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THE POISON PEN

Bupropion, Bayesian Logic and Serotonin Toxicity

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I suggest it is important to note that there are some powerful reasons for doubting the attribution of serotonin toxicity (ST) being caused by bupropion that is made in the report by Thorpe et al. [1]. It is well recognised that case reports are low-grade scientific evidence and can be misleading, to the extent of misdirecting doctors down blind alleys [2]. This can be especially counterproductive in emergency situations where less experienced physicians may not have time for protracted deliberation. I have emphasised previously that there is overwhelming evidence that potent serotonergic activity is an absolute prerequisite if a drug is to be capable of precipitating ST [3]. It may seem obvious to state that vitamin C cannot cause ST. A case report claiming that would be regarded sceptically because there is simply no basis for supposing that vitamin C is able to affect serotonin. That is Bayesian logic in operation, i.e., using the prior probability to weigh the expected outcome [4]. As I have pointed out before, drugs like bupropion and mirtazapine, that have no significant serotonergic activity, are no more likely to cause ST than is vitamin C [5]. This scenario has already been enacted, over a decade, with the antidepressant mirtazapine, which was claimed, erroneously, to have serotonergic activity. Many poor quality case reports of ST with mirtazapine were published. This probably led to misdirected treatment of overdoses, some of which may have caused morbidity. It took several reviews to correct this error and establish that mirtazapine cannot cause ST [6–8].

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These authors appear to be inviting us to repeat this time-wasting saga. There is no evidence that bupropion can increase 5-HT. Thorpe et al. carelessly and fallaciously represent Piacentini et al.'s results as reporting increased 5-HT when, to the contrary, they clearly and specifically state that "5-HT showed no significant change after bupropion injection (Fig. 1C)." [9]. Bupropion has no potency as a serotonin re-uptake inhibitor [10]. There are large case series of overdoses and none of which have shown serotonergic toxicity, not even serotonergic side effects [11]. These would be expected if it had some other mysterious effect on 5-HT that is still unknown, which is unlikely after 30 years of use and research. One case report carries negligible weight when set in that context.

Despite the apparent presence of clonus, this case does not meet the Hunter serotonin toxicity criteria, specifically because no drug with established serotonergic activity was given. Bayesian logic indicates there is a low probability that this case represents ST. It is both fundamentally implausible and has other possible interpretations. It is a typical example of a report that is likely to mislead rather than illuminate, about which I have previously written [2].

Conflicts of interest None.

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