NHS Greater Glasgow & Clyde

Mental Health Services

Prescribing Management Group

Guidance on the management of Extrapyramidal Side Effects

Extrapyramidal side effects (EPSE) and movement disorders can manifest as several symptoms, detailed in the tables below. It is important that staff are aware of the clinical features and treatments for the different EPSE symptoms.

All antipsychotics have the potential to cause EPSE but it is more common with first generation antipsychotics (e.g. flupentixol, haloperidol) and the effect tends to be dose related. Caution should be used in prescribing other medication likely to cause EPSE such as sodium valproate, lithium and some antidepressants and the patient should be monitored closely for additive effects.

Following initiation of an antipsychotic patients should be monitored for emergence of EPSEs on a weekly basis and for 2 weeks after target dose reached. After dose increases patients should be monitored for 2 weeks.

Akathisia - A state of inner restlessness, with a strong desire/compulsion to move	
Clinical features	- Foot stamping when seated - Crossing/uncrossing legs - Rocking from foot to foot - Pacing up and down - Akathisia may be mistaken for psychotic agitation and has been linked with suicidal ideation and aggression towards other
Rating scales	Barnes akathisia scale (appendix 1)
Prevalence	Approximately 25%, less with second generation antipsychotics in decreasing order; aripiprazole, lurasidone, risperidone, olanzapine, quetiapine and clozapine.
Time taken to develop	Occurs within hours to weeks of starting antipsychotics or increasing the dose. Tardive akathisia can take longer to develop and persist after antipsychotics have been withdrawn
Treatment	Depending on the clinical circumstances; - Reduce antipsychotic dose - Change to an antipsychotic with a lower propensity for akathisia - Anticholinergics (e.g. procyclidine) are usually ineffective - Benzodiazepines can be used short term during initiation - The following drugs may reduce akathisia (all unlicensed for this indication- see Maudsley for dosing);

	○ Propranolol ○ Clonazepam (low dose) ○ H_2 antagonists e.g. Mirtazapine, trazodone The Maudsley- Practice guidelines for physical health conditions in psychiatry has a good flow chart showing treatment options (Athens login required)

The following guidance is adapted from The Maudsley Prescribing Guidelines in Psychiatry [1] and The Maudsley Practice Guidelines for Physical Health Conditions in Psychiatry [2]

Dystonia - Uncontrolled muscular spasm in any part of the body	
Clinical features	- Abnormal face and body movements - Oculogyric crisis (eyes rolling upwards) - Torticollis (head and neck twisting to the side) - Inability to swallow or speak clearly - In extreme cases, back may arch or jaw dislocate
Rating scales	No specific scale
Prevalence	Approximately 10% but more common; - In young males - In neuroleptic naïve - With high potency antipsychotics Rare in the elderly
Time taken to develop	Can occur within hours of starting antipsychotics (minutes if given via IM or IV)
Treatment	Anticholinergic drugs given PO, IM or IV depending on the severity of the symptoms; - Example PO anticholinergic*: procyclidine 2.5mg three times daily, increased in steps of 2.5mg-5mg daily if required, up to maximum 30mg daily in 2-4 divided doses* [3] - For procyclidine IM dosing please consult the summary of product characteristics. The maximum IM procyclidine dose is 20mg daily [4] but in acute crisis doses of up to 30mg can be used. - Elderly patients may be more susceptible to the anticholinergic effects of procyclidine and a reduced dosage may be required - Response to IM takes ~20 minutes - If after 3 doses of IM, symptoms have not resolved then patient should be transferred to acute care

	- Remember: patient may be unable to swallow Reduce dose or switch to an antipsychotic with lower propensity

