



RAPID TRANQUILLISATION

Clinical Guidelines for the Pharmacological Management of Severely Disturbed Patients or of Violent Behaviour by Psychiatric Inpatients in the Mental Health Directorate (including Algorithm for Management of Disturbed Behaviour)

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1. INTRODUCTION

- 1.1 Sedative medication is one of several strategies commonly used in the management of severely disturbed behaviour in inpatient settings. The severity of the disturbed behaviour and associated risk to the patient or to other people, and the apparent imminence of that risk, often determine the strategies that are employed in a particular situation. Where the risk is assessed as both severe and imminent rapid tranquillisation may be employed.
- 1.2 Rapid tranquillisation has a limited evidence base because clinical trials are difficult to conduct. These guidelines provide prescribers and nurses with background information that will allow them to make appropriate clinical decisions based on the characteristics of an individual patient and situation.
- 1.3 The *Health Board Algorithm for Management of Disturbed Behaviour* (forming part of this document) should be used in conjunction with these broader guidelines.
- 1.4 The Guideline for the short-term management of disturbed/violent behaviour in psychiatric inpatient settings and emergency departments, published by the National Institute for Clinical Excellence, provides valuable further reading¹.

2. WHAT IS RAPID TRANQUILLISATION?

- 2.1 Rapid tranquillisation (RT) is a pharmacological strategy used to manage a high risk of imminent violence. "Tranquillisation" means calming without sedating. "Rapid" implies that it is necessary to achieve calming as quickly as is safely possible. Occasionally sedation will be unavoidable but this is not an optimal result.

3. WHEN SHOULD RAPID TRANQUILLISATION BE USED?

- 3.1 The need for RT requires a careful clinical judgement. Violence among psychiatric inpatients is predicted by florid psychotic symptoms – particularly, disorganisation symptoms, mania, lack of insight, anger and hostility – and drug or alcohol intoxication.²⁻⁴

- 3.2 Imminence of violence may be suggested by rapidly increasing verbal aggression or anger, perhaps associated with explicit threats of violence, changes or extremes of behaviour, outward signs of inner tension.⁵
- 3.3 RT is a pharmacological strategy. There are a variety of other approaches for managing a high risk of imminent violence. These include de-escalation, distraction techniques, consideration of placement, physical restraint and seclusion. All of these strategies should be considered in each case. RT is likely to be appropriate only when some of these have been tried and have failed. Even when RT is used, the other strategies should continue to be used alongside RT as each is likely to augment the effect of the others. Particular caution is necessary if combining RT with seclusion. Patients who are sedated should not be secluded.
- 3.4 The aim of RT is not to treat any underlying illness or disorder. This must proceed alongside RT but is distinct from RT. An underlying condition does not necessarily predict response to RT or preclude RT. Violence need not be associated with psychosis for RT to be an appropriate therapy. Similarly, violence that is associated with psychosis may respond to non-pharmacological intervention.
- 3.5 RT should not be carried out without an assessment of the physical health of the patient and a consideration of concurrent medication. In particular, the presence of delirium or intoxication should always be considered before RT is commenced.
- 3.6 RT is potentially hazardous. Medical support must be available in case of adverse reactions, over-sedation or the need to administer Flumazenil. Therefore, if RT is to be attempted out of hours, the duty doctor should be contacted. This requires nursing staff to make an important clinical judgement, distinguishing between what is rapid tranquillisation and what is administration of PRN medication. This decision should be made in advance of administration of medication. The level of the disturbed behaviour and apparent imminence of the risk of violence are relevant to this decision. In particular it should be considered rapid tranquillisation, if:
- Medication is to be given without the consent of the patient; or
 - More than one dose of sedative medication is likely to be required (consider the patient's previous history of response to such medication); or
 - It is considered necessary to give i.m. medication.

