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VIEWPOINT

Enriching Global Perspectives Through a Regional Lens: Recognition, Assessment, and Management of Tardive Dyskinesia in Southeast Asia

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INTRODUCTION

Tardive dyskinesia (TD) is a medication-induced movement disorder characterized by abnormal, involuntary movements of the face, trunk, limbs, and, occasionally, the respiratory system that lasts at least four weeks.[1,2] These movements may appear choreiform, athetoid, or semirhythmic.[1] TD typically develops after exposure to dopamine receptor blocking agents (DRBAs), most commonly antipsychotics and antiemetics such as metoclopramide.[1,3] Other medications, including tricyclic antidepressants, flunarizine, and cinnarizine, have also been associated with TD.[3-5]

Globally, the prevalence of TD among patients on antipsychotics is 25.3% and is higher with first-generation antipsychotics (30%) than with second-generation antipsychotics (20.7%).[6] In Southeast Asia (SEA),[7] TD prevalence data are obtained from single-center studies: Singapore (26.8%),[8] Malaysia (35.9%),[9] and the Philippines (20.3%).[10] In the United States, only about 10% of patients with irregular movements receive a TD diagnosis,[11] but there are no comparable data available from SEA.

Recognition of TD in patients on DRBAs is vital to ensure appropriate treatment, prevent sequelae, and address its psychosocial burden. TD can cause stigma, social isolation, behavioral challenges, and medication nonadherence, further impairing functioning and quality of life.[2,12-14]

The objective of this consensus study was to consolidate expert-derived best practices and recommendations on the recognition, screening, diagnosis, impact, and management of TD within the region. Information exchange among countries within a region can inspire cross-border collaborations and the adoption of best practices and innovations.

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MATERIALS & METHODS

The consensus development panel consisted of a chair, a co-chair, and eleven panel members from Indonesia (*n*=2), Singapore (*n*=3), Malaysia (*n*=3), and Thailand (*n*=3). All participants were licensed neurologists, neuropsychiatrists, or psychiatrists from their country of practice, with substantial experience in the diagnosis and evidence-based management of TD. Given that this study involved the collection of expert opinions among the authors/panel members through a structured rating system, institutional review board review was not needed.

The consensus development methodology (Supplementary Material 1, Supplementary Figures 1 and 2 in the online-only Data Supplement) in this study was based on the modified RAND Corporation/University of California–Los Angeles Appropriateness Method (RAND-UCLA), which incorporates both scientific evidence and clinical experience.[15] The consensus process involved 1) a structured literature review to aid decision-making by panelists; 2) the creation of clinical scenarios/statements on the recognition, screening, diagnosis, treatment, and impact of TD; 3) an online rating (9-point Likert scale, with 1–"strongly disagree" to 9–"strongly agree") of each clinical scenario/statement; 4) a face-to-face meeting to discuss the current landscape of TD in the region, review the results of the first round of rating, and revise the clinical scenarios/statements as appropriate; 5) an onsite second round of rating of revised clinical scenarios/statements; and 6) the conversion of clinical scenarios to consensus recommendations. In accordance with the RAND-UCLA methodology, the panel was instructed to rate the clinical scenarios/statements independently without consideration of costs to ensure that the rating focused solely on clinical appropriateness (Supplementary Material 2 in the online-only Data Supplement).[15,16]

The results of the discussion of the current landscape of TD in countries from SEA were synthesized and reported in this study, while ratings of the appropriateness of the clinical scenarios/statements were summarized using descriptive statistics (median and interquartile range).[16] A statement was considered in "disagreement" when one-third or more of the panelists rated it both in the lowest (1–3) and highest (7–9) points of the appropriateness scale.[16] In the absence of "disagreement," a rating with a median score of 7–9 was considered "appropriate" (benefits outweigh the risks), a median score of 4–6 was "equivocal/uncertain," and a median score of 1–3 was "not appropriate" (risks outweigh the benefits).[16]

RESULTS AND DISCUSSION

The current landscape of TD in SEA and the consensus recommendations are presented and discussed in this section. Table 1 describes the challenges and barriers in the recognition, assessment, and management of TD. Table 2 outlines the second round of ratings, while Table 3 lists the expert panel consensus recommendations.

Recognition, screening, and diagnosis of TD

Current landscape in SEA

The panel estimates that approximately 90% of TD cases are underrecognized in their respective countries. This finding is similar to that of a United States electronic health records study showing that only 10% of patients were diagnosed with TD, even though 90% of patients in the records had documented abnormal movements suggestive of TD.[11] In SEA, no formal studies have evaluated the diagnostic gap in TD.

