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CLINICAL REFLECTION

# The pharmacological management of acute behavioural disturbance in pregnancy

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**SUMMARY**

Acute behavioural disturbance is relatively common during the perinatal period. The management of agitation in pregnant women is similar to that in the general population, although with some additional considerations, such as modifications to restraint techniques, careful medication selection, monitoring of maternal and fetal well-being and the importance of a debrief. There are benefits of agreeing a pre-determined care plan for women who are at risk.

**Keywords**

Perinatal psychiatry; antipsychotics; drug interactions and side-effects; psychotic disorders; bipolar affective disorder.

Pregnancy is a risk factor for first onset of affective psychosis, as well as relapse of a pre-existing mental illness such as schizophrenia or bipolar disorder. Acute behavioural disturbance is accordingly a significant and relatively common presentation during the perinatal period. However, clinicians often lack confidence in treating behavioural disturbance in pregnancy and so we offer a pragmatic approach to this clinical problem, with a focus on pharmacological management. We include a summary of the current guidelines, a brief review of evidence regarding the safety of rapid tranquillisation in pregnancy, and a suggested treatment algorithm (Fig. 1).

## De-escalation

Pregnant women may present with acute agitation in a range of settings: psychiatric in-patient environments, the emergency department, obstetric settings or in the community. Early identification of warning signs and triggers should be attempted, accompanied by efforts to remedy any reversible causes, such as a specific psychological, social or physical stressor, including pain. Medical or obstetric problems, delirium and drug or alcohol intoxication/withdrawal should also be ruled out.

It is important for staff to feel equipped in de-escalation techniques, and in community settings this may be the limit of available interventions, aside from requesting support from emergency services. It is beyond the scope of this reflection to describe de-escalation strategies in full; however, these include verbal techniques such as speaking calmly and concisely and listening carefully to establish the woman's concerns, which can then be addressed. Staff should be aware of their body language, respect personal space and attempt to remove environmental stressors, for example by moving to a quiet space. If these efforts are unsuccessful and the level of agitation is felt to put the patient or others at risk, physical restraint and rapid tranquillisation may be considered as a final resort.

## Physical restraint

There are precautions that need to be taken when planning any form of physical restraint on a woman who is pregnant, to avoid discomfort or injury to the woman and harm to the fetus. Any prone position should be avoided at any stage of pregnancy but particularly after the first trimester. Women in the second and third trimesters are at risk of aortocaval compression and therefore must not be restrained supine. Recommendations are that pregnant women should be restrained on their side (ideally, the left) or in a semi-recumbent position, for example with the use of a large beanbag. If intramuscular medication is required, administration into the deltoid muscle may offer benefits as regards accessibility.

In non-psychiatric settings there may be difficulty obtaining sufficient trained staff to carry out a safe restraint, and restraint is inadvisable until adequate personnel can attend. It is important that the restraint time is as short as possible and that the woman's physical health is monitored during and after the restraint. It is also advisable to ensure a midwife or obstetrician review as soon as this is practicable, particularly if the restraint has been difficult or prolonged.

The emotional impact of restraint on the woman should be recognised, with particular consideration

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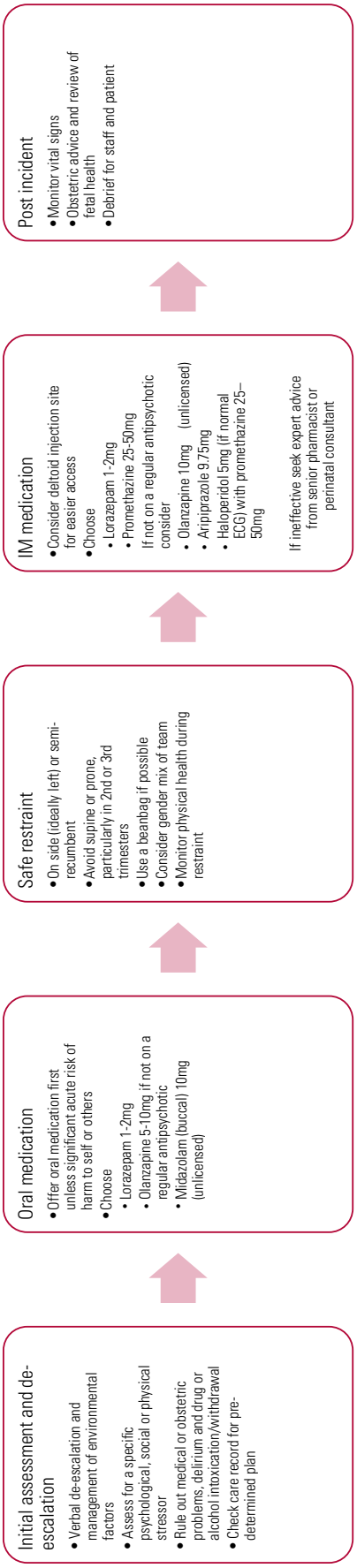


**FIG 1** Suggested algorithm for management of acute agitation in pregnant women. IM, intramuscular; ECG, electrocardiogram.

of her trauma history and the gender mix of attending staff. Post-incident debrief is essential to allow staff involved to reflect on the events, identify the antecedents and consider how future incidents might be prevented. The patient should be involved in the debrief if appropriate or supported by a separate discussion with staff.

## Medication for acute behavioural disturbance

The safety of psychotropic medication in pregnancy cannot be robustly tested owing to ethical restrictions, particularly on prospective trials. Often women prefer to minimise the use of psychotropic medication during pregnancy or avoid it altogether. This makes decisions about prescribing in pregnancy without patient consent even more significant (for example when a woman is detained under the Mental Health Act). In an emergency there is often little or no opportunity to discuss with the woman the rationale and potential risks of rapid tranquillisation.

Rapid tranquillisation typically refers to the use of intramuscular medication but can include oral medication. Oral medication should be offered initially, and intramuscular medication should be administered only if that is refused. When the need for rapid tranquillisation arises in a pregnant woman it may engender anxiety in the treating team, including prescribers, who may be relatively junior, and nursing staff, who may lack specific experience of restraints and medication administration in pregnancy. In the context of acute agitation there may not be time for specialist advice to be sought. Unfortunately, there is a lack of clear guidance for non-specialist clinicians, who may subsequently practise in an over-cautious manner, which may in itself lead to negative outcomes such as patient self-harm, harm to staff or members of the public, or distress to the patient or fetus.

## Existing guidelines

The National Institute for Health and Care Excellence (NICE) guidelines (CG192) (NICE 2014) advise that pregnant women who present with violent and aggressive behaviour in the context of mental disturbance should be treated according to the general guidelines for non-pregnant people (NICE guideline NG10). NICE does stipulate some specific caveats, for example to avoid the use of seclusion after rapid tranquillisation and to adapt restraint procedures to minimise harm to the fetus. The medications suggested for rapid tranquillisation (not specific to perinatal cases) are lorazepam alone or haloperidol combined with promethazine. NICE advises that antipsychotics or benzodiazepines used as rapid tranquillisation should be given at the

minimum effective dose, although it can be difficult to predict this, particularly during the third trimester, when higher doses may be required. NICE also gives preference to medications with shorter half-lives, which is particularly relevant during the last few days of pregnancy or during labour, when there may be a risk of neonatal extrapyramidal side-effects (associated with maternal antipsychotic use) or floppy baby syndrome (with benzodiazepines).

The British Association for Psychopharmacology consensus guidance advises that any woman at risk of relapse ought to have a predetermined plan written in their care record to indicate what should happen in the case of acute behavioural disturbance (McAllister-Williams 2017). It advises that the type of medication is considered in advance, in accordance with the individual risk to the woman and fetus, as well as previous response to and tolerance of specific medications. It is advised that if a pregnant woman is given rapid tranquillisation, mental health teams ought to work with obstetric and midwifery colleagues to ensure there is no evidence of harm to the fetus. The guidance highlights the importance of checking physical observations after rapid tranquillisation.

## Choice of medication

There is a lack of research into medication used as rapid tranquillisation specifically in pregnancy. However, it may be useful to look at the medications typically used as rapid tranquillisation, for example benzodiazepines, haloperidol, atypical antipsychotics and promethazine, and consider their safety in pregnant women. All these drugs are known to cross the placenta but there are no clear associated teratogenic effects. It may be presumed that once only or occasional use of these medications would be less likely to affect the developing fetus than regular oral use. The timing of use is significant. Medication use in the first trimester generally carries the highest risk of fetal malformations, whereas use towards the end of pregnancy or during labour risks complications such as neonatal withdrawal and requires extended neonatal observations after birth. Choice of medication may be guided by various factors, including patient preference, previous response and tolerability, physical comorbidities and access to physical health investigations (such as a recent electrocardiogram (ECG) before haloperidol administration). Concomitant or recent medication administration should also be taken into account, for example if a patient is on a regular high-dose antipsychotic, additional antipsychotic use may not be advised. Intramuscular olanzapine should not be used with benzodiazepines because of the risk of excess sedation and respiratory depression.

### *Benzodiazepines*

Some older studies linked exposure to benzodiazepines in the first trimester with an increased risk of cleft palate (e.g. Dolovich 1998), but more recent studies have not found this association (e.g. Ban 2014). There are minimal data on lorazepam specifically. Tinker et al (2019) found an association between lorazepam and pulmonary valve stenosis but the sample size was small. Buccal midazolam has been shown to be effective for rapid tranquillisation (Taylor 2008) and could be a useful option for pregnant women as it avoids the risks associated with prone or supine restraint. A consideration in later pregnancy with high-dose or frequent use of benzodiazepines is floppy baby syndrome with associated mild sedation, hypotonia and feeding difficulties. In addition to this, neonatal withdrawal may cause vomiting, diarrhoea and poor weight gain.

### *First-generation antipsychotics*

First-generation antipsychotics are believed to be safe in pregnancy, with no clear association with any congenital malformations. Huybrechts et al (2016) found no increased risk of malformation when examining a group of 733 women taking a typical antipsychotic compared with those who did not take antipsychotics. Haloperidol is recommended by NICE in the context of rapid tranquillisation (NICE guideline NG10) but there is a risk of acute dystonia, and a pre-treatment ECG is usually advised.

### *Second-generation antipsychotics*

A recent systematic review (Tosato 2017) concluded that second-generation antipsychotics were not associated with an increased risk of fetal malformation and had no adverse effect on child neurodevelopment. Huybrechts et al (2016) found no significant association between atypical antipsychotics and malformations, and included individual analysis for aripiprazole and olanzapine. Olanzapine is commonly chosen as an agent for rapid tranquillisation, and data generally support this as being safe for the developing fetus (Ennis 2015), although it is noted that intramuscular olanzapine is not formally licensed in the UK. There is relatively little information on aripiprazole, although a recent review found no evidence of adverse outcomes (Cuomo 2018).

### *Promethazine*

Promethazine is sometimes used as a sedative or it is co-prescribed with haloperidol to prevent extrapyramidal side-effects. It is generally felt to be safe,

with no evidence of association with congenital malformations or other pregnancy complications (UK Teratology Information Service 2019), and it is commonly prescribed in pregnancy because of its antiemetic effects. However, its effectiveness is limited owing to slow onset of action.

## Summary

Acute agitation in pregnancy should be managed in most situations with de-escalation and non-pharmacological methods. Where this is not possible, restraint (with or without intramuscular medication) should be planned collaboratively by a multidisciplinary team, with due consideration of the welfare of the woman and developing fetus. It may be challenging in an acute scenario to hold discussions and to seek advice, therefore where possible a plan should be made in advance, for example at the pre-birth planning meeting, for women already known to perinatal mental health services. Clear communication between psychiatric and obstetric teams is essential, and sharing this pre-determined plan may be reassuring to professionals involved.

Women in the perinatal period encounter several different services, and professionals working across these need to have some knowledge of how to manage acute agitation in this specific patient population. Training may be beneficial for emergency services, emergency department clinicians and security staff, midwives and other maternity staff, as well as general and specialist mental health teams. Health professionals, police and security staff who may be involved in physical restraint should be familiar with the adaptations required.

In situations where intramuscular medication is necessary, medication choice should be guided by multiple factors, including patient preference, the source of agitation, and previous response to and tolerance of medication. Guidelines suggest medications similar to those used in the general adult population, including haloperidol with promethazine, short-acting benzodiazepines such as lorazepam and atypical antipsychotics such as olanzapine. Women who have undergone or witnessed physical restraint may benefit from a debrief about the intervention soon after the incident as well as at a later point in their recovery.

## Data availability

Data availability is not applicable to this article as no new data were created or analysed in this study.

## Author contributions

J.P. was the lead author, writing the majority of the article, including the initial and final drafts. D.T. reviewed the content, re-wrote sections, advised on the algorithm and medications, and participated in final review of the article. M.M. was the project supervisor, involved in initial ideas/conception, reviewing drafts, providing clinical overview with specialist perinatal experience, and final review of the article.

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## Declaration of interest

None.

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