4. WHAT DRUGS MAY BE USED FOR RAPID TRANQUILLISATION?

- 4.1 Traditionally antipsychotics, such as Haloperidol, have been used for RT in psychiatry, because violence is commonly associated with psychosis. Benzodiazepines are also used commonly and have important advantages over antipsychotics in terms of side effects and toxicity. Increasingly benzodiazepines are a recommended choice⁶⁻¹⁰. Atypical antipsychotics may also produce effective calming and are tolerated better than older antipsychotics.¹¹⁻¹³
- 4.2 It is common for combinations of benzodiazepines and antipsychotics to be used. In patients where antipsychotics are considered necessary this may be beneficial because it reduces the dose of the more toxic antipsychotic that is required¹⁴. It has been suggested that the two classes of drug have a synergistic action^{15;16} and that benzodiazepines may counteract the lowering of seizure threshold by antipsychotics⁷. Antipsychotics are best avoided in those with cardiovascular disease, benzodiazepines are best avoided in those with compromised respiratory function and Haloperidol is best avoided in those who are neuroleptic naïve or who have a history of severe extrapyramidal side effects.
- 4.3 Suitable drugs for rapid tranquillisation need to have a rapid onset of action. Frequent small doses are safer and more effective than single large doses, but this may lead to a risk of accumulation. Therefore, the drugs used should have a short duration of action and the prescriber should bear in mind the pharmacokinetics of the agents used. The previous medication taken by the patient must be considered in this regard. The agents which have the most rapid onset of action are Lorazepam, intramuscular Olanzapine and intramuscular Haloperidol.
- 4.4 Zuclopentixol Acetate (acuphase) is not an appropriate drug for use in RT and there is limited evidence for its value in the treatment of schizophrenia¹⁷.
- It has a significantly delayed onset of action and a relatively long duration of action.
 - It may have a role in the ongoing management of a risk of violence once tranquillisation has been satisfactorily achieved. But it is important to consider the pharmacokinetics of other drugs when

prescribing it. For example, caution is necessary in a patient who has recently received a dose of depot antipsychotic which has not yet reached peak levels.

- It should only be given after calming has been achieved, in those situations when it is likely that repeated doses of i.m. antipsychotics will be necessary.
- It should never be used in those who are struggling, who are sensitive to EPSE, those with cardiac disease, hepatic or renal impairment or in pregnancy.
- Doses of 50-150 mgs may be given up to a maximum of 400 mgs in two weeks, with at least 24 hours between doses. NB. There is no such thing as “a course of acuphase”!

Table 1 – Drugs used in RT, their properties and side effects

Drug	Route	Pharmacokinetics	Major Side Effects	Notes
Short-acting antipsychotics				
Aripiprazole	Oral	Peak 3-5 hours t½ 75 hours	Orthostatic hypotension Tachycardia Dry mouth	
	i.m.	Peak 1-3 hours t½ 75 hours		
Haloperidol	Oral	Peak 4 hours t½ 21 hours	EPSE Hypotension NMS Increased QTc, Arrhythmias Seizures Sudden death	Note risk of acute dystonias and ensure that an appropriate antimuscarinic is to hand. Not recommended for i.v. use because of the risk of arrhythmias
	i.m.	Peak 20 minutes t½ 21 hours		
Olanzapine ^{11,13}	Oral	Peak 5-8 hours	Hypotension Bradycardia syncope	Less likely to cause EPSE than haloperidol i.m. administration results in initial maximum plasma concentration 5× higher than same dose given orally
	i.m.	Peak 15-45 minutes t½ 30 hours		
Risperidone ¹⁸	Oral	Peak 2 hours t½ 18 hours	EPSE ? hypotension	Limited clinical experience or trial data
Quetiapine	Oral	Peak 1.5-1.8 hours t½ 6-7 hours	? hypotension	Limited clinical experience or trial data
Benzodiazepines				
Lorazepam	oral	Peak 2 hours t½ 12 hours	Respiratory depression Disinhibition	A wide therapeutic index & respiratory depression is readily reversed with the specific antagonist Flumazenil Disinhibition is more likely to occur in those with organic brain disease, including learning disabilities, the under 18s and the over 65s, and perhaps those with impulse control problems ¹⁹
	i.m.	Peak 60-90 mins t½ 12-16 hours		
Diazepam	oral	Peak 60 minutes t½ 24-48 hours	IM must be diluted with equal volume of WFI/saline	
	i.v.	n/a		
	i.m.	Onset 1-2 hours t½ 7-15 hours		
Other				
Promethazine ²²	i.m.	Onset of action 20 minutes t ½ 9.8 +/- 3.4 hours	Sedation, EPSE reactions, Tachycardia, bradycardia, faintness, dizziness, transient minor increases in BP, and hypotension have been reported	Monitor for sedation and cardiac side effects

Note: The pharmacokinetics of Lorazepam are similar whether given orally or parenterally. Therefore, the only reason to give Lorazepam parenterally is if the patient refuses oral.

