Rapid tranquilization experiences of Turkish psychiatrists: A preliminary online survey

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SUMMARY

Objective: In this study, we aimed to determine the clinical experiences and preferences of Turkish psychiatrists regarding rapid tranquilization of acutely agitated individuals and to evaluate the variables affecting these approaches.

Method: A cross-sectional online survey was conducted between November 2019 and March 2020. The survey link was mailed to a sample of 131 Turkish psychiatrists. A significant proportion of the study sample worked in academic institutions like universities. The questionnaire consisted of mostly single-choice questions about rapid tranquilization, the use of zuclopenthixol acetate, and experiences with intravenous haloperidol.

Results: Only 34.4% of the clinicians adhered to a guideline and almost half of the clinicians did not follow up with the patients after the rapid tranquilization. Intramuscular drug administration was preferred to a greater extent, and haloperidol was the most preferred first-line agent. Simultaneous anticholinergic administration was an almost established practice. The most preferred use of zuclopenthixol acetate was sedation whereas intravenous haloperidol was applied most frequently for delirium.

Discussion: In Turkey, mental health resources are still limited. Moreover, some pharmacological agents or different administration forms are not available. These difficulties seem to increase improper use of rapid tranquilization approaches. A national consensus text is needed and clinicians should be invited to periodic courses. Since the study's sample tends to be clustered in certain institutions, the findings should be evaluated with caution refraining from overgeneralization.

Key Words: Agitation, intravenous haloperidol, rapid tranquilization, sedation, zuclopenthixol acetate

INTRODUCTION

Agitation consists of abnormal, excessively verbal, and physically aggressive or repetitive and purposeless motor behaviors such as rhythm with feet, pulling hair, and rubbing hands that require intervention (1,2). It is characterized by increased arousal and significant impairment in functionality (1). Agitation can be seen in many psychiatric diseases, especially in schizophrenia and other psychotic disorders (3). For the intervention in case of agitation, primarily verbal de-escalation techniques and environmental regulations are recommended, but sometimes physical restraint or seclusion are also used (4). Studies have shown that patients are exposed to traumatic experiences associated with seclusion and restraint, they feel humiliated and lonely, and the most frequently associated theme is staff violence against them (5,6). On the other hand, agitation endangers the person's own or others' safety and hinders medical care. Different studies have shown that agitated patients exhibit significant physical or verbal aggressive behaviors towards healthcare professionals (7,8).

In some countries, seclusion and restraint have been prohibited or policies have been developed to reduce such practices (9). In a follow-up study conducted in nine centers for eleven years in line with policies aimed at reducing coercive interventions, a decrease was observed in the rates and duration of restraint and seclusion, while no increased risk was

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found in terms of violence against staff (10). Studies have shown that with increasing involuntary pharmacological treatments, restraint and seclusion are reduced (11, 12). When appropriate psychological and behavioral approaches fail to reduce agitated behaviors, the use of pharmacological agents through various routes of administration is referred to as rapid tranquilization (13). Benzodiazepines and typical, and atypical antipsychotics are frequently used in rapid tranquilization. No superiority was found between antipsychotics and benzodiazepines in studies. There is also no difference in terms of different antipsychotics when applied in equivalent doses and in the same route (14).

Various guidelines were prepared to ensure certain standards, taking into account the effectiveness, side effects, and post-application follow-up of the drugs used in rapid tranquilization. In England, the National Institute of Health and Clinical Excellence (NICE) recommends the administration of oral preparations first and lorazepam as the first choice (15). On the other hand, the Canadian Psychiatric Association (CPA) recommends oral second-generation antipsychotics as a priority, and an intramuscular haloperidol-lorazepam combination will be used in patients who refuse to take oral medications (16). Similar to CPA, the American Psychiatric Association (APA) also recommends second-generation antipsychotics as first-line but also recommends haloperidol as a first-line agent (17). In Turkey, the Psychiatric Association of Turkey (PAT) stated a series of pharmacological recommendations focused on the underlying etiology in its publications (18). Guidelines cannot always be adapted to clinical practice, many factors are effective in this situation. In a study conducted in Belgium, only 26.9% of clinicians followed the guidelines (19). In another study, 25% of the participants stated that no guidelines were used in their institutions. The rate of adherence to the guidelines did not reach even 50% in total (20). The practice of rapid tranquilization also differs between countries. In countries such as the USA and England, the goal of rapid tranquilization is to calm, while in resource-limited countries such as Brazil, it is ideal to sedate (21).