The panel identified time constraints and high patient load as the causes of inadequate recognition and screening. Other factors cited by the panel included limited awareness and knowledge of TD, prioritization of psychopathology over TD symptoms, and medicolegal concerns related to this treatment-related adverse effect. Failing to inquire about TD during patient consultations further contributes to the lack of awareness and understanding. Limited access to effective treatment can also discourage recognition of TD, as mentioned by the panel during the discussion.

Most patients have limited awareness of TD symptoms, with studies reporting that only half to two-thirds of patients recognize these symptoms.[17-19] When the panel rated the statement, "*Patients are aware of their TD symptoms*," it was assessed as "disagreement" (Table 2, statement 23; median: 6; interquartile range: 3–7). In cases where awareness is present, embarrassment can limit consultation despite the impact of TD on quality of life.[20] Indifference may result from the pathology for which antipsychotics were prescribed (negative/positive symptoms, sensory agnosia, or anosognosia).[21] Patients' limited understanding of the origins and consequences of TD, fluctuating symptoms (i.e., the waxing and waning nature of TD), and severity also influence reporting.[22] Experiences in the region align with global perspectives, where treatment seeking is shaped by psychiatric illness.[21]

Consensus recommendations on the recognition and screening of TD

The panel recommends continuing medical education for psychiatrists on the recognition, screening, diagnosis, and man-

Table 1. Challenges and barriers in the clinical recognition, assessment, and management of TD

	Challenges and barriers
Recognition and screening	i) Prioritization: Time-constraint/high patient load • Busy clinical settings with limited time to assess patients - Prioritization of psychoeducation and focusing on suicidal ideations shifts attention away from TD screening - Inability to accommodate a complete examination • Patient reliability/Caregiver role in diagnosis - May not always be reliable due to lack of awareness and inability to detect/recognize the problem ii) Knowledge and skills deficit • Lack of familiarity in neurological assessment and tools (e.g., AIMS) - May lead to low confidence and anxiety in practice, especially among graduate students iii) Under-recognized and under-reported • Timing/Phase of illness - During the acute phase of illness, tackling psychosis and disorganized behavior takes precedence over dyskinesia screening • Medicolegal issues - Treatment-emergent adverse effects such as TD may pose legal concerns, especially when symptoms are reported (e.g., in the self-rated questionnaire) and not properly or promptly addressed
Assessment and diagnosis	• Identification and differentiation of movement disorders based on phenomenology - e.g., TD, akathisia, dystonia • Use of proper nomenclature within the specialists' community • Uniformity in methods/criteria used • Access to specialists, i.e., neurologists, movement disorder specialists - For evaluation of TD among psychiatric patients

TD, tardive dyskinesia; AIMS, Abnormal Involuntary Movements Scale.

agement of TD. Similarly, training and involving allied health care professionals in screening for TD is recommended. Nurses in particular can play a role; their ratings in TD screening studies were not significantly different from those of specialists.[23,24]

The screening should include interviews and examinations every 6 months, which are consistent with American Psychiatric Association guidelines.[25] Patients and caregivers should also receive educational materials and access to patient- or caregiver-rated screening tools.

Consensus recommendations for TD diagnosis

The diagnosis of TD should include the use of scales, such as the Schooler–Kane Abnormal Involuntary Movements Scale (AIMS) and the Diagnostic Statistical Manual of Mental Disorders. Clinicians should consider differential diagnoses, use precise nomenclature, involve neurologists in complex cases, and consider telehealth for some patients with TD.

If TD is suspected, the severity, distribution, and phenomenology should be documented using the AIMS or other scales. Laboratory investigations and neurologic consultation should be performed when necessary.[12] Alignment between psychiatrists and movement disorder specialists is vital to ensure consistency in terms of terminology and approach.[22] The term "extrapyramidal symptoms", or EPS, is discouraged because it contributes to the continued misguided and incorrect use of therapies. It is a term that does not differ by presentation, phenomenology, pathophysiology, or treatment, as it lumps together a range of distinct movement disorders.[26]

Telehealth may support diagnosis but cannot replace in-person visits. Limitations include poor connection, poor camera placement, and reduced neurological examination capacity.[22] Virtual assessment of TD may be enhanced by creating standardized instruction or guidance documents for clinicians and patients or caregivers, which may include camera and environment set-up, among others, to enhance reliable remote assessments.

