SPAGG

Coversheet for Specialist Palliative Audit and Guideline Group Agreed Documentation

This sheet is to accompany all documentation agreed by SPAGG. This will assist maintenance of the guidelines as well as demonstrating the governance process undertaken prior to members seeking local approval in their areas of work.

Document Title	**Guidelines for the use of naloxone in palliative care in adult patients**
Document Date	September 2020
Document Purpose and Intended Audience	This guideline provides information about the use of naloxone, an opioid antagonist in the palliative patient who is receiving prescribed opioid medication in the clinical setting.
Authors	Dr Christina Radcliffe and Tarun Nayyar
References	At end of document
Consultation Process	Discussed and ratified at SPAGG
Monitoring	Review by SPAGG
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Approval Signatures: SPAGG chair SPAGG deputy chair SPAGG secretary	 Dr Jon Tomas Dr Nik Sanyal
Date Approved by SPAGG:	4/11/2020
Date submitted to Area Prescribing Committee:	

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Pan Birmingham NHS
Cancer Network

Guidelines for the Use of Naloxone in Palliative Care in Adult Patients

Version History

Version	Date	Summary of Change/Process
0.1	17/12/08	Draft guideline discussed at Specialist Palliative Care Audit and Guidelines Sub Group (SPAGG)
0.2	18/03/09	Amended draft re-discussed
0.3	15/06/09	Received comments from Professor Ferner and circulated document to SPAGG for discussion at meeting on 17.6.09
0.4	19/08/09	Approved at SPAGG meeting pending minor changes
0.4	25/08/09	Endorsed at Governance Committee Sub Group subject to minor amendment and clarification of 6.1
1.0	28/09/09	Amendments made following Governance Committee Sub Group
1.1	20/12/11	Prepared for discussion by Supportive and Palliative Care Network Site Specific Group
1.2	17/01/12	Author identified at NSSG 16/1/12 template updated and sent to Trisha Castanheira for review
1.3	February 2012	With updating by Trisha Castanheira
1.4	February 2012	With comments by Anna Lock and Lara Barnish
1.5	March 2012	Updated by Trisha Castanheira and forwarded to the NSSG for comments
1.6	March 2012	With Lara Barnish comments for Trisha Castanheira and Network Site Specific Group
2.0	May 2012	Reviewed and endorsed by Guidelines Sub Group and prepared for uploading on to website
3.0	March 2017	Reviewed and updated by Louise Seager. Endorsed by SPAGG.
4.0	November 2019	Reviewed and updated by Christina Radcliffe. Circulated to SPAGG for comments.
4.1	September 2020	Comments from SPAGG and review by Tarun Nayyar, pharmacist, incorporated

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Changes between Version 1 and 2

1. Guideline background
2. Guideline statements
3. Diagnosis and treatment of opioid induced respiratory depression
4. Monitoring after first naloxone administration
5. Patient information and counselling
6. Clinical trials

Changes between Version 2 and 3

1. Guideline background
2. Section 4.2
3. References

Changes between Version 3 and 4

1. **Scope of the guideline**
2. **Guideline statements**
3. **Diagnosis and treatment**
4. **Patient advice and counselling**
5. **References**

Scope of the guideline

1.1. This guideline provides information about the use of naloxone, an opioid antagonist in the palliative patient who is receiving prescribed opioid medication in the clinical setting.

1.2. It is **not** intended to cover the management of acute opioid overdose

1.3. It is **not** intended to cover alternative uses of naloxone in the palliative care setting

1.4. It does **not** cover administration in the patient's home environment

2. Guideline background

2.1. This guideline was initially produced in response to the National Patient Safety Agency recommendation (May 2006) that naloxone is available in all clinical locations where morphine and diamorphine injections are administered or stored.[1] Subsequent patient safety alerts NHS/PSA/W/2014/016 [2] and NHS/PSA/Re/2015/009 [3] recommended that naloxone must be given with great caution to patients who have received longer-term opioid/opiate treatment for pain control or who are physically dependent on opioids/opiates. It acknowledges that the BNF doses recommended for opioid/opiate overdose may not be appropriate for the management of opioid/opiate induced respiratory depression and sedation in those receiving palliative care and in chronic opioid/opiate use.

2.2. This guidance on the use of naloxone for overdose of prescribed opioids in palliative care patients has been developed to address this. They are based on information in PCF 6 Palliative Care Formulary accessed on 27.11.19

Guideline statements

3. General principles

3.1. Naloxone should only be used in palliative care in those circumstances where a clinician suspects opioid-induced toxicity.

3.2. Naloxone is not indicated for:

- patients on opioids who are dying as a natural result of their disease progression
- symptoms induced by non- opioids e.g. barbiturates, benzodiazepines
- opioid induced drowsiness and/or delirium which is not life threatening

3.3. It is important, in the management of patients in pain, that the signs of advanced progressive disease are not confused with those of opioid overdosage, leading to inappropriate use of naloxone.

3.4. Patients on regular opioids for pain and symptom control are physically dependent; naloxone given in too large a dose or too quickly can cause an acute withdrawal reaction and an abrupt return of pain that is difficult to control.

3.5. Total antagonism of opioids can result in severe pain with hyperalgesia. Physical withdrawal symptoms and marked agitation can also occur. Opioid withdrawal syndrome is characterised by anxiety, irritability, muscle aches, nausea and vomiting. In severe cases, this can include life-threatening tachycardia and hypertension. Cardiac arrhythmias, pulmonary oedema and cardiac arrest have been described.

3.6. Patients who are taking opioids and have recently received another intervention e.g. Radiotherapy or nerve block are at risk of opioid toxicity

3.7. Naloxone's antagonism of buprenorphine is less complete because of the latter's high receptor affinity. See section 5 for reversal of buprenorphine induced respiratory depression.