In this study, we aimed to determine the clinical experiences and preferences of psychiatrists in Turkey regarding rapid tranquilization of acute agitated cases and to evaluate the variables affecting these management approaches.

METHODS

A cross-sectional online survey created using Google Forms© was conducted between November 2019 and March 2020. The survey link was mailed to the "Google Psikiyatri" Gmail group where a sample of 1496 psychiatrists is present within the mailing list. The mailing list aims to provide information sharing and to help each other on certain issues among psychiatrists in Turkey. To improve the participation rate, the survey link was shared once a month via the mail list. At the beginning of the survey, a consent form and checkbox accepted as valid by the Ethical Committee of Gazi University are included. Participants who were informed about the study and gave informed consent were invited to fill in the questionnaire. A total of 143 survey forms were received as filled and 131 participants who fully completed the questionnaire constituted the sample of the study.

A semi-structured online questionnaire consisting of four sections was designed by the researchers. The responses were mostly single-choice, and in some questions, more than one option could be chosen. A limited number of open-ended responses were also included. In order to ensure content validity and ease of expression, the questionnaire was first evaluated by three senior psychiatrists, necessary corrections were made, and then the survey was sent to the mailing list. Participants were asked to give demographic and professional information in the first section. In the study, no special information was requested from the participants that would violate anonymity, and action was taken within the scope of the Personal Data Protection Law.

In the second section, questions about rapid tranquilization experiences of clinicians were included. The administration of drugs using oral, parenteral or other routes of administration to calm patients with acute agitation was defined as rapid tranquilization. In this section, information about rapid

tranquilization indications, preferred drug administration routes and factors affecting this preference, post-administration vital monitoring frequency and measured vital parameters, and the number of rapid tranquilization cases in the last one month were collected. Moreover, clinicians were asked questions about whether they followed any rapid tranquilization guidelines, which guidelines they followed, and if not, the reasons why. In addition, clinicians were asked about the first and second-line agents they preferred for rapid tranquilization by different administration routes and also simultaneous anticholinergic use.

The following two sections had questions about the use of intramuscular zuclopenthixol acetate (ZA) and intravenous haloperidol (IVH) experiences of participants. In the section on intramuscular ZA, clinicians were asked about their purpose and frequency of ZA use, possible contraindications, and concurrent use with other rapid tranquilization agents. In the next section, there were questions about the indications for use of IVH, the average dose and method of administration, and the vital and laboratory parameters followed.

Ethical approval of this study was granted by the Ethical Committee of Gazi University 04.11.2019 with the number 2019-353. This study is in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the World Medical Association (WMA) Declaration of Helsinki – Ethical Principles For Medical Research Involving Human Subjects revised in 2013.

Statistical analysis was performed using SPSS 22.0 for Windows (SPSS, Inc.; Chicago, USA) package program. Descriptive values are stated as number (n), percentage (%), mean and standard deviation (SD).

RESULTS

A hundred and thirty-one completed questionnaires were returned (9,5% response rate). Participants were predominantly under the age of 40 (84.7%) and more than half were women (62.6%). 41.2% of the participants were in the first five years of their professional experience. Psychiatry specialists and residents were mostly involved in the study. 6.1% of the participants were associate professors and 4.6% were professors. The sociodemographic characteristics of the participants are provided in Table 1.