5. WHAT ABOUT YOUNG PEOPLE UNDER 18 YEARS OF AGE?

- Many drugs are not licensed for use with children. Some may be used because over time clinical experience has been built up amongst experts and there is peer support for usage. There is an expectation that in the future drug companies will have to give fuller information on the effects of their drugs on children.
- The weight of the young person needs to be considered in deciding dosages. Over a weight of 40kg dosages up to adult BNF limits may be used. Calculate dosage by weight for under 40kg (size of average 12-13 yr old).

- 5.3 It is not acceptable practice to use doses over that given in the BNF for young people as there is no body of evidence or experience to support such usage.
- 5.4 Haloperidol, Diazepam and Promethazine are used with young people.
- 5.5 Risperidone is licensed for use for those aged 15 and over.
- 5.6 Currently oral Olanzapine is used for treating young people off licence and there is clinical peer support for this. There is no body of clinical evidence to support the use of the newer IM formulation, so this should not be used.
- 5.7 Quetiapine and Zuclopenthixol Acetate are being used clinically by specialists but are not licensed for use with young people.
- 5.8 Levomepromazine is not used.
- 5.9 Lorazepam is not recommended for use with young people although specialists do use it. There is experience of disinhibition occurring. After some hours irritability can be marked and there is a risk of further behavioural disturbance related to this.

6 Rapid Tranquilisation for Older Adults

6.1 If in doubt at any stage, duty doctor to seek advice from covering Consultant, SpR or Staff Grade.

6.2 Pre RT Considerations

- Review use of non-pharmacological strategies
 - Distraction, Environment, Talking Down, Time Out, Privacy
- Consider other medical causes
 - Akathisia, Diabetes, Acute Infection, Delirium, Intoxication, Dehydration, Metabolic Disturbance, Respiratory Diseases, Discomfort, Pain, Constipation.
- Review Consent to Treatment
- Consider other important characteristics which may impact on choice / dose of treatment
 - Body Weight, Metabolic Disturbance, Cardiac Pathology, Abnormal ECG, Lewy Body Dementia, Parkinson's Disease, Previous Tolerance of Antipsychotics
- If disturbed behaviour due to alcohol withdrawal, avoid antipsychotics
- Check medication given in last 24 hours including prn.

6.3 Pre RT – Oral and Buccal

Step 1 : PO Lorazepam 500micrograms to 1mg

If after 45 minutes, inadequate or no effect, proceed to Step 2

Step 2 : PO Lorazepam 500micrograms to 1mg

Other options if the patient has previously had antipsychotic therapy, has a recent ECG available and does not have LBD, Parkinson's Disease or significant cardiac pathology include :-

- PO Haloperidol 0.5mg – 1mg
- PO Olanzapine 2.5mg
- With the following less commonly used :*
- PO Aripiprazole 5mg
- PO Promethazine 10mg – 25mg [avoid in dementia due to anticholinergic effect]
- PO Risperidone 0.5mg – 2.5mg

6.4 RT: Intramuscular Monotherapy

If refusing oral medication

Step 1 : IM Lorazepam 0.5-1mg

If after 45 minutes, inadequate or no effect, proceed to Step 2

Step 2 : IM Lorazepam 0.5mg-1mg repeated

Other options if the patient has previously had antipsychotic therapy, has a recent ECG available and does not have LBD, Parkinson's Disease or significant cardiac pathology include :-

- IM Haloperidol 0.5mg [May prolong QT interval]
- IM Olanzapine 2.5mg [Not within 1 hour of IM Lorazepam]

With the following less commonly used :-

- IM Aripiprazole 5.25mg [Less sedating but minimal hypotensive effect]
- IM Promethazine 12.5mg [Avoid in dementia due to anticholinergic effect]

6.5 RT : Combination Therapies

Combination therapies e.g. lorazepam combined with haloperidol are used less commonly in old age populations and as such if the above measures fail to adequately treat agitation / aggression, discussion with senior on call registrar or consultant is advised.