<u>Tardive Dyskinesia</u> – Abnormal movements	
Clinical features	- Lip smacking or chewing - Tongue protrusion 'fly catching' - Pill rolling or piano playing (choreiform hand movements) - Pelvis thrusting - Severe orofacial movements can lead to difficult speaking, eating or breathing. Symptoms can worsen under stress.
Rating scales?	Abnormal Involuntary Movement Scale (AIMS) (appendix 2)
Prevalence	5% of patients per year of antipsychotic exposure. More common in; - Older age - Affective illness - Those who have had acute EPS early in treatment - Genetic predisposition - Length of exposure to antipsychotics
Time taken to develop	Months to years. Approximately 50% of cases are reversible
Treatment	Depending on the clinical circumstances; - Stop anticholinergic if prescribed - Reduce dose of antipsychotic - Change to an antipsychotic with lower propensity for tardive dyskinesia - Clozapine is the antipsychotic most likely to be associated with resolution of symptoms, quetiapine may also be useful. - Tetrabenazine is licensed for the treatment of TD, starting at 12.5mg and titrating to 25-75mg/day.

Pseudoparkinsonism	
Clinical features	- 'mask like' face - Resting tremor - Rigidity - Cogwheeling - Bradykinesia - Bradyphenia
Rating scales	Simpson-Angus EPS Rating Scale (appendix 3)
Prevalence	Approximately 20%. More common in: - Elderly females - Those with pre-existing neurological damage
Time taken to develop	Days to weeks after initiation or dose changes
Treatment	Depending on the clinical circumstances; - Consider cautious dose reduction of causative agent - If side effects persist, consider switching to an antipsychotic with lower propensity to cause parkinsonism (aripiprazole, quetiapine, olanzapine, clozapine) - Prescribing an anticholinergic, monitoring for side effects (dry mouth, constipation, urinary retention, cognitive impairment). Review use regularly. *Example agents: procyclidine 2.5mg three times daily, increased in steps of 2.5mg-5mg daily if required, up to maximum 30mg daily in 2-4 divided doses* [3] - After 3 months should be gradually withdrawn, to prevent cholinergic rebound, and restarted if symptoms reappear [5]

[1] Taylor, D. et al.The Maudsley Prescribing Guidelines in Psychiatry 12th Edition; 2015

[2] Taylor, D. et al. The Maudsley Practice Guidelines for Physical Health Conditions in Psychiatry. 2021.

[3] BNF

[4] Summary of Product Characteristics. Kemadrin 5mg/ml solution for injection. [Accessed 23/12/21] https://www.medicines.org.uk/emc/product/2336/smpc

[5] Psychotropic drug directory 2020/21. Stephen Bazire.

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Appendix 1- Barnes akathisia scale (BARS)

Instructions:
Patient should be observed while they are seated, and then standing while engaged in neutral conversation (for a minimum of two minutes in each position). Symptoms observed in other situations, for example while engaged in activity on the ward, may also be rated. Subsequently, the subjective phenomena should be elicited by direct questioning.

Objective
0 Normal, occasional fidgety movements of the limbs
1 Presence of characteristic restless movements: shuffling or tramping movements of the legs/feet, or swinging of one leg while sitting, *and/or* rocking from foot to foot or "walking on the spot" when standing, but movements present for less than half the time observed
2 Observed phenomena, as described in (1) above, which are present for at least half the observation period
3 Patient is constantly engaged in characteristic restless movements, *and/or* has the inability to remain seated or standing without walking or pacing, during the time observed

Subjective
Awareness of restlessness
0 Absence of inner restlessness
1 Non-specific sense of inner restlessness
2 The patient is aware of an inability to keep the legs still, or a desire to move the legs, *and/or* complains of inner restlessness aggravated specifically by being required to stand still
3 Awareness of intense compulsion to move most of the time *and/or* reports strong desire to walk or pace most of the time