Table 1: Sociodemographic Characteristics of the Participants

	N	%
Age (years)		
20-30	48	36.6
30-40	63	48.1
40-50	12	9.2
50 >	8	6.1
Gender		
Female	82	62.6
Male	49	37.4
Professional Experience Period (years)		
5<	54	41.2
5-10	44	33.6
10-20	23	17.5
20>	10	7.6
Academic Degree		
Psychiatry Resident	57	43.5
Psychiatrist	60	45.8
Associate Professor	8	6.1
Professor	6	4.6
Institution		
State Hospital	21	16
Mental Health Hospital	11	8.4
University Hospital	44	33.6
Training and Research Hospital	40	30.5
Private Hospital	4	3.1
City Hospital	9	6.9
Private Clinic	2	1.5

It has been reported that rapid tranquilization is most commonly used in cases of self-harm (98.5%), physical aggression (95.4%) and damage to property (93.1%). 34.4% of the clinicians stated that they followed a guideline for rapid tranquilization, and PAT guideline was the most frequently followed one. The remaining clinicians did not follow any guidelines and cited unawareness of the guidelines as the most common reason (30.5%). Clinicians stated that they preferred intramuscular drug administration more frequently (58.8%). The most common factors affecting drug administration routes were reported as the severity of agitation (95.4%) and previous clinical experiences (63.4%). 80.9% of the clinicians stated that anticholinergic drugs were administered simultaneously during intramuscular drug administration. In patients who were administered rapid tranquilization, the most common monitored vital signs were pulse rate (75.6%) and blood pressure (69.5%). Most of the participants stated that vital monitoring was performed at least once in the first hour. 29% of the clinicians stated that they inspected the patient every 15 minutes, and 16.8% every 30 minutes after

Table 2: Rapid Tranquilization Experiences of Psychiatrists

	N	%
Rapid tranquilization indications		
Physical aggression	125	95.4
Verbal aggression	70	53.4
Damage to property	122	93.1
Harm oneself	129	98.5
Drug rejection	66	50.4
Difficulty falling asleep	9	6.9
Risk of escape	71	54.2
Staff shortage	13	9.9
Following a guideline	45	34.4
Followed guidelines		
APA guidelines	25	19.1
CPA guidelines	4	3.1
NICE guidelines	20	15.3
RANZCP guidelines	1	0.8
AAEP guidelines	4	3.1
PAT guidelines	29	22.1
Reasons for not following any guidelines		
Lack of awareness	40	30.5
Lack of common agreement	11	8.4
Guidelines not functional	9	6.9
Clinical experiences are sufficient	33	25.2
Preference for drug administration route		
Oral	54	41.2
Intramuscular	77	58.8
Reasons for preferring the drug administration route		
Patient preference	51	39
Patient s family preference	5	3.8
Severity of agitation	125	95.4
Presence of comorbidity	37	28.2
Presence of drug abuse	20	15.3
Lack of some drugs	45	34.4
Having too many patients	16	12.2
Limited time	50	38.2
Probability of side effects	57	43.5
Patient s age	40	30.5
Previous clinical experiences	83	63.4
Simultaneous anticholinergic administration	106	80.9
Vital monitoring		
Pulse rate	99	75.6
Blood pressure	91	69.5
Temperature	64	48.9
Respiratory rate	58	44.3
Oxygen saturation	32	24.5
Peripheral circulation findings	61	46.6
Frequency of vital monitoring		
Every 5 minutes	3	2.3
Every 15 minutes	46	35.1
Every half hour	31	23.7
Every one hour	22	16.8
Every two hours	4	3.1
No vital monitoring	23	17.6
Duration variable depending on medical conditions	1	0.8
Physician follow-up		
Every 15 minutes	38	29
Every 30 minutes	22	16.8
Every one hour	13	9.9
Every two hours	4	3.1
Not follow-up	2	1.5
No time for follow-up	8	6.1
Follow-up is done by the nurse	44	33.6
Number of RT events in the last 1 month		
10>	69	52.7
10≤	8	6.1

AAEP: American Association for Emergency Psychiatry, APA: American Psychiatric Association, CPA: Canadian Psychiatric Association, NICE: National Institute of Health and Clinical Excellence, RANZCP: Royal Australian and New Zealand College of Psychiatrists, RT: Rapid Tranquilization, PAT: Psychiatric Association of Turkey

rapid tranquilization. On the other hand, 41.2% of the psychiatrists stated that no follow-up was made by the clinician for different reasons. Other parameters on practices of clinicians for rapid tranquilization are shown in Table 2.

