12 Cappellari M, Bovi P. Direct oral anticoagulants in patients with cervical artery dissection and cerebral venous thrombosis. A case series and review of the

- Successful Use of DOAC in the Treatment of Cerebral Venous Sinus Thrombosis (CVST): A Case Report. *J Stroke Cerebrovasc Dis*; **29**:105261. doi:10.1016/j.jstrokecerebrovasdis.2020.105261
- 16 Saito K, Ishii K, Furuta K, et al Recurrent Cerebral Venous Thrombosis Treated with Direct Oral Anticoagulants in a Japanese Man with Hereditary Protein C Deficiency. *J Stroke Cerebrovasc Dis*; **29**:105320. doi:10.1016/j.jstrokecerebrovasdis.2020.105320
- 17 Sugiyama Y, Tsuchiya T, Tanaka R, et al Cerebral venous thrombosis in COVID-19-associated coagulopathy: A case report. *J Clin Neurosci*; **2020**; **79**:30–2. doi:10.1016/j.jocn.2020.07.038
- 18 Chiu D, Weinberger J. Cerebral Venous Sinus Thrombosis and Acute Myocardial Infarction in a Patient with PAI-1 4G/4G Homozygosity. *J Stroke Cerebrovasc Dis* **2020**; **29**:105250. doi:10.1016/j.jstrokecerebrovasdis.2020.105250
- 19 Bolaji P, Kukoyi B, Ahmad N, et al Extensive cerebral venous sinus thrombosis: a potential complication in a patient with COVID-19 disease. *BMJ Case Rep* **2020**; **13**:e236820. doi:10.1136/bcr-2020-236820
- 20 Huang Q, Chai X, Xiao C, et al A case report of oral contraceptive misuse induced cerebral venous sinus thrombosis and dural arteriovenous fistula. *Medicine (Baltimore)*; **2019**; **98**:e16440. doi:10.1097/MD.00000000000016440
- 21 Hu Y, Tang Z, Zhu W, et al Clinical Reasoning: A teenager with persistent headache. *Neurology*; **2019**; **92**:e1526–31. doi:10.1212/WNL.00000000000007184
- 22 Yasushi S. Successful Treatment of Cerebral Sinus Thrombosis with Edoxaban Alone. *Int J Crit Care Emerg Med*; **2017**; **3**. doi:10.23937/2474-3674/1510029
- 23 Sui J, Zhang Y, Yang L, et al Successful treatment with rivaroxaban of cerebral venous thrombosis and bone marrow necrosis induced by pegaspargase: A case report and literature review. *Medicine (Baltimore)*; **2017**; **96**:e8715. doi:10.1097/MD.00000000000008715
- 24 Becerra AF, Amuchastegui T, Tabares AH. Decreased Rivaroxaban Levels in a Patient with Cerebral Vein Thrombosis Receiving Phenytoin. *Case Rep Hematol* **2017**; **2017**:3. doi:10.1155/2017/4760612
- 25 Budhram A, Shettar B, Lee DH, et al Bilateral Cavernous Sinus Thrombosis in Lemierre's Syndrome. *Can J Neurol Sci / J Can des Sci Neuro*; **2016**; **44**:424–6. doi:10.1017/cjn.2016.438
- 26 Hsu Y, Juan C, Le J, et al Anti-N-methyl-D-aspartate-receptor encephalitis complicated with antiphospholipid syndrome and cerebral venous thrombosis. *J Clin Rheumatol*; **2017**; **23**:294–5. doi:10.1186/2047-2994-1-19.
- 27 Inche Mat LN, Wan Sulaiman WA, Hoo FK, et al A rare case of vein of Galen thrombosis: Exploring a potential role for novel oral anticoagulants (NOACs) in cerebral deep vein thrombosis. *Rawal Med. J.* **2017**; **42**:432–4.

- 30 Cho Y, Chae MK, Cha JM, et al Cerebral venous thrombosis in a patient with Crohn's disease. *Intest Res* 2016;**14**:96. doi:10.5217/ir.2016.14.1.96
- 31 Micieli JA, Derkatch S, Pereira VM, et al Development of dural arteriovenous fistulas after cerebral venous sinus thrombosis. *J Neuro-Ophthalmology* 2016;**36**:53–7. doi:10.1097/WNO.0000000000000288
- 32 Mutgi SA, Grose NA, Behrouz R. Rivaroxaban for the treatment of cerebral venous thrombosis. *Int J Stroke* 2015;**10**:167–8. doi:10.1111/ijs.12592
- 33 Sugie M, Iizuka N, Shimizu Y, et al Cerebral Venous Thromboembolism in Antiphospholipid Syndrome Successfully Treated with the Combined Use of an Anti-Xa Inhibitor and Corticosteroid. *Intern Med* 2015;**54**:3051–6. doi:10.2169/internalmedicine.54.5045
- 34 Mathew T, Lobo A, Kukkuta Sarma G, et al A case of post varicella cortical venous thrombosis successfully treated with dabigatran. *Neurol India* 2013;**61**:531. doi:10.4103/0028-3886.121939
- 35 Hon SFK, Li HLT, Cheng PW. Use of direct thrombin inhibitor for treatment of cerebral venous thrombosis. *J Stroke Cerebrovasc Dis* 2012;**21**:915.e11-915.e15. doi:10.1016/j.jstrokecerebrovasdis.2012.02.004