Management of TD

Current landscape in SEA

The management of TD symptoms aims to reduce disability and improve quality of life.[27,28] Reported practices by the panel include modification of DRBA treatment (dose reduction, discontinuation, and switching medications); augmentation with anticholinergics, benzodiazepines, vesicular monoamine transporter 2 (VMAT-2) inhibitors, vitamin B6, or vitamin E; referrals to neurologists or neuropsychiatrists; use of sulfas or atropine; or no treatment (Supplementary Table 1 in the online-only Data Supplement).

Table 2. Rating of clinical scenarios or statements

Indications	Ratings	Median (IQR)
Recognition and screening of TD		
Based on your opinion or experience, the following patients taking antipsychotics should be screened for TD.		
1. All patients taking antipsychotics should be screened for TD.	Appropriate	9 (9,9)
2. All patients who have received antipsychotics at any point in time should be screened for TD.	Appropriate	9 (8,9)
3. All patients taking antipsychotics should be screened for TD regardless of the risk.	Appropriate	8 (8,9)
In a busy clinical practice, the following should be prioritized when screening for TD:		
4. … effect on quality of life and functioning	Appropriate	9 (8,9)
5. … symptom severity	Appropriate	9 (9,9)
6. … ocular inspection of abnormal movements during mental status examination	Appropriate	9 (9,9)
7. … patient recognition or report of abnormal movements, which affects function and quality of life of the patient	Appropriate	9 (8,9)
8. … caregiver recognition or report of abnormal movements, which affects function and quality of life of the patient	Appropriate	9 (8,9)
9. … body parts affected	Appropriate	8 (8,9)
Frequency of TD screening		
10. Screening of TD with standardized tools should be performed every 6 months.	Appropriate	9 (9,9)
11. Screening of TD using visual examination as part of routine should be performed every clinical consultation.	Appropriate	9 (8,9)
Diagnosis of TD		
When diagnosing TD, the following factors should be considered:		
12. ... differential diagnosis from disorders with abnormal movements	Appropriate	9 (8,9)
13. ... involuntary and abnormal movements that emerges during use of antipsychotics or within 4 to 8 weeks of antipsychotic withdrawal	Appropriate	9 (9,9)
14. ... duration of exposure to antipsychotic medication	Appropriate	9 (9,9)
15. ... severity of abnormal movements in affected areas	Appropriate	9 (8,9)
16. ... number of areas with involuntary movements	Appropriate	8 (8,9)
17. ... duration of abnormal movements	Appropriate	8 (8,9)
18. ... patient or caregiver report on abnormal movements affecting function or quality of life	Appropriate	8 (8,9)
Role of neurologist in ideal situations		
19. In ideal situations, neurologists should confirm the diagnosis of TD and rule out other problems.	Appropriate	8 (8,9)
20. In ideal situations, neurologists should be involved in treatment of difficult to treat and/or complex TD.	Appropriate	9 (8,9)
Diagnosis/assessment of TD during a remote/online consultation		
21. Diagnosing TD could be done during a remote/ online consultation if face-to-face diagnosis is not possible.	Appropriate	8 (7,9)
22. Assessment for TD could be done during a remote/ online consultation.	Appropriate	8 (8,9)
Impact of TD on patients		
Patients' awareness of TD symptoms		
23. Patients with TD are aware of their TD symptoms.	Disagreement	6 (3,7)
Management of TD		
Importance of managing TD		
24. Managing TD is important in clinical practice.	Appropriate	9 (9,9)
The following are relevant when deciding on the management approach for patients with TD:		
25. … involuntary, abnormal movements, which occurs during treatment with antipsychotics or within four to eight weeks of withdrawal from the antipsychotics	Appropriate	9 (9,9)
26. ... patient or caregiver report on abnormal movements affecting function or quality of life	Appropriate	9 (8,9)
27. ... daily function	Appropriate	9 (9,9)
28. ... severity of abnormal movements in affected areas	Appropriate	9 (8,9)
29. ... duration of abnormal movements	Appropriate	9 (8,9)
30.... duration of exposure to antipsychotic medication	Appropriate	8 (8,9)
31. ... number of areas with involuntary movements	Appropriate	8 (8,8)

Table 2. Rating of clinical scenarios or statements (continued)

Indications	Ratings	Median (IQR)
VMAT-2 inhibitors for TD, as part of an overall integrated, pharmacologic management, should be used …		
32. ... as first-line treatment if available	Appropriate	9 (8,9)
33. … after determining the response to antipsychotic modification	Appropriate	9 (8,9)
34. … before determining the response to antipsychotic modification	Appropriate	8 (6,8)
35. … during the same time of antipsychotic switch	Appropriate	7 (7,8)
36. … during the same time of antipsychotic dose reduction	Appropriate	7 (6,8)
37. … during the same time of antipsychotic dose increase	Disagreement	6 (1,7)
38. … after determining the response to anticholinergic discontinuation	Appropriate	8 (7,9)
39. … before determining the response to anticholinergic discontinuation	Equivocal	5 (3,7)
40. … during the same time of anticholinergic discontinuation	Disagreement	7 (2,8)

TD, tardive dyskinesia; VMAT-2, vesicular monoamine transporter 2; IQR, interquartile range.