Lorazepam was the first-line oral agent, followed by olanzapine, quetiapine, and clonazepam for rapid tranquilization (Figure 1). For intramuscular administration, clinicians most frequently preferred haloperidol followed by chlorpromazine. There was no change in the preference of clinicians in terms of second-line agents (Figure 2). Intravenous administration was not specified as the first choice and was preferred as the second line, diazepam was most frequently preferred (5.3%).

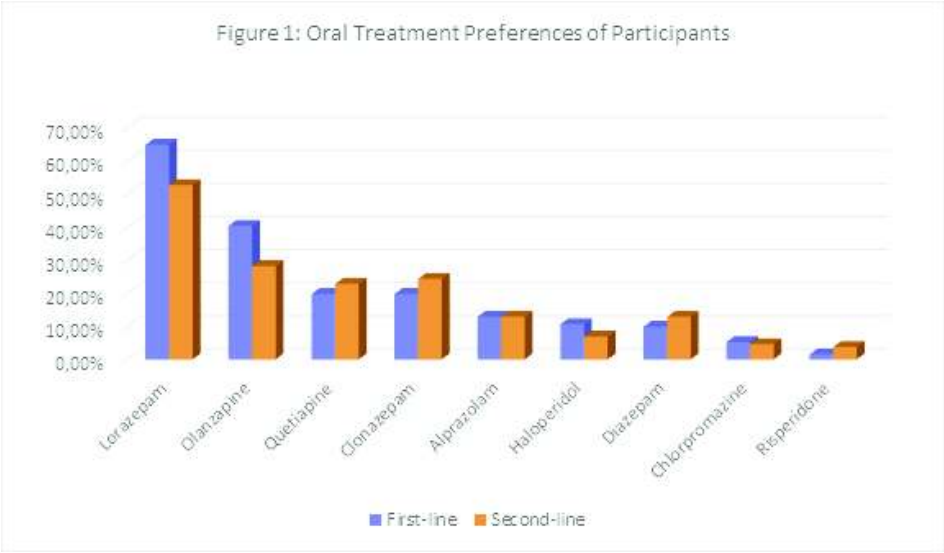
ZA was most commonly preferred for sedation (65.6%), followed by rapid tranquilization (63.4%). Furthermore, 30.5% of clinicians stated that they also used ZA for evaluating tolerance to long-action injectable form. Some clinicians (19.1%) reported that they used other intramuscular drugs simultaneously with ZA. ZA was mostly preferred as an administration for 72 hours. Other findings are shown in Table 3.

More than half of the participants (52.7%) stated that they had at least one experience administering IVH. It was most commonly preferred for delirium (42.7%) and most clinicians reported using haloperidol in the 5-10 mg dose range. The intravenous 30-minutes infusion was preferred most commonly by clinicians (22.1%). Other findings related to the IVH experiences of participants are shown in Table 4.

DISCUSSION

The main findings of this study are that almost half of the clinicians did not follow up with the patients after the rapid tranquilization, adherence to the rapid tranquilization guidelines was low, the intramuscular drug administration was preferred more and the simultaneous anticholinergic drug use was an almost established practice.

A significant proportion of the psychiatrists inclu-



ded in the study were under the age of 40 and most of them worked in universities or training and research hospitals. Therefore, the present results more often reflect the common practice of academic institutions. It is expected that in these institutions responsible for psychiatry residency training, medical practices will be more evidence-based and these institutions are more open to innovations in the field of psychiatry (22). However, on the other hand, these results may not fully reflect the existing practices in mental health hospitals with larger bed capacities, where more chronic and severe patients are treated. In a study conducted at Bakırköy Mental Health Hospital, which has the largest bed capacity in Turkey, physical restraint was applied to 311 acute agitation cases within one month (23). In a 3-month study that included only two wards in the same hospital, physical restraint was used in a total of 174 cases (24). Indeed, it is supported by the fact that only 52.7% of clinicians reported more than ten rapid tranquilization cases in the last month.