Distress related to restlessness
0 No distress
1 Mild
2 Moderate
3 Severe

Global Clinical Assessment of Akathisia
0 *Absent.* No evidence of awareness of restlessness. Observation of characteristic movements of akathisia in the absence of a subjective report of inner restlessness or compulsive desire to move the legs should be classified as pseudoakathisia
1 *Questionable.* Non-specific inner tension and fidgety movements
2 *Mild akathisia.* Awareness of restlessness in the legs *and/or* inner restlessness worse when required to stand still. Fidgety movements present, but characteristic restless movements of akathisia not necessarily observed. Condition causes little or no distress.
3 *Moderate akathisia.* Awareness of restlessness as described for mild akathisia above, combined with characteristic restless movements such as rocking from foot to foot when standing. Patient finds the condition distressing
4 *Marked akathisia.* Subjective experience of restlessness includes a compulsive desire to walk or pace. However, the patient is able to remain seated for at least five minutes. The condition is obviously distressing.
5 *Severe akathisia.* The patient reports a strong compulsion to pace up and down most of the time. Unable to sit or lie down for more than a few minutes. Constant restlessness which is associated with intense distress and insomnia.

The Barnes Akathisia Rating Scale is scored as follows:
Objective Akathisia, Subjective Awareness of Restlessness and Subjective Distress Related to Restlessness are rated on a 4-point scale from 0 – 3 and are summed yielding a total score ranging from 0 to 9.
The Global Clinical Assessment of Akathisia uses a 5-point scale ranging from 0 – 4.

Appendix 2- Abnormal Involuntary Movement Scale (AIMS)

Instructions:

There are two parallel procedures, the examination procedure, which tells the patient what to do, and the scoring procedure, which tells the clinician how to rate what he or she observes.

Examination Procedure:

Either before or after completing the examination procedure, observe the patient unobtrusively at rest (e.g., in the waiting room).

The chair to be used in this examination should be a hard, firm one without arms.

1. Ask the patient whether there is anything in his or her mouth (such as gum or candy) and, if so, to remove it.

2. Ask about the 'current' condition of the patient's teeth. Ask if he or she wears dentures. Ask whether teeth or dentures bother the patient 'now'.

3. Ask whether the patient notices any movements in his or her mouth, face, hands, or feet. If yes, ask the patient to describe them and to indicate to what extent they 'currently' bother the patient or interfere with activities.

4. Have the patient sit in the chair with hands on knees, legs slightly apart, and feet flat on floor. (Look at the entire body for movements while the patient is in this position.)

5. Ask the patient to sit with hands hanging unsupported – if male, between his legs, if female and wearing a dress, hanging over her knees. (Observe hands and other body areas).

6. Ask the patient to open his or her mouth. (Observe the tongue at rest within the mouth.) Do this twice.

7. Ask the patient to protrude his or her tongue. (Observe abnormalities of tongue movement.) Do this twice.

8. Ask the patient to tap his or her thumb with each finger as rapidly as possible for 10 to 15 seconds, first with right hand, then with left hand. (Observe facial and leg movements.) [±activated]

9. Flex and extend the patient's left and right arms, one at a time.

10. Ask the patient to stand up. (Observe the patient in profile. Observe all body areas again, hips included.)

11. Ask the patient to extend both arms out in front, palms down. (Observe trunk, legs, and mouth.) [activated]

12. Have the patient walk a few paces, turn, and walk back to the chair. (Observe hands and gait.) Do this twice. [activated]

Scoring Procedure

Complete the examination procedure before making ratings.

According to the original AIMS instructions, one point is subtracted if movements are seen only on activation, but not all investigators follow that convention.

