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Use of benzodiazepines during pregnancy. A survey in a cohort of pregnant women in northern Italy

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To the Editor,

In almost all western countries, Benzodiazepines (BZD), typically used to treat insomnia and anxiety disorders, are widely prescribed in every field of medicine. There is a wide gap between the recommendations for a rational use and the actual medical practice. Several epidemiological studies have shown a quite high prevalence of their use among the general population, with variations from one country to another and from one study to another (1, 2).

BDZ misuse is a widespread phenomenon, but it is paradoxically of little interest for scientific researchers.

In literature, rates of BZD use in the general population vary between 2.2% and 17% (3). The use of BZD tends to increase with age and in 2/3 of cases involving female (3). A large study conducted among the Northern Italy general population reported a prevalence of recent use (last month prevalence) of BZD in 7% of childbearing age women (4).

For all these reasons, we read with great interest the article by Leppèe *et al*. published by your journal on the use of BZD in pregnant women (5). The subject is relevant because the use of BZD during pregnancy involves a small but significant risk of birth defects (6). All BZD spread across the placenta to the foetus. The risk of malformation is higher when foetus is exposed between two and eight weeks after conception. If drugs are administered at or near term, they may cause foetal withdrawal symptoms (7). Leppèe et coll. reported a high prevalence of use of diazepam in pregnant women: 8.3% in the first trimester of pregnancy, 14.2% in the second, 23.7% in third trimester (5).

For completeness we report a similar study, performed by our group at the University Hospital of Verona (Italy), dealing with the problem of the misuse of BZD for many years, managing an inpatient unit for the most serious cases of addiction.

We agree with Leppèe that the problem of misuse of BZD is largely underestimated and not adequately assessed, but there are differences that, in our opinion, need to be reported.

We evaluated 109 serum samples collected from same number of pregnant women, median age 29 years. 31 were in the first, 13 in the second and 65 in the third trimester of pregnancy, respectively. The serum was collected during routine clinical evaluation after informed consent and sent anonymously to the laboratory. The presence of metabolites of BZD was investigated with test BZD Serum Assay Syva Emit Tox. Samples with an absorbance value lower than the lowest calibrator (0.3 mcg/ml) were interpreted as negative.

All samples were completely negative for BZD.

These data have some limitations compared to Leppèe's one: the sample is smaller and there was no follow-up. Also no other anamnestic or diagnostic data except age and time of pregnancy were collected. Of course, a negative test does not exclude an intermittent use of BZD.

Our conclusions are that the pregnancy may have led to greater awareness among these women about the possible harm of anxiolytics to the foetus. We agree that health professionals should keep in mind the problem of anxiety disorders during pregnancy and the ensuing potential use of BZD.

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