Clinicians frequently stated that they apply rapid tranquilization in patients with indications of self-harm, physical aggression, and damage to property. These indications were also frequently emphasized in various previous studies (25, 26). However, 54.2% of the participants stated that they administered rapid tranquilization at the risk of escape. In a study conducted in acute psychosis wards over one month in Turkey, 32.2% of the reasons for physical restraint were caused by the ward environments, and in 18.6% of these cases, there was an attempt to leave the ward without permission (23). In Turkey, resources are still limited compared to many countries and there is a serious lack of staff in health care (27). In fact, 9.9% of the participants stated that they applied to rapid tranquilization due to lack of staff. Furthermore, there is no mental

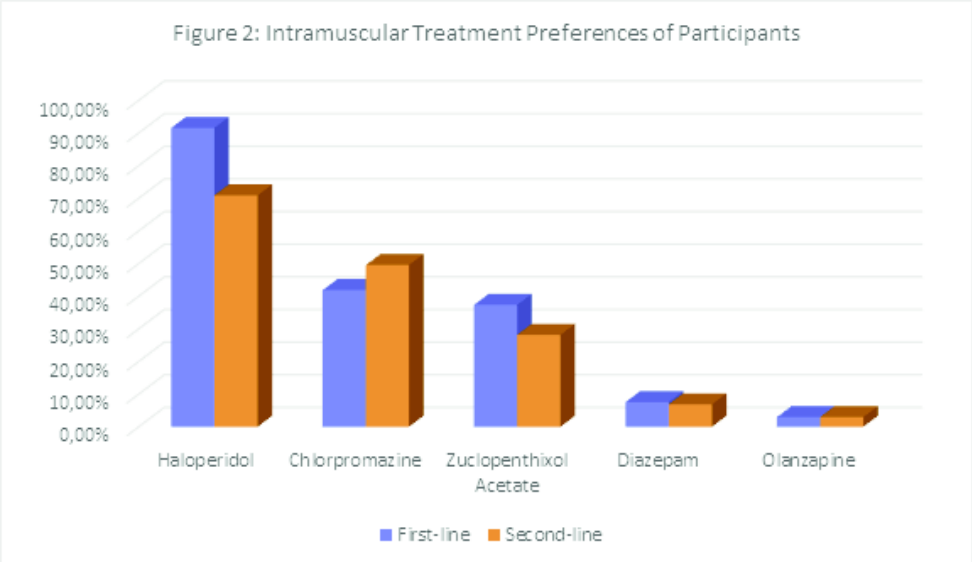


Table 3: Zuclopenthixol Acetate Experiences of Psychiatrists

	N	%
Use of zuclopenthixol acetate	128	97.7
Purposes of zuclopenthixol acetate use		
Sedation	86	65.6
Rapid tranquilization	83	63.4
Maintaining antipsychotic therapy	29	22.1
Evaluating tolerance in zuclopenthixol decanoate	40	30.5
Need for repeated tranquilization procedure	35	26.8
Increasing antipsychotic efficacy	51	38.9
Failure of rapid tranquilization	2	1.6
Long-distance patient transfer	1	0.8
Concurrent use with tranquilizing agents	25	19.1
Frequency of use		
Every 12 hours	3	2.3
Every 24 hours	15	11.5
Every 36 hours	5	3.8
Every 48 hours	26	19.8
Every 72 hours	74	56.5
Contraindications		
If taking oral medication	35	26.7
Antipsychotic-naive patient	42	32.1
Extrapyramidal symptoms prone patient	77	58.8
Confusion	84	64.1
Pregnancy and lactation	83	63.4
Liver and kidney impairment	61	46.6
Presence of cardiac disease	46	35.1
Old patient	47	35.9
Clozapine use	9	6.9
Typical antipsychotic use	9	6.9

health law and there are difficulties in compulsory treatment practices (28). There are also different opinions among the healthcare professionals who personally carry out physical restraint regarding the legal framework of restriction practices (29). Therefore, clinicians may prefer to restrict chemically the patients who are at risk of escaping. The other preventable and correctable rapid tranquilization indication was difficulty falling asleep (6.9%). Maybe, clinicians may have evaluated the additional doses of current treatment regimen given to patients who have difficulty falling asleep and voluntarily want a drug, within the scope of rapid tranquilization.