Most approaches to managing TD in SEA align closely with the suggestions found in the global literature. In practice, it is common to consider switching from typical to atypical agents or discontinuing DRBA treatment, particularly for nonpsychotic patients who can safely undergo tapering of medications.[12] However, the evidence of benefits is limited, and discontinuation can initially worsen TD by unmasking symptoms.[29] Similar to the recommendations reported in the literature, benzodiazepines are also utilized.[28]

Nevertheless, patients with TD may remain untreated regardless of severity. Anticholinergics continue to be used despite the potential to worsen symptoms.[26] Although supported by limited evidence, *Ginkgo biloba* and amantadine were not reported.[28] Chemodenervation with botulinum toxin and pallidal deep brain stimulation, used for intractable TD,[12,30] were also not cited. Sulfas and atropine, mentioned in practice, are not supported in the literature.

The panel identified barriers to management that mirror those in recognition and diagnosis, including the absence of guidance in psychiatric care pathways, limited awareness or access to effective treatments, and medicolegal issues.

Within three weeks, vitamin B6 (pyridoxine) may alleviate akathisia and TD by acting as a cofactor to dopamine carboxylase.[31] The use of VMAT-2 inhibitors, which act on presynaptic monoamine transporters, is supported by a number of high-quality evidence studies.[25,30,32] Tetrabenazine, the first VMAT-2 inhibitor used for off-label treatment for TD, was limited by a short half-life and adverse effects (akathisia, somnolence, depression, and suicidality).[33] Newer agents, such as deutetrabenazine and valbenazine, have been developed to address these issues.[34] Valbenazine is approved in Indonesia, Malaysia, Singapore, and Thailand.[35] Both are supported by Level A evidence in the updated evidence-based guideline of the American Academy of Neurology on the treatment of tardive syndromes[30,36] and are recommended by the American Psychiatry Association for TD regardless of severity.[25]

Consensus recommendations on the management of TD

The panel recommends switching from first-generation antipsychotics. Utilizing antipsychotic dose equivalents may be helpful to clinicians when switching between antipsychotics. A comprehensive list of antipsychotic dose equivalents was presented in a publication by Leucht et al.[37] in 2016, which was followed by an online dose calculator cited in a 2020 publication by Leucht et al.[38] Vitamin B6 may be helpful in patients with mild-to-moderate TD based on a randomized controlled trial.[31] Concomitant use of anticholinergic agents and antipsychotics should be avoided. Where available, VMAT-2 inhibitors are recommended as part of overall integrated pharmacologic management as a first-line treatment. Policy-makers in the region may consider the cost of newer technologies when developing policy recommendations on reimbursement, pricing negotiations, and formulary inclusion. Future studies on patient and caregiver preferences and challenges may improve educational materials, screening tools, and the delivery of appropriate management strategies.

LIMITATIONS

The expert panel included participants from only four SEA countries, which may limit the generalizability of the findings to the other seven countries in the region. However, the treatment options are broadly similar across countries, except for the availability and regulatory approval of newer treatment options. As such, the expert panel was selected from countries that have experience in using VMAT-2 inhibitors to manage TD, enabling them to potentially provide insights to other countries in the region. Furthermore, this consensus development study may be updated in the future to include most SEA countries once

Table 3. Recommendations on recognition and screening, assessment and diagnosis, and management of TD

