

to countries with better provision of intensive care units. However, for the United Kingdom, non-invasive ventilation for patients with mild to moderate acidosis due to decompensated chronic obstructive pulmonary disease is a highly effective technique that improves clinical outcomes, reduces demand for intensive care, and, from the hospital's perspective, reduces costs.

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Loss of tolerance and overdose mortality after inpatient opiate detoxification: follow up study

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In many countries opiate overdose remains the main source of the 10-fold excess mortality among opiate addicts, notwithstanding the effects of HIV/AIDS.¹ Treatment reduces mortality but can sometimes increase mortality transiently—for example, during the first few weeks of methadone maintenance treatment and among former opiate addicts after their release from prison.^{2,3} The increase in mortality among released prisoners who were formerly opiate addicts has been attributed to loss of tolerance and erroneous judgment of dose when they returned to opiate use.^{1,3} We wished to investigate whether opiate addicts who have undergone inpatient detoxification might have a

similarly increased mortality after treatment. We followed up patients who received inpatient opiate detoxification, looked for evidence of increased mortality, and investigated the distinctive characteristics of patients who died.

Participants, methods, and results

Over 20 months we recruited 137 consecutive opiate addicts who were receiving opiate detoxification as part of a 28 day inpatient treatment programme and who consented to be followed up. Five patients died within 12 months after their discharge from the

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Predictors of mortality among patients who underwent inpatient opiate detoxification. Values are numbers (percentage) of patients unless stated otherwise

Characteristic	Patients who died (n=5)	Other patients (n=132)	Statistical test results
Mean age in years (SD)	31.4 (7.1)	32.6 (7.3)	$t=0.36$, $P=0.72$
Male sex	5 (100)	99 (75)	Fisher's exact, $P=0.34$
Previous inpatient treatment	4 (80)	92 (70)	Fisher's exact, $P=1.0$
Ever overdosed	1 (20)	50† (39)	Fisher's exact, $P=0.65$
Was prescribed methadone*	5 (100)	92 (70)	Fisher's exact, $P=0.32$
Mean dose (mg) of prescribed methadone (SD)	51.0 (20.7)	29.2 (23.1)	$t=2.08$, $P=0.04$
Mean number of days of heroin use* (SD)	14.4 (14.4)	24.5 (10.2)	$t=2.15$, $P=0.03$
Living alone*	4 (80)	21† (16)	Fisher's exact, $P=0.004$
Physical health (MAP‡ score) (SD)*	38.6 (10.2)	29.9 (12.3)	$t=1.59$, $P=0.12$
Mean length of stay (days) in unit (SD)	24.6 (7.6)	15.6 (8.1)	$t=2.44$, $P=0.02$
Completed detoxification	5 (100)	89 (67)	Fisher's exact, $P=0.33$
Completed full treatment programme	4 (80)	33 (25)	Fisher's exact, $P=0.02$

*In the month before admission.

†Of 130 patients.

‡Maudsley Addiction Profile (see www.ntors.org.uk/map.pdf).

inpatient unit, of whom three had died after a drug overdose within the first four months after discharge. We successfully interviewed 103 patients (at a mean interval of 8.7 months after discharge). A search of records indicated that the remaining 29 patients were still alive one year after discharge.

To test whether loss of tolerance increased the risk of overdose, we grouped the patients into three categories, according to their opiate tolerance at the point of leaving treatment: 43 “still tolerant” (ST) patients who failed to complete detoxification; 57 “reduced tolerance” (RT) patients who completed the prescribed phase of detoxification but who prematurely left the treatment programme; and 37 “lost tolerance” (LT) patients who completed the detoxification and also completed the inpatient treatment programme.

The three overdose deaths that occurred within four months after treatment were all from the LT group; the two deaths unrelated to overdose (although both these patients had relapsed) were one LT patient with end stage renal failure and one RT patient with *Clostridium welchii* infection; no deaths occurred in the ST group (Fisher’s exact test, $df=2$, $P=0.02$). This clustering did not derive from differences in duration to the follow up interview (mean durations were 9.5 months (ST), 8.7 months (RT), and 7.8 months (LT)).

We also considered length of time in treatment as a continuous variable. The five patients who died had stayed longer in the inpatient unit (mean 24.6 days (SD 7.6)) than the other 132 patients (15.6 days (8.1)) ($t=2.44$, $P=0.02$) (table). We looked for distinctive premorbid characteristics among the patients, all men, who died—possible clinical markers of risk of mortality after detoxification. Before admission these patients were more likely than the other patients to have been living alone, to have been taking higher doses of methadone, and to have been using heroin less often. They stayed longer in the inpatient unit and were more likely to have completed the treatment programme.

Comment

Patients who “successfully” completed inpatient detoxification were more likely than other patients to have died within a year. No patients who failed to complete detoxification died. Heroin addicts are known to have excess mortality.⁴ However, on the basis of previously published data we would have expected that in our group only one or two patients would have died within a year and only one from overdose.⁵ The clustering of the deaths from overdose in the group of patients who had successfully completed treatment is counterintuitive and illogical—unless it derives from loss of tolerance and consequent unpredictability of resumed heroin use. This study urgently requires replication, and if its results are confirmed these will need to be addressed within existing inpatient, residential, and custodial and associated aftercare programmes.

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Changing prescription patterns for lithium and valproic acid in old age: shifting practice without evidence

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Over the past decade, valproic acid (prescribed as divalproex in North America) has been marketed as an alternative to lithium for treating bipolar disorders. For elderly patients, however, there is no clear evidence that valproic acid is more beneficial than lithium. Moreover, the evidence for the superiority of valproic acid in treating bipolar disorders—mixed episodes and rapid cycling—has been challenged in a recent Cochrane review.¹ Valproic acid has not benefited patients with manic and psychiatric symptoms in dementia, despite the growing use of the drug in the management of these conditions.² Recently, the relatively rapid shift in prescription patterns has been questioned.³ We describe trends in the use of lithium and valproic acid in a large population of people over 65.

Methods and results

We obtained information on drug use from the Ontario Drug Benefit Program, which provides comprehensive drug benefits to all residents aged 65 or older in Ontario, Canada. We identified all patients who had been taking lithium or valproic acid between 1993 and 2001 (prevalent users) and we further identified those patients who had not previously taken lithium or valproic acid (new users). We restricted our study to patients aged 66 or more to enable us to examine their previous drug use for a minimum of one year. Using unique encrypted health card numbers, we linked data on this cohort to two other large datasets—the Canadian Institute for Health