In our study similar to the literature, referring to a guideline on rapid tranquilization is very low. In a study conducted in Belgium in which 108 psychiatrists and emergency physicians participated, guideline following was found to be 26.9% and it was reported that local guidelines were followed frequently (19). In another study, 75% of the participants reported that there is a guideline for rapid tranquilization in their institutions. However, the rate of compliance with these guidelines in this study did not reach 50% in total (20). In a survey conducted by the European Violence in Psychiatry Research Group in 21 countries, it was reported that there are national guidelines in only three countries, and there are no guidelines in 11 countries. In this study, it was reported that there is no national guideline in Turkey, and APA and PAT guidelines are frequently used by Turkish clinicians (30). In our study, PAT publications related to agitation management were followed most frequently, and APA guidelines were the second most frequently followed guideline with 19.1%. Participants who did not follow any guidelines reported that the most common reasons were that they were not aware of the guidelines and thought that their clinical experiences were sufficient. Similarly, in a study conducted with emergency physicians in Australia, it was reported that 68.7% of the participants were not aware of the NICE guidelines, and only 44.8% found the NICE guidelines useful (31). As a result, the applicability of agitation guidelines in daily clinical practice is low. There should be policies at the national level in Turkey to improve care of agitated patients and clinicians should be given periodic training on this subject.

More than half of the participants reported that they preferred the intramuscular route primarily in the management of agitation. Most guidelines recommend primarily oral treatments for rapid tran-

Table 4: Intravenous Haloperidol Experiences of Psychiatrists

	N	%
Use of intravenous haloperidol	69	52.7
Indications		
Agitation	38	29
Physically Aggression	30	22.9
Delirium	56	42.7
Alcohol or substance withdrawal symptoms	4	3.1
Extrapyramidal symptoms prone patient	8	6.1
Liver and kidney impairment	3	2.3
Intravenous haloperidol dose		
5 mg >	8	6.1
5-10 mg	36	27.5
10 mg ≤	20	15.3
Type of usage		
Intravenous slow push	14	10.7
Intravenous 30-minutes infusion	29	22.1
Intravenous 60-minutes infusion	12	9.2
Intravenous 2-hours infusion	13	9.9
Vital signs and laboratory examinations		
Pulse rate	54	41.2
Blood pressure	43	32.8
Temperature	22	16.8
Respiratory rate	27	20.6
Oxygen saturation	23	17.6
Evaluation of extrapyramidal symptoms	26	19.8
Complete blood count	5	3.8
Serum electrolytes	6	4.6
Liver and kidney function tests	7	5.3
Arterial blood gas analysis	2	1.5
Electrocardiogram	49	37.4
Creatinine phosphokinase	9	6.9

quilization (15-17). Also, the oral route is more preferred by clinicians in the management of agitated patients in recent studies (32-34). In our study, the severity of agitation and previous clinical experiences were indicated as the most effective reasons for the choice of administration route. Patients with high agitation severity generally do not accept taking medications voluntarily, so oral treatments are difficult to implement (35). Therefore, clinicians in our study may have reported that they predominantly preferred the intramuscular route. Moreover, it was shown that the subjective experiences of clinicians, institutional culture, and attitudes are effective in changing pharmacological preferences in rapid tranquilization practices (31). The third most common cause was the probability of drug side effects. In some previous studies investigating attitudes towards agitation management, similar safety concerns were reported to be effective in the pharmacological preferences of clinicians (20, 31). Despite the recommendations of the current guidelines to encourage patient participation (3, 15), only 39% of the participants stated that the patient's preference was effective in choosing the route of drug administration.

NICE recommends the measurement of at least one vital parameter per hour after rapid tranquilization (15). In our study, 75.6% of the participants reported that vital monitoring was performed at least once within one hour after rapid tranquilization. Similarly, in a study, 64% of clinicians reported that vital signs were measured at least once between 15-60 minutes (20). However, these results reflect the attitudes of clinicians based on their past experiences, as in our study. In a study in which rapid tranquilization cases recorded retrospectively were examined, vital signs were followed up in the first hour in 21% of the cases, and in 40% of the cases, no document record was found (26). In a study that included the data of 45 Mental Health Trusts in England, 55.5% of the centers did not have any audit reports after rapid tranquilization, and physical monitoring findings were recorded in the audit reports only in 40% of them (36). Therefore, real-life data on vital monitoring in Turkey will yield more accurate results.