	Recommendations
TD recognition and screening	i) Clinician education and training/ re-training • Training on screening for all clinicians, including general practitioners, and allied health professionals. ▪ Include allied health care professionals. Experienced and trained nurses and pharmacists are or can be capable in identifying physical and mental symptoms. • Continuing medical education and workshops on recognition, awareness, diagnosis and management for specialists. ii) Patient and caregiver education • Accessible educational materials for patients and/or caregivers in the clinic, e.g. pamphlets, videos to take home • Patient/Caregiver-rated screening tools that are brief and easy to use iii) In the waiting room: • A patient self-rated questionnaire may be provided in the waiting room. • A clinic assistant can do a simple screening prior to consultation. • Increase general awareness to, e.g., educational poster in the clinic. iv) During consultation • Interview: ▪ Ask the caregiver/relative and patient to report any involuntary movements. ▪ Include patients in decision-making, particularly when stable and able to provide reliable information. Patient reports of TD symptoms may be reliable if they are well-informed about their condition. They may not be as underinformed as perceived. • Clinical examination: ▪ Relying on observations during the psychiatric interview may lead to overlooked symptoms (e.g., facial twitching, fasciculations, tardive movements). Dedicate time focused on keen observation of presence of abnormal movements. ▪ Two-tiered approach: - Step 1: Visual inspection of the patient upon entering the room and throughout the patient course of the interview. - Step 2: Perform a full AIMS assessment if there are abnormal movements detected (Note: will only take 2–3 minutes with training). ▪ Doing a “mini-AIMS” orofacial examination only takes 30 seconds if a full AIMS assessment is not feasible. Four out of the 12 AIMS items useful in a quick assessment of facial and oral movements/dyskinesia. v) Frequency of evaluation • Visual screening (clinical observation) must be done in every clinical consultation. • All patients on antipsychotic medications are recommended to be routinely screened for TD every 6 months. While 3 months may be ideal especially with patients on FGAs, most experts agreed that AIMS at 6 month-intervals is more feasible due to limited consultation time.
TD assessment and diagnosis	i) Awareness of risk of TD among patients with exposure to antipsychotics • Assess involuntary abnormal movements which may occur during treatment or within 4–8 weeks of withdrawal from antipsychotics. ii) Identification and differentiation of movement disorders • Consider the other differentials of TD assessment. • Observe the phenomenology of the movement disorder. • Note that movement disorders may not always appear in isolation. • Evaluate not only hyperkinesia and dyskinesia but also hypokinesia such as drug-induced parkinsonism (including decrease in arm swing). iii) Use of proper nomenclature and reporting • Avoid using the term “EPS” due to the lack of a formal definition which may lead to confusion. • Define movement disorder phenomenologically. • Note the duration of exposure to antipsychotic medication, duration of presence of abnormal movements; severity of these movements in affected areas; number of bodily regions affected; and any patient or caregiver report regarding their impact on patient’s functioning and quality of life. iv) Uniformity in methods / criteria in diagnosis • When possible, use the same methods/criteria recommended for movement disorders. • Schooler–Kane AIMS Criteria plays a greater role in diagnosis than in screening. v) Role of neurologists and movement disorder specialists • Involve neurologists in difficult-to-treat or complex TD. vi) Telemedicine • Telemedicine or remote online consultation is not a substitute for face-to-face evaluation and should only be used if the latter is not possible. While remote assessment is limited, a limited assessment is better than no assessment at all.

Table 3. Recommendations on recognition and screening, assessment and diagnosis, and management of TD (continued)

	Recommendations
Treatment	*Recommendations for General Management of TD*
	• If possible, switch out of first-generation antipsychotics.
	• Vitamin B6 (pyridoxine) may be helpful in patients with mild-to-moderate TD.
	• Avoid concomitant use of anticholinergic agents and antipsychotics.
	• Use VMAT-2 inhibitors when available.
	- After determining response to anticholinergic discontinuation
	- Regardless of timing of antipsychotic modification
	Recommendations for Clinical Indication of VMAT-2 Inhibitors
	• Clinical Presentation
	- Illness Severity: moderate to severe*
	- Impairment in functioning
	- Decrease in quality of life due to TD symptoms
	• Other factors
	- Patient and family preferences

*including the elderly population.
TD, tardive dyskinesia; AIMS, Abnormal Involuntary Movements Scale; FGAs, first generation antipsychotics; EPS, extrapyramidal symptoms; VMAT-2, vesicular monoamine transporter 2.

treatment options for TD with higher levels of evidence become available.

CONCLUSIONS

A comprehensive understanding of global perspectives on TD undoubtedly influences local or regional practice. Regional studies aim to provide relevant and applicable guidance to populations with similar characteristics among patients. This consensus enhances the knowledge that can improve local health care practices, particularly with the availability of first-line TD treatments in the region. With global health equity in mind, international exchanges can inspire cross-border partnerships, encourage the adoption of best practices, and promote innovations and reforms in health care.

Ethics Statement

Not applicable

Supplementary Materials

The Data Supplement is available with this article at https://doi.org/10.14802/jmd.25146.

Conflicts of Interest

The authors have no financial conflicts of interest.

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