Medication profiles for older adults (over 65 years)					
Aripiprazole IM	Max 15.75mg/24hrs	Peak 1-3hrs	Olanzapine IM	Max 10mg/24hrs	Peak 15-45min
Haloperidol IM	Max 5mg/24hrs	Peak 15-60min	Olanzapine PO	Max 10mg/24hrs	Peak 5-8hrs
Haloperidol PO	Max 5mg/24hrs	Peak 2-6hrs	Promethazine IM	Max 50mg/24hrs	Peak 2-3hrs
Lorazepam IM	Max 2mg/24hrs	Peak 60-90min	Promethazine PO	Max 50mg/24hrs	Peak 2-3hrs
Lorazepam PO	Max 2mg/24hrs	Peak 2hrs	Risperidone PO	Max 2mg/24hrs	Peak 1 hr

7 PHYSICAL MONITORING BEFORE AND DURING RAPID TRANQUILLISATION

7.1 Before prescribing medication for rapid tranquillisation, the prescribing doctor should:

Review the patient's notes with regard to his/her general medical history and consider the possibility of a physical examination.

Check for recent ECG, U&E and urine drug screen results, a previous history of severe extrapyramidal effects, previous response to RT or other methods of managing imminent violence.

Review current prescribed medication and recently administered medication, taking note of administrations of PRN prescriptions.

7.2 During rapid tranquillisation:

7.3 Close monitoring by nursing staff is necessary to ensure prompt recognition of the serious complications. The frequency must be agreed with the prescriber and will vary according to the clinical state of the patient. Observations should be particularly frequent when a patient is sedated.

7.3.1 Some observations may be difficult if a patient remains agitated or aggressive. Problems in this regard should be clearly documented and discussed with the prescriber or the clinical team.

7.3.2 Observations should be recorded on the 'Observation & NEWS Score' chart, the chart should be annotated on the entry date and in the comments box with 'RT administered' (See page 13).

Table 2 – Suggested scheme for physical monitoring after parenteral drug administration

<ul style="list-style-type: none"> • Alertness • Temperature • Pulse • Blood pressure • Respiratory rate 	<ol style="list-style-type: none"> 1. Every 5-10 minutes for 1 hour 2. Then every 30 minutes until patient is ambulatory 3. Then continue to monitor alertness, mental state and behaviour. Restart physical observations if there are any concerns.
Fluid balance & electrolyte balance should be monitored as clinically indicated	
ECG monitoring is recommended when parenteral antipsychotics have been given in high doses	
If a patient is unconscious continuous pulse oximetry is recommended	

8 MANAGEMENT OF SIDE EFFECTS AND COMPLICATIONS

Table 3 – Common or serious side effects and management

Complication	Symptoms/signs	Management
Acute dystonia	Severe painful muscular stiffness	Procyclidine 5-10 mgs im
Hypotension	Fall in blood pressure (orthostatic or <50mmHg diastolic)	Lie patient flat and raise legs Monitor closely
Neuroleptic malignant syndrome	Increasing temperature, fluctuating blood pressure, muscular rigidity, confusion/altered consciousness	Withhold antipsychotics Monitor closely Liaise with general medical team
Arrhythmias	Slow (<50/minute) or irregular pulse	Monitor closely and liaise with general medical team immediately
Respiratory depression	Reducing respiratory rate, reducing consciousness	Give oxygen, raise legs. If necessary ventilate mechanically If respiratory rate drops below 10/minute in a patient who has received benzodiazepines, give Flumazenil : 1. 200mcg i.v. over 15 seconds 2. if consciousness not resumed within 60 seconds give 100mcg over 10 seconds 3. repeat at 60 second intervals. Maximum dose 1mg/24 hours Continue to monitor after respiratory rate returns to normal. Flumazenil has a short duration of action so further doses may be required. Patients may become agitated or anxious on waking.

