Managing unplanned severe opiate withdrawal after Vivitrol

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Having deliberately precipitated opiate withdrawal with naltrexone (NTX) in several thousand opiate-dependent patients, using a variety of techniques, between 1985 and my retirement two decades later, I think I can comment usefully on the difficulties experienced by Wightman et al. [1] in managing severe and unexpected opioid withdrawal precipitated by Vivitrol®. The drug that is notably absent from their attempts at symptom control is octreotide. Other researchers have confirmed my original observation [2] that it effectively prevents the profuse diarrhea and vomiting that distress medical and nursing staff as well as patients and it is now routine in most rapid NTX induction/transfer programmes [3,4]. 100–200 μg s/c or slow i/v is usually adequate for an average-sized patient. It can be repeated 8-hourly and may need to be continued for several days after initiating NTX; occasionally longer.

Most of my patients transferred seamlessly from opiates to NTX using techniques that did not involve general anaesthesia [5] but mainly after 1995, some 700 were treated in ICUs using a variety of anaesthetic techniques and agents. Dexmedetomidine was not then routinely available in Britain but i/v clonidine very effectively controlled both hypertension and tachycardia and has effective antidotes if BP or pulse-rate drops too far. I should add that the only (relatively minor) anaesthetic complication among those 700+ patients involved an ectopic bronchus, requiring re-intubation after chest x-ray.

In the sort of emergencies described in the paper, clonidine should be given i/v or at least i/m and usually in much larger doses than 100 μg. Many of my patients initiated NTX using an in-patient version of the 24-hour 'Asturian' NTX induction technique, developed originally in northern Spain as a domiciliary procedure without doctors or nurses [6]. It involves premedication with 450 μg of oral clonidine (as well as octreotide, other anti-emetics, gastro-protectants and oral midazolam) and a further 300 μg of clonidine an hour after administering 50 mg of oral NTX. Clonidine is a very safe drug.

The transient but sometimes profound restlessness and delirium that are usual in precipitated withdrawal can be managed by physical restraint but this may need two or three people. In the long-established Perth day-patient NTX induction programme [7] using modest levels of sedation with midazolam, family members or friends provide the muscle-power. In most ICUs, that is probably not acceptable but provided cardiovascular and gastrointestinal disturbances are well-controlled, the choice of anaesthetic is probably not very important. Intramuscular ketamine was sometimes used as an induction agent in patients with no easily accessible veins, allowing venous access to be obtained at leisure, and might be a suitable agent for quickly and safely controlling patients in acute withdrawal. My sole contribution to the anaesthetic literature was a paper describing its use for electro-convulsive treatment [8] in patients in a developing country who were often very psychotic by the time they arrived at the hospital. In subsequent correspondence, we noted that "…the induction of distraught, uncooperative or agitated patients was made considerably easier and less unpleasant for staff and patients" [9].

Antipsychotic drugs like haloperidol have little effect on the delirium of precipitated opiate withdrawal (or *delirium tremens*) and should be avoided. Prevention, by giving a naloxone challenge before Vivitrol, is obviously preferable. However, I also recall a newly-detoxified patient who showed no withdrawal response after successive doses of 400 μg and 800 μg of i/m naloxone but telephoned me 20 min after I then inserted a NTX implant to describe classic but fortunately relatively mild precipitated withdrawal symptoms.

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Dangerous manifestations of reversible cerebral vasoconstriction syndrome

The spectrum of dangerous manifestations of reversible cerebral vasoconstrictive syndrome (RCVS) includes, not only the subtype characterised by rapid-onset headache, as in the recently reported case [1], but also subtypes characterised by potentially life-threatening manifestations such as status epilepticus (SE) [2], and Guillain-Barre syndrome (GBS) [3, 4], respectively.

In one report, ten cases of SE were identified from a clinical database of 77 patients with RCVS (alternatively known as posterior reversible encephalopathy syndrome) in one university center [2]. Their mean age was 38.6 years (range 7 to 73 years). At the time of diagnosis of SE two patients had generalised convulsive SE, and eight had nonconvulsive SE with or only subtle clinical signs such as lip smacking and lateralised automatism, twitching, blinking, and spontaneous nystagmus. During the course of their hospital admission eight patients had generalised tonic-clonic seizures. Six patients responded to first line antiepileptic drugs. Four patients, however, developed refractory SE, and required general anaesthesia to control seizure activity. All ten patients eventually recovered from SE, along with resolution of imaging studies [2].

RCVS can also present with Guillain-Barre syndrome (GBS) [3] or its brainstem variant, Bickerstaff's brainstem encephalitis [4]. Guillain-Barre syndrome was reported in a previously healthy 63 year old woman initially presented with paresthesiae in both feet, and subsequent headache, bilateral visual loss, and hypertension. Magnetic resonance imaging (MRI) studies were consistent with a diagnosis of RCVS. Three days later she developed clinical features of GBS, complicated by respiratory failure requiring mechanical ventilation. Her symptoms improved only after plasmapheresis, and she was eventually weaned off the mechanical ventilation. Brain MRI performed 6 weeks after onset of her symptoms disclosed complete resolution of the abnormalities documented on admission [3]. The authors of the report documented eight other cases of RCVS-related GBS (age range 57–76) in the medical literature. They postulated that the association might be attributable to GBS-related dysautonomia that can lead to life-threatening arterial pressure instability and alteration in brain circulatory self-regulation.