DRUG POINTS

Galactorrhoea may be associated with methadone use

Jennifer Bennett, Richard Whale

We report persistent galactorrhoea and raised prolactin in a woman taking methadone, which is commonly prescribed for the treatment of opiate dependence.

A heroin smoking 28 year old mother of two (younger child aged 4), with hepatitis C (of nine years' duration), weighing 50 kg, was first prescribed 30 mg methadone a day for opiate dependence. She reported newly emergent galactorrhoea after four months of taking methadone, when the dose was increased to 40 mg. The subsequent persistent galactorrhoea required her to use breast pads. Her prolactin concentrations over the next year were raised at 1500, 780, and 910 mIU/l. We confirmed methadone use and intermittent misuse of heroin and cocaine at these times and others by urinalysis. She took no other drugs. Two years later, she still takes methadone and has galactorrhoea.

We found no breast abnormalities other than tenderness; a negative pregnancy test; normal thyroid status; normal range concentrations of oestrogen, follicle stimulating hormone, and luteinising hormone; and an unremarkable head magnetic resonance imaging scan with contrast. She remains amenorrhoeic.

Hyperprolactinaemia with chronic methadone use is described in three reports to the UK Committee for the Safety of Medicines but is not mentioned in the *British National Formulary* or the summary of product characteristics for methadone.

Tolis and colleagues (in 1978) showed a clear rise in plasma prolactin after acute administration of methadone in humans, reversed by dopamine agonists.[1] Pituitary prolactin release is tonically inhibited by dopamine secreted from hypothalamic tuberoinfundibular neurones.[2] Tuberoinfundibular activity is suppressed by opiate agonists, via μ and κ receptors, thereby increasing release of prolactin.[3] This case suggests that tolerance does not occur to the prolactin enhancing effect of methadone, consistent with experimental studies.[4]

Drug rechallenge could not be done, so causality is not proved. But together with previous reports and experimental findings, this case indicates an association between galactorrhoea and methadone use.

Galactorrhoea and other effects of hyperprolactinaemia may be under-reported in patients using methadone.

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Southdowns Health NHS Trust, Brighton BN2 3EW
Jennifer Bennett *consultant in public health/staff grade psychiatrist*
University of Brighton, Postgraduate Medical School, Brighton BN1 9PH
Richard Whale *senior lecturer/ consultant psychiatrist*
Correspondence to: R Whale Richard.whale@brighton.ac.uk

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Ditch the digraph

A surgeon uses a ligature to tie off a bleeding vessel, although the word is somewhat archaic and conjures up an image of John Hunter tying off a popliteal aneurysm. Yet lexical ligatures cast a long shadow, at least on this side of the Atlantic. Medical language is full of words containing *ae* and *oe*: although these pairs are now printed as separate vowels (digraphs), a look in an older text will reveal their earlier form as ligatures *æ* and *œ*. *Haemoglobin* and *oesophagus* show no signs of losing *ae* and *oe* respectively, and some august surgeons and physicians are inordinately proud of these Old World discriminators. This convention, however, does not stand up to close inspection.

In classical Latin the ligature *æ* was used inconsistently for the digraph *ae*, which was found both in native words and in imported words that in their original Greek form had the digraph *αι*. Old English used *æ* as a distinct intermediate vowel; having fallen into disuse in the English language, this sturdy ligature made a comeback in Renaissance scholarly neologisms. Its use hailed back to one of its classical forms, the Greek *αι*. Thus *Ὑμο* became *hæmo*. In due course the ligature *æ* morphed into the digraph *ae*, and so became *haemo*. Perhaps this was because of the very strangeness of the ligature, or perhaps the ligature lost out simply because it required an extra print character.

Classical scholars concur that the correct pronunciation of the sound is a long *e* as in *sheep*. This is respected in *haemoglobin*, but not in *haemorrhoid*. Moreover, the *ae* digraph clashes with the Latin plural suffix *–ae* (as in *fistulae*), which church Latin pronounces like *eye*. Furthermore, its non-medical use in British English is in decline, a notable example being the demise of *encyclopaedia* in favour of *encyclopedia*. Americans binned the *ae* digraph a long time ago, and one must admit a sneaking admiration for their revolutionary spirit.

Use of the digraph *oe* is just as questionable. In earlier borrowings the ligature *œ*, also pronounced as a long *e*, was used to represent the Greek digraph *οι*. The ligature rapidly morphed into *e* alone, thus *œconomy* became *economy*. In later medical borrowings the ligature was also popular, but in due course it morphed into the *oe* digraph, thus *oesophagus*. Derivations can, however, show remarkable inconsistency. *Coeliac* and *koilonychia* both come from *κοιλο* (hollow); but, while the former took the ligature-digraph route, the latter did not. Anyway the *oe* digraph has great potential to confuse. Recently, I was shocked and saddened to hear a healthcare colleague pronounce *oedema* with the first syllable like *toe*.

On grounds of phonetic utility and historical consistency, surely the time has come to call time on this use of *ae* and *oe*. Hard as it is to accept, perhaps our US colleagues got it right when they replaced both with a simple *e*. Might I suggest that the *BMJ*, proponent of all things progressive in British medicine, sets an example by ditching these dodgy digraphs?

Marcus Gore *resident surgical officer, St Mark's Hospital, Harrow (davidmarcusgore@aol.com)*