After rapid tranquillisation

8.1 All patients should be offered the opportunity to discuss their experiences and should be provided with a clear explanation of the decision to use RT. They should be given an opportunity to write their account of their experience in the notes.

8.2 Similarly, staff and other patients should have the opportunity to discuss the incident.

8.3 RT provides a short-term strategy for managing a high risk of imminent violence. Medium- and longer-term measures should be considered at an early stage with the aim of avoiding repeated RT. The diagnosis and its relationship to violence should be considered. Regular treatment should be reviewed. There may be two types of patient requiring RT²¹:

8.3.1 Those who require repeated injections due to persistent refusal of oral medication and resulting aggressive behaviour;

8.3.2 Those who require only one or two injections early on in their treatment.

For the former group, the use of longer-acting parenteral medications such as Zuclopenthixol Acetate (acuphase) or depot antipsychotics may be appropriate. It may be appropriate to administer both Zuclopenthixol Acetate and a depot antipsychotic simultaneously. Such strategies are likely to be less appropriate for the latter group.

9 IMPLEMENTATION OF GUIDELINES AND PROTOCOL

- 9.1 Following ratification of the document awareness raising sessions are planned. These will be organised on a multidisciplinary basis with presentations to all groups of staff who will be required to implement the guidelines set out in this document.
- 9.2 Awareness and training sessions will be available to all staff and information will be circulated to all relevant clinical areas.

10 AUDIT

- 10.1 When the clinical need indicates the use of rapid tranquillisation guidelines in the management of severely disturbed patients this will trigger a submission of an IR1 form (Adverse Incident Reporting).
- 10.2 Incidents will be logged on the Datix system by the Governance Support Unit. This will enable accurate records of the number and types of instances in which the procedure was required. Details held on the system will serve as an audit trail. This will enable a case note audit of all cases in which rapid tranquillisation was used and to check compliance with the protocol and compliance with NICE Clinical Guideline 25: Violence¹. An annual audit will be undertaken and will be included in the directorate audit plan.

11 REFERENCE LIST

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Pre-RT Considerations

- Review the use of non-pharmacological strategies for managing an imminent risk of violence
- Review the patient's consent to treatment. Is it necessary to use a section 62?
- Junior doctor to consult with senior doctor, e.g. Consultant, at any stage if unsure. RC to be informed
- If disturbed behaviour is due to alcohol withdrawal, avoid use of antipsychotics, see alcohol detox guidelines

Pre-RT - Oral & Buccal

Oral Lorazepam 1-2mg

OR

Oral Promethazine 25-50mg

OR

Oral Antipsychotics
Haloperidol 5mg
Olanzapine orodispersible 10mg

RT: Intramuscular Monotherapy

IM Lorazepam 1-2mg

OR

IM Promethazine 50mg

OR

IM Aripiprazole 9.75mg
IM Haloperidol 5-10mg
IM Olanzapine 5-10mg

RT: Intramuscular Combinations

IM Promethazine 25-50mg
PLUS
IM Haloperidol 5-10mg

OR

IM Lorazepam 2mg
PLUS
IM Haloperidol 5mg

Management of possible complications of RT which may require urgent medical attention	
N.B. IV administration by medical staff only	
Problem	Remedial Measures
Irregular/ Slow pulse <60/minute	Contact Doctor. Consider urgent referral to physicians
Fall in Blood Pressure Orthostatic or <50mmHg diastolic	Contact Doctor. Lie patient flat. Raise legs if possible. Monitor closely. May need physician referral.
Acute Dystonia (including oculogyric crisis)	Administer procyclidine 5-10mg IM (or IV) Review antipsychotic medication
Reduces Respiratory Rate <10/minute O ₂ sats <95	Phone 999 and contact doctor immediately. Give Flumazenil if benzodiazepine induced. Initial Dose: 200mcg IV over 15 sec – if required level of consciousness not achieved after 60 seconds then: Subsequent dose: 100mcg over 10 seconds, repeated after 60 seconds if necessary. Maximum dose: 1mg in 24hours
Increase in Temperature >38°C	Consider Neuroleptic Malignant Syndrome

