An open letter from Professor John Strang, chair of the clinical guidelines update working group

22 July 2015

Dear colleagues,

Naloxone – preliminary advice from the working group updating Drug Misuse and Dependence: UK Guidelines on Clinical Management

Background

An NHS England Patient Safety Alert[i] in 2014 raised questions about naloxone dosing in overdose situations. There have also been questions about take-home naloxone products that can be supplied and training that should be provided, now and following legislation to make naloxone more widely available from October 2015 onwards.

The 2007 national clinical guidelines[ii] are currently being updated and a new edition will be published in 2016. The working group updating the clinical guidelines has decided to publish some preliminary advice on these naloxone questions before addressing its supply and use more fully in the published update next year.

This advice was developed by a small subgroup led by Dr Ed Day, to whom I am grateful.

Naloxone and its use

Across Europe, illicit opioid users are 10 times more likely to die than their peers of the same age group and gender, and 6,100 deaths were attributed directly to opioid overdose in 2012.

Naloxone is a potentially life-saving medicine when used in settings associated with opiate misuse and overdose. There is evidence that take-home naloxone given to service users, and training family members or peers in how to administer naloxone, can be effective in reversing heroin overdoses. Its legal status means that anyone can administer naloxone for the purpose of saving a life, and it has been supplied by some drug treatment services since 2005.

However naloxone is only licensed for use in injectable form and remains a prescription-only medicine. This means that at present it can only be distributed to patients with a prescription or via an alternative mechanism (patient group direction (PGD) or patient specific direction (PSD)).

Naloxone is an opioid/opiate antagonist and is already licensed for use in:

1. complete or partial reversal of central nervous system depression and especially respiratory depression, caused by natural or synthetic opioids; and

2. treatment of suspected acute opioid overdose or intoxication.

An NHS England Patient Safety Alert[i] in November 2014 highlighted risks associated with the use of naloxone in patients where it is not indicated, or in larger than recommended doses.

Naloxone dosing

UK Medicines Information (UKMi) Q&A document on naloxone[iii] highlights that there are two distinct scenarios where naloxone may be used, and that appropriate dosing needs to be mindful of a range of patient factors (including the scenario).

The first scenario is palliative care which is not the focus of this letter.

The second is the case of drug misuse and dependence. In an **emergency scenario** where an individual has used sufficient opioid to reduce their rate of respiration to life-threatening levels, prompt administration of naloxone can reverse these effects and restore adequate levels of oxygen in the bloodstream. The risks of giving too much naloxone when it is not required are well documented (see box) but the UKMi document is clear that, in the reversal of acute opioid toxicity with severe respiratory depression or arrest, **'Higher initial dose regimens'** are of particular value.

The recommended intramuscular dose is 400 micrograms initially, with further 400 microgram doses given incrementally every 2-3 minutes until an effect is noted or the ambulance arrives.

Total available naloxone in a community overdose situation before an ambulance arrives is unlikely to exceed 2mg (five 400 microgram doses), which is the amount at which the BNF recommends the diagnosis of opiate overdose should be reviewed.

Risks of giving too much naloxone
Acute withdrawal syndrome from opioids can have both unpleasant and potentially serious effects. Physical effects such as vomiting, agitation, shivering, sweating, tremor and tachycardia are unpleasant, and may lead to aggression and a refusal to accept further treatment (i.e. refusal to go in ambulance or to stay in hospital). Furthermore, life threatening withdrawal reactions may also occur in as many as 1% of cases of naloxone administration, with the potential to cause a sympathetic excess and resultant pulmonary oedema and ventricular arrhythmia.

Naloxone products

A number of products are licensed for use in reversing acute opioid overdose, and all have both advantages and disadvantages in terms of assembly, dose, dose calculation and ease of administration. Consideration should also be given to storage and transportation of the product when identifying the appropriate product to supply.

One product (Prenoxad) has a licence that specifies use in community settings, and comes in a pre-filled syringe containing five 400-microgram doses.

UKMi is producing a product safety assessment report on naloxone products used in emergency situations, which will guide on the issues associated with giving different naloxone products in practice.

It is essential that a minimum level of training in how to assemble and use the particular product should be given to complement provision of that product. Other training will also be helpful.

Training

There is already advice from Public Health England[iv] that training need not be complicated, but it should cover the identification of overdose and how to then respond to overdose. This should certainly cover first calling an ambulance. Where a naloxone product is supplied a minimum level of training in how to assemble and use that product should be given.

People being trained in how to respond to opiate overdose, including using any available naloxone, should, after training, be able to demonstrate an understanding of the following:

- How to identify a suspected opiate overdose
- When to call 999
- Rescue breathing, cardiopulmonary resuscitation (CPR) and the recovery position
- What naloxone is:
    - What it does
    - What it can't do
    - Its short acting nature
- Using naloxone:
    - When to administer naloxone
    - How to administer naloxone
- The importance of staying with a casualty

Yours faithfully,

Professor John Strang
Chair, Clinical guidelines update working group

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[i] NHS England (2014) Patient Safety Alert. Stage One: Warning – Risk of distress and death from inappropriate doses of naloxone in patients on long-term opioid/opiate treatment. NHS/PSA/W/2014/016 www.england.nhs.uk/wp-content/uploads/2014/11/psa-inappropriate-doses-naloxone.pdf

[ii] Department of Health (England) and the devolved administrations (2007) Drug Misuse and Dependence: UK Guidelines on Clinical Management. London: Department of Health (England), the Scottish Government, Welsh Assembly Government and Northern Ireland Executive www.nta.nhs.uk/uploads/clinical_guidelines_2007.pdf

[iii] UK Medicines Information (2015) What naloxone doses should be used in adults to reverse urgently the effects of opioids or opiates www.medicinesresources.nhs.uk/GetDocument.aspx?pageId=797289

[iv] PHE (2015) Take-home naloxone for opioid overdose in people who use drugs www.nta.nhs.uk/uploads/take-home-naloxone-for-opioid-overdose-feb-2015.pdf