A suicidal fatality following an overdose with varenicline

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Introduction. Varenicline is a selective $\alpha_4\beta_2$ nicotinic receptor partial agonist used as an aid for smoking cessation (Champix®, Chantix®). Adverse effects are generally mild and self-limiting, with gastro-intestinal effects most commonly reported. Varenicline use has also been associated with psychiatric troubles and adverse effect reporting has resulted in warnings of a possibly increased risk of suicide. Here, we describe the first fatality associated with an intentional suicidal ingestion of a varenicline overdose, resulting in extremely high blood concentrations. **Case Report**. On a cold morning, a man was found dead, lying almost naked at the side of the street. The direct vicinity of the body suggested that he had been rooting up the sandy earth and leaves. His car, parked a bit further, contained his clothes, as well as a farewell note and six empty blisters of Champix® 1 mg. Peripheral blood, urine and vitreous were sampled *on site* for routine toxicological analysis. The results indicated that, apart from ethanol and caffeine, varenicline was the only drug present. **Methods.** Quantitative determination of varenicline encompassed an optimized solid phase extraction, derivatization and analysis by GC-MS. Linearity of the established calibration line was evaluated, as were precision and accuracy at the lower (1.56 ng/ml) and upper (50 ng/ml) limit of quantification and at low (3 ng/ml) and high (30 ng/ml) QC levels. In addition, we evaluated the validity of the approach for haemolysed blood and urine and for samples with ultrahigh concentrations that were diluted in blank serum. **Results**. Acceptable precision (<15% RSD) and accuracy (100% ± 15% of the nominal concentration) were obtained at LLOQ, ULOQ and both QC levels. Also the analysis of matrices other than serum - using the approach of standard addition- and of diluted highly concentrated samples resulted in acceptable precision and accuracy. The blood (vena subclavia *resp.* vena femoralis), urine and vitreous of the deceased had varenicline concentrations of 262, 257, 687 and 165 ng/ml, respectively. **Conclusion.** The blood concentration of more than 250 ng/ml is almost 10-fold higher than the highest concentration described in plasma (28.3 ng/ml) so far. Although, with respect to the *mechanism of death* in this case, confounding factors were concomitant ethanol consumption and, importantly, potentially fatal hypothermia, this is the first report of a fatality associated with the ingestion of an overdose of varenicline.