It is important that the patient is evaluated face-to-face by the physician at a certain frequency after rapid tranquilization. In our study, 33.6% of the clinicians stated that they left the follow-up to the nurses, and 7.6% stated that they did not re-evaluate the patient after rapid tranquilization. In a study conducted in England, 52% of the participants reported that they left the follow-up to nurses (20). However, in the USA, the Joint Commission recommends that the patient should be evaluated face-to-face by the responsible physician within the first hour (37). Therefore, it is necessary to provide more training to physicians in Turkey on the follow-up of agitated patients and to carry out more strict audits on the recording of agitation cases.

Lorazepam and olanzapine were the most frequently preferred agents among first-line oral treatments. Among the intramuscular treatments, haloperidol was reported most frequently as the first-line agent. The preferences for both routes of administration did not change in the second-line agent preference. When previous studies are examined, in a study conducted in Africa, clinicians reported that they prefer chlorpromazine most frequently among parenteral agents in the management of acute agitation (38). In a retrospective study in Turkey where acute agitation cases were evaluated, the most frequently used agent was found to be intramuscular haloperidol (41.6%) (39). In an older Turkish study, it was reported that chemical restraint was used in 65% of acute agitation cases, and haloperidol was used in 67.3% of them. However, in this study, no information was given about the administration route (23). In an English study, clinicians preferred benzodiazepines as the first-line agent in neuroleptic naïve patients, benzodiazepine+antipsychotic combinations, and then antipsychotic monotherapy most frequently in non-neuroleptic naïve patients. Lorazepam was the most commonly used benzodiazepine, and haloperidol was the most commonly used antipsychotic (20). In another study, benzodiazepines were most frequently preferred as first-line agents by emergency physicians, while psychiatrists reported atypical antipsychotics as first-line agents most frequently (19). Therefore, different factors are effective in the pharmacological agent preference of clinicians in the management of agitated patients. Many factors such as the rapid onset of action, neuroleptic naivety, current treatment of the patient,

relative safety, easy applicability, availability, and allowing psychiatric evaluation are effective in the choice of pharmacological agents (20, 31, 38, 40). The oral drug preferences of clinicians in our study are in line with the recommendations of current guidelines. However, benzodiazepines and atypical antipsychotics are still not used adequately in parenteral administration for agitated patients. There is no parenteral form of lorazepam in Turkey (41), and although parenteral olanzapine is licensed, it is difficult to obtain (42). Therefore, in our study, the main factor in the preference of clinicians for parenteral agents was availability. Interestingly, although intramuscular ziprasidone exists, it was never preferred by clinicians. QT prolongation concerns about this drug may have been effective in this situation (43). Therefore, haloperidol still maintains its place as the first-line agent. Haloperidol is the most commonly used parenteral agent in the treatment of acute agitation (44). However, the manufacturer recommends using haloperidol in parenteral administration after an ECG recording (45).

In our study, 80.9% of the participants stated that they used anticholinergic drugs simultaneously with antipsychotics for rapid tranquilization. In a Turkish study in which acute agitation cases were evaluated retrospectively, the use of haloperidol in 41.6% of the patients and biperiden in 37.9% of the patients supports similar simultaneous use (39). The prophylactic use of anticholinergic drugs is not recommended (46). Only in a guideline for the treatment of schizophrenia, there are recommendations supporting the use of haloperidol combined with anticholinergics (14). There is a risk of extrapyramidal side effects with the use of high-potency antipsychotics such as haloperidol. In a study conducted with neuroleptic-naive first-episode psychosis patients, the incidence of extrapyramidal side effects with haloperidol was found to be 77.9% (47). Since the participants preferred haloperidol most frequently among intramuscular agents, they may be using anticholinergics prophylactically in order to avoid the risk of possible extrapyramidal side effects. In countries like Turkey, where resources and staff are insufficient, it may be difficult for clinicians to follow the patient and administer anticholinergics if necessary. Studies have shown that the use of agents such as lorazepam, promethazine, and diphenhydramine concurrent with haloperidol both produce a more rapid reduction in agitation and also reduce the incidence of extrapyramidal side effects (3, 44, 48). In a study conducted in Brazil, it was determined that clinicians most frequently preferred the combination of haloperidol and promethazine in the treatment of agitation (49). Therefore, these agents may be an alternative to the anticholinergic prophylaxis approach. Unfortunately, only the diphenhydramine parenteral form is licensed in Turkey and there is difficulty in obtaining this form (50).