Time to peak				
	Injection	Injection Cost	Oral	Notes
Haloperidol	15-60 mins	£	2-6 hours	↑ risk of acute dystonia. Not recommended for IV use due to arrhythmias
Lorazepam	60-90 mins	£	5-8 hours	Respiratory depression reversed with flumazinil
Promethazine	2-3 hours	£	2-3 hours	Monitor for sedation and cardiac side-effects
Aripiprazole	1-3 hours	££	3-5 hours	
Clonazepam	-	-	1-4 hours	
Olanzapine	15-45 mins	££££	5-8 hours	Less likely to cause EPSEs than haloperidol. Initial plasma concentration is 5x higher than equivalent oral dose
Flumazinil	Response within 3 mins. Peak 6-10 mins. Duration depends on type & dose of benzodiazepines			

Suggested scheme for physical monitoring after parenteral drug administration	
<ul style="list-style-type: none"> Alertness Temperature Pulse Blood pressure Respiratory Rate 	<ol style="list-style-type: none"> Every 5-10 minutes for 1 hour Then every 30 minutes until the patient is ambulatory Then continuously to monitor alertness, mental state and behaviour. <p>Restart physical observations if there are any concerns</p>
Fluid balance & electrolyte balance should be monitored as clinically indicated	
ECG monitoring is recommended when parenteral antipsychotics have been given in high doses	
If a patient is unconscious continuous pulse oximetry is recommended	

Once adequate tranquillisation has been achieved

1. Maintain monitoring of physical and mental state according to guidelines
2. Review causes of violence, diagnosis and consider ongoing management. This is likely to require a review of continuing pharmacological treatment.
3. Consider debriefing of patients, staff and other observers. Offer the patient an opportunity to describe his/her experience in the notes.
4. All 'prn' medication, including rapid tranquilisation should be reviewed on a weekly basis.

Surname:
Forename:
M/F:
Hospital No:

Comments
Day 4 - Rapid Tranquilisation administered

	3	2	1	0	1	2	3
Resp rate	≤8		9-11	12/20		21-24	≥25
SpO ₂	≤91	92-93	94-95	≥96			
Any O ₂				No		Yes	
Systolic BP	≤90	91-100	101-110	111-219			≥220
HR	≤40		41-50	51-90	91-110	111-130	≥131
AVPU				Alert			V,P or U
Temp °C	≤35.0		35.1-36.0	36.1-38.0	38.1-39.0	≥39.1	

Date	1	2	3	4	5												
RESP. RATE	≥25																
	21-24																
	12-20	x	x	x	x	x											
	9-11																
	≤8																

SpO ₂	≥96	x	x	x	x	x											
	94-95																
	92-93																
	≤91																
No O ₂																	
Any o ₂																	

BLOOD PRESSURE (If BP unrecordable score 3)	250																
	230																
	210																
	190																
	170																
	150																
	130																
	110																
	90																
	70																
	50																
	30																

HEART RATE	≥140																
	120				x												
	100					x											
	80	x	x	x													
	60																
	40																

CONSCIOUS LEVEL	ALERT																
	V																
	P																
	U																


TEMP	≥39°																
	39°				x												
	39°	x		x		x											
	37°		x														
	36°																
	≤35°																



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Authorisation Form for Publication onto COIN

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Has NICE guidance been considered/referenced when producing this guidance? If yes, please state the title or reference number.	Yes
Is the document relevant to the GP Portal?	No
Equality Statement (Mandatory for Policies). ⁽¹⁾	Yes
Please specify keywords to assist with searching. ⁽²⁾	Rapid tranquillisation
Published.	October 2015
Last Review.	June 2019
Next Review/Expiry Date.	June 2022

(1) All policies need to comply with the Policy for the production, consultation, approval, publication and dissemination of strategies, policies, protocols, procedures and guidelines

(2) Relevant keywords will assist COIN users with searching for documents.