

Letter to the Editor

Thrombosis and Antipsychotics

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The Virchow triad, described in 1856, corresponds to three factors inducing the development of venous thrombosis. Those factors are abnormalities in blood flow, in vascular constituents and/or in the vascular lumen. Several drug classes are known to have pro-thrombotic effects as estroprogestin therapies, non steroidal anti-inflammatory drugs... Neuroleptics may also determine this adverse drug reaction. The first cases of venous thrombosis are reported with chlorpromazine in 1953 and 1954 [1,2].

A case-control study [3] focused on 677 patients hospitalized for deep vein thrombosis or pulmonary embolism without thrombosis risk factor and 677 cases acquired and comparable control for sex and age. Neuroleptics, including "hidden" neuroleptics (for instance some antiemetics as domperidone, metoclopramide and some H1 antihistamines phenothiazine structure), was associated with an increased risk of thrombosis (OR = 2.1, 95% CI: 1.4 to 3.2). Antipsychotic, whether first or second generation, was specifically correlated with an increase (OR = 3.5; 95% CI: 2.0 to 6.2) of the risk of thromboembolism. The correlation was independent of age, sex, BMI, and classic major risk factors that are surgery, cancer, long immobilization, pregnancy and two minor genetic factors (Factor V Leiden and prothrombin G20210A).

The risk increased with "atypical" antipsychotic and in newly treated patients (less than three months) [4,5]. The parenteral route also appears to be an additional risk factor [6]. More recently, a review in the 1990-2012 intervals, for studies involving antipsychotic medication and thromboembolic events, confirm the link and those risk factors [7]. Higher doses and concomitant multiple antipsychotic therapy increase also the thrombosis risk.

Several pharmacodynamic hypotheses are made: neuroleptics block alpha 1 adrenergic receptors, induce arterial hypotonia which is resulting in peripheral vasodilation and blood stasis [8]. Sedation and obesity induced by these drugs are also implicated. The role of hyperprolactinemia with platelet activation through

ADP, the increased anti-lupus or anticardiolipin antibodies, the hyperhomocysteinemia or a hyperleptinemia, the presence of antiphospholipid antibodies and a pro-coagulant effect or pro-aggregating are also suggested.

Psychiatric patients have many risk factors which can lead to venous thrombosis. They should be then closely monitored because of the high mortality rate in pulmonary embolism [9,10].

Neuroleptics are therefore a risk factor for thromboembolism, mostly with "atypical" antipsychotics [7].

There is a need to strengthen the knowledge of patients and health professionals about thromboembolic risk factors. Risk factors of thrombosis are numerous. They include for instance major surgery, multiple trauma, increasing age, prolonged immobility, hematological disease, cigarette smoking, metabolic syndrome, hypertension and hyperlipidemia [11]. Drug-induced thrombosis should be also considered. Caution is then needed in prescription of neuroleptic to avoid thrombosis and maybe unexplained death...

References

1. Labhardt F. [Technic, side effects and complications of largactil therapy]. *Schweiz Arch Neurol Psychiatr.* 1954; 73: 338-345.
2. Thomassen R, Vandenbroucke JP, Rosendaal FR. Antipsychotic medication and venous thrombosis. *Br J Psychiatry.* 2001; 179: 63-66.
3. Lacut K, Le Gal G, Couturaud F, Cornily G, Leroyer C, Mottier D, et al. Association between antipsychotic drugs, antidepressant drugs and venous thromboembolism: results from the EDITH case-control study. *Fundam Clin Pharmacol.* Dec. 2007; 21: 643-650.
4. Parker C, Coupland C, Hippisley-Cox J. Antipsychotic drugs and risk of venous thromboembolism: nested case-control study. *BMJ.* 2010; 341: c4245.
5. Wu CS, Lin CC, Chang CM, Wu KY, Liang HY, Huang YW, et al. Antipsychotic treatment and the occurrence of venous thromboembolism: a 10-year nationwide registry study. *J Clin Psychiatry.* 2013; 74: 918-924.
6. Liperoti R, Gambassi G. Antipsychotics and the risk of venous thromboembolism. *BMJ.* 2010; 341: c4216.
7. Shulman M, Jennifer Njoku I, Manu P. Thrombotic complications of treatment with antipsychotic drugs. *Minerva Med.* 2013; 104: 175-184.
8. Pantel J, Schroder J, Eysenbach K, Mundt C. Two cases of deep vein thrombosis associated with a combined paroxetine and zotepine therapy. *Pharmacopsychiatry.* 1997; 30: 109-111.
9. Barnhorst A, Xiong GL. Pulmonary embolism in a psychiatric patient. *Am J Psychiatry.* 2014; 171: 1155-1157.
10. Allenet B, Schmidlin S, Genty C, Bosson JL. Antipsychotic drugs and risk of pulmonary embolism. *Pharmacoepidemiol Drug Saf.* 2012; 21: 42-48.
11. Anderson FA, Spencer FA. Risk factors for venous thromboembolism. *Circulation.* 2003; 107: I9-16.