As the first-line intramuscular agent, 37.4% of the participants reported that they preferred ZA. The most common purposes of ZA use were reported as sedation and rapid tranquilization, respectively. When intramuscular ZA is used, the sedation effect occurs in only 2-4 hours in a minority of patients, while the antipsychotic efficacy is seen after the 8th hour. Therefore, it is not expected for a certain change in the agitation level of the patient for a long time when administered for rapid tranquilization (13). In a Cochrane review, the authors stated that there were methodological problems in existing studies and that ZA is more effective in reducing the frequency of repetitive injections since it does not have a rapid onset of action (51). Therefore, clinicians' view of ZA in rapid tranquilization should be changed in Turkey. Furthermore, in our study, 30.5% of the clinicians stated that they used ZA to evaluate the tolerance to the long-acting depot form of zuclopenthixol. The use of a long-acting pharmacological agent is inconvenient for the assessment of tolerance to an antipsychotic. A test dose consisting of a small dose of active drug in a small volume is recommended for the assessment of tolerance to long-acting depot typical antipsychotics (13). ZA should be avoided for this purpose, especially in neuroleptic naive patients, because it may cause prolonged extrapyramidal side effects (13).

In our study, slightly more than half of the participants reported that they had at least one experience of using IVH in patients, and used it most frequently for delirium. Low-dose IVH was recommended for use in the treatment of delirium by expert groups such as the Cochrane Collaboration (52). Intravenous use of haloperidol in delirium

patients has many advantages over the intramuscular route, such as rapid onset of action, high bioavailability, and ease of administration (53). However, in 2007, based on case reports of potentially fatal cardiac events, the Food and Drug Administration (FDA) warned clinicians of an increased risk of QT prolongation and torsades de pointes within higher-than-recommended doses or intravenous use of haloperidol (54). Therefore, clinicians should be careful about possible complications when using IVH. In our study, the participants stated that they used haloperidol intravenously most frequently at doses of 5 to 10 mg. The most common form of administration was infusion within 30 minutes. In the American Association for Emergency Psychiatry guidelines, when IVH administration is required, it is recommended to limit the dose to 5 to 10 mg/day with continuous ECG monitoring, while CPA recommends its use at an average dose of 1-2 mg and monitoring of respiratory rate, blood pressure, and pulse rate every 5 minutes (3, 16). A recent systematic review recommended ECG monitoring only when using >5 mg intravenous doses of haloperidol and telemetry only for high-risk patients who received a cumulative dose of at least 100 mg or QTc >500 ms (55). Similar to the current recommendations, clinicians in our study reported that while using IVH, they most frequently followed ECG, heart rate, and blood pressure.

The study has several limitations. First, the study sample was quite small and tended to cluster in certain institutions. Therefore, the results mostly reflect the practice of academic institutions in Turkey. Secondly, the preference of clinicians may have been determined by the most probable scenario in their minds, since no specific feature was given about the agitation. It would be more accurate to make a similar assessment on hypothetical cases with factors affecting pharmacological interventions such as etiology, special groups, and comorbidity. Thirdly, drug-related factors such as the rapid onset of action, possible interactions, and mean sedation duration, which affect clinicians' pharmacological preferences are not presented in detail. Fourth, clinicians were not asked about their preference for combinations in the management of agitated patients. However, in real life, polypharmacy is common in the psychiatric population (25, 49). Also, in the study differences between emergency and inpatient services were not examined. Finally, documentation and audit processes in institutions were not included in the survey. With these limitations, our study should be still considered to be a preliminary study on rapid tranquilization in Turkey.

The present results in our study show that there are preventable and correctable problems in the management of agitated patients, and clinicians have improper use of rapid tranquilization agents. There is no national consensus text on the management of agitated patients in Turkey, and professional organizations do not have a policy text on rapid tranquilization. Clinicians