Items 1-9 are scored based on: None (0); Minimal (1); Mild (2); Moderate (3); Severe (4)	
Facial and oral movements	
1. Muscles of facial expression e.g. movements of forehead, eyebrows, periorbital area, cheeks. Include frowning, blinking, grimacing of upper face	1 2 3 4
2. Lips and perioral area e.g. puckering, pouting, smacking	1 2 3 4
3. Jaw e.g. biting, clenching, chewing, mouth opening, lateral movement	1 2 3 4
4. Tongue Rate only increase in movement both in and out of mouth, not inability to sustain movement	1 2 3 4
Extremity movements	
5. Upper (arms, wrists, hands, fingers) Include movements that are choreic (rapid, objectively purposeless, irregular, spontaneous) or athetoid (slow, irregular, complex, serpentine). Do not include tremor (repetitive, regular, rhythmic movements)	1 2 3 4
6. Lower (legs, knees, ankles, toes) e.g. lateral knee movement, foot tapping, heel dropping, foot squirming, inversion and eversion of foot	1 2 3 4
Trunk movements	
7. Neck, shoulders, hips e.g. rocking, twisting, squirming, pelvic gyrations. Include diaphragmatic movements	1 2 3 4
Global judgements	
8. Severity of abnormal movements. Based on the highest single score on the above items.	1 2 3 4
9. Incapacitation due to abnormal movements.	1 2 3 4
10. Patient's awareness of abnormal movements. No awareness (0); Aware, no distress (1); Aware, mild distress (2); Aware, moderate distress (3); Aware, severe distress (4)	1 2 3 4
Dental status	
Current problems with teeth and/or denture	Yes (1) No (0)
Does patient usually wear dentures?	Yes (1) No (0)

Appendix 3- Simpson-Angus scale

Scaling:

The Simpson Angus Scale is composed of 10 items investigating 5 domains.

Domains	Number of items	Cluster of items	Direction of domains
Gait	1	1	Higher score = Greater impact of Neuroleptic-induced parkinsonism
Rigidity	6	2-7	
Glabella tap	1	8	
Tremor	1	9	
Salivation	1	10	

Scoring of domains:

		Sources
Item scaling	5-point Likert Scale with 0 meaning complete absence of the condition, and 4 meaning presence of the condition in extreme form	Simpson GM and Angus JW (1970)[1]
Weighing of items	No	Simpson GM and Angus JW (1970)[1]
Range of scores	Global score ranging from 0 to 4.	Simpson GM and Angus JW (1970)[1]
Scoring procedure	Global score: Sum of item scores divided by 10	Simpson GM and Angus JW (1970)[1]
Interpretation and Analysis of missing data	NA- clinician rated	
Interpretation of multiple answers for one item	NA- clinician rated	
Interpretation of scores	Simpson GM and Angus JW considered scores up to 0.3 within the normal range. Janno S et al. found that the optimal SAS mean score cut-off value is higher than the commonly used 0.3 and suggested a new cut-off value of 0.65 for screening Neuroleptic-induced parkinsonism.	Simpson GM and Angus JW (1970)[1] And Janno S et al. (2005)[2]

[1]Simpson GM, Angus JW. A rating scale for extrapyramidal side effects. Acta Psychiatr Scand Suppl. 1970; 212:11-9

[2]Janno S, Holi MM, Tuisku K, Wahlbeck K. Validity of Simpson-Angus Scale (SAS) in a naturalistic schizophrenia population. BMC Neurol. 2005 Mar 17; 5(1):5

1. GAIT: The patient is examined as he walks into the examining room, his gait, the swing of his arms, his general posture, all form the basis for an overall score for this item. This is rated as follows:	
0 = Normal	☐
1 = Diminution in swing while the patient is walking	☐
2 = Marked diminution in swing with obvious rigidity in the arm	☐
3 = Stiff gait with arms held rigidly before the abdomen	☐
4 = Stooped shuffling gait with propulsion and retropulsion	☐

2. ARM DROPPING: The patient and the examiner both raise their arms to shoulder height and let them fall to their sides. In a normal subject a stout slap is heard as the arms hit the sides. In the patient with extreme Parkinson's syndrome the arms fall very slowly:	
0 = Normal, free fall with loud slap and rebound	☐
1 = Fall slowed slightly with less audible contact and little rebound	☐
2 = Fall slowed, no rebound	☐
3 = Marked slowing, no slap at all	☐
4 = Arms fall as though against resistance; as though through glue	☐