4. Diagnosis and treatment of opioid induced respiratory depression

4.1. If respiratory rate > 8 breaths/min and the patient is easily rousable and not cyanosed, adopt a policy of 'wait and see'; consider reducing or omitting the next regular dose of morphine or reducing rate of/discontinuing continuous parenteral administration

4.2. Administer high flow oxygen via face mask if the patient is hypoxic

4.3. If respiratory rate < 8 breaths/min, and the patient is comatose/unconscious and/or cyanosed:[4,5]

- Stop opioid administration
- Dilute naloxone 400 mcg (1 ampoule) to 8ml with 0.9% sodium chloride for injection to give a 50mcg/ml solution
- Initially administer 100mcg (2ml of diluted naloxone) intravenous (IV) as a slow bolus then flush the cannula with 0.9% sodium chloride
- Administer 100 mcg (2ml) IV every 2 minutes until the patient's respiratory status is satisfactory
- Flush the cannula with 0.9% sodium chloride after each bolus injection
- Further boluses may be necessary because naloxone is shorter acting than morphine (and other opioids)
- Lower doses (20-80micrograms) may be used by diluting naloxone in larger volumes of 0.9% saline if appropriate for the individual patient
- The aim is for slow, paced administration of the drug to avoid a surge of pain from complete antagonism of opioid
- After the last dose of naloxone, monitor consciousness and respiratory rate every 15 mins for 2 hours then hourly for 6hours after immediate release opioid, 12 hours after sustained release opioid, and 24hours after methadone or transdermal opioid.
- Wait until there has been a sustained improvement in consciousness before restarting a lower dose of opioid, it may be preferable to switch the type of opioid
- If there is little or no response consider other causes (e.g. other sedatives)

4.3 If repeated naloxone doses (more than 3 repeat bolus doses) are required, consider starting a continuous intravenous infusion of naloxone [4]

- In this circumstance, transfer to the acute hospital setting should be considered and discussed with the patient or their advocate, and the consultant in charge of the patient's care or the on call consultant.
- Nursing and medical staff should be competent at IV administration and monitoring of opioid toxicity and withdrawal prior to a decision to utilise a continuous intravenous infusion in the hospice setting

- Dilute 1 ampoules containing naloxone 400micrograms in 100 ml 0.5% glucose or 0.9% saline to 100ml to produce a 4microgram/ml solution (or 5 amps in 500ml if 100ml infusion bags not available)
- Administer via a large peripheral vein (or central venous catheter)
- Use a IVI device e.g. volumetric infusion pump to deliver dose
- Use 60% of the stat dose which had previously maintained satisfactory ventilation for more than 15mins, every hour. If 60% equates to a difficult dose, it is possible to round up or down to the nearest whole number.
- For example, if 60mcg has been the last dose to previously maintain respiratory rate, start infusion of 36mcg/hr or 9ml/hr of 4mcg/ml solution.

Adjustment of infusion rate may be required according to patient respiratory rate (aim to keep above 8/min)

- continue to monitor the patient closely with minimum of respiratory rate, oxygen saturations and alertness (AVPU) measured every 30 minutes
- continue the infusion until the patient's condition has stabilised, and respiratory rate is greater than 10/min with oxygen saturations greater than 92% on air
- When the decision is taken to cease the infusion, close observation should again take place in case of ongoing toxicity being masked by the naloxone infusion
- Nursing and medical staff should take care to review for signs of opioid withdrawal and adjust the naloxone infusion rate as required.
- additional IV boluses may need to be given using naloxone diluted in sodium chloride 0.9% as above
- There is no current evidence for use of naloxone via continuous subcutaneous syringe driver. However, the authors are aware of cases where this has been done where hospital transfer was not appropriate or

5. Buprenorphine

5.1 Due to very strong receptor affinity (reflected in its high relative potency with morphine), naloxone in standard doses does not reverse the effects of buprenorphine and higher doses must be used, see table below

Reversal of buprenorphine induced respiratory depression
1. Discontinue buprenorphine (remove transdermal patch) 2. Give Oxygen by mask 3. Give IV naloxone 2mg stat over 90 seconds 4. Commence naloxone 4mg/hour by CIVI 5. Continue CIVI until the patient's condition is satisfactory (probably <90min) 6. Monitory the patient frequently for the next 24h, and restart CIVI if

respiratory depression recurs

7. If the patient's condition remains satisfactory, restart buprenorphine at a reduced dose, e.g. half of the previous dose

6. Other management issues

6.1. Intra-venous is the preferred route of administration for naloxone, but can be given intra-muscularly or sub-cutaneously if venous cannulation is not possible (If using IM/SC route, be aware that onset of action will be slower, approx 2-5 minutes, though duration of action may be more prolonged).

6.2. Administer high flow oxygen via face mask, if the patient is hypoxic.

7. Monitoring after first Naloxone administration

7.1. Naloxone has a much shorter half life than morphine. There is a risk that opioid toxicity will recur as the naloxone wears off and the opioid is still active. Respiratory rate and oxygen saturation should be monitored closely until stable. The length of this period of monitoring will be dependant on the half life of the opioid causing toxicity. The half life of morphine and some other opioids is prolonged in renal failure and other metabolic disturbance.

7.2. It may be appropriate to transfer the patient to a facility where naloxone infusion and monitoring can be initiated. This course of action should be considered if respiratory depression continues to recur despite repeated administration of naloxone (as above).

8. Patient information and counselling

As per the NICE Guidance for use of opioids in palliative care, all patients, should be offered access to appropriate written information during their investigation and treatment, including information about opioid side effects and signs of toxicity

9. Monitoring of the guideline

Adherence to the Network guidelines may from time to time be formally monitored.

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