3. SHOULDER SHAKING:
The subject's arms are bent at a right angle at the elbow and are taken one at a time by the examiner who grasps one hand and also clasps the other around the patient's elbow. The subject's upper arm is pushed to and fro and the humerus is externally rotated. The degree of resistance from normal to extreme rigidity is scored as follows:

0 = Normal	☐
1 = Slight stiffness and resistance	☐
2 = Moderate stiffness and resistance	☐
3 = Marked rigidity with difficulty in passive movement	☐
4 = Extreme stiffness and rigidity with almost a frozen shoulder	☐

4. ELBOW RIGIDITY:
The elbow joints are separately bent at right angles and passively extended and flexed, with the subject's biceps observed and simultaneously palpated. The resistance to this procedure is rated. (The presence of cogwheel rigidity is noted separately.)

0 = Normal	☐
1 = Slight stiffness and resistance	☐
2 = Moderate stiffness and resistance	☐
3 = Marked rigidity with difficulty in passive movement	☐
4 = Extreme stiffness and rigidity with almost a frozen elbow	☐

5. FIXATION OF POSITION or Wrist Rigidity: The wrist is held in one hand and the fingers held by the examiner's other hand, with the wrist moved to extension, flexion and both ulner and radial deviation:	
0 = Normal	☐
1 = Slight stiffness and resistance	☐
2 = Moderate stiffness and resistance	☐
3 = Marked rigidity with difficulty in passive movement	☐
4 = Extreme stiffness and rigidity with almost a frozen wrist	☐

6. LEG PENDULOUSNESS: The patient sits on a table with his legs hanging down and swinging free. The ankle is grasped by the examiner and raised until the knee is partially extended. It is then allowed to fall. The resistance to falling and the lack of swinging form the basis for the score on this item:	
0 = The legs swing freely	☐
1 = Slight diminution in the swing of the legs	☐
2 = Moderate resistance to swing	☐
3 = Marked resistance and damping of swing	☐
4 = Complete absence of swing	☐

7. HEAD DROPPING: The patient lies on a well-padded examining table and his head is raised by the examiner's hand. The hand is then withdrawn and the head allowed to drop. In the normal subject the head will fall upon the table. The movement is delayed in extrapyramidal system disorder, and in extreme parkinsonism it is absent. The neck muscles are rigid and the head does not reach the examining table. Scoring is as follows:	
0 = The head falls completely with a good thump as it hits the table	☐
1 = Slight slowing in fall, mainly noted by lack of slap as head meets the table	☐
2 = Moderate slowing in the fall quite noticeable to the eye	☐
3 = Head falls stiffly and slowly	☐
4 = Head does not reach the examining table	☐

8. GLABELLA TAP: Subject is told to open his eyes wide and not to blink. The glabella region is tapped at a steady, rapid speed. The number of times patient blinks in succession is noted:	
0 = 0 - 5 blinks	☐
1 = 6 – 10 blinks	☐
2 = 11 – 15 blinks	☐
3 = 16 - 20 blinks	☐
4 = 21 and more blinks	☐

9. TREMOR: Patient is observed walking into examining room and is then reexamined for this item:	
0 = Normal	☐
1 = Mild finger tremor, obvious to sight and touch	☐
2 = Tremor of hand or arm occurring spasmodically	☐
3 = Persistent tremor of one or more limbs	☐
4 = Whole body tremor	☐

10. SALIVATION: Patient is observed while talking and then asked to open his mouth and elevate his tongue. The following ratings are given:	
0 = Normal	☐
1 = Excess salivation to the extent that pooling takes place if the mouth is open and the tongue raised.	☐
2 = When excess salivation is present and might occasionally result in difficulty in speaking	☐
3 = Speaking with difficulty because of excess salivation	☐
4 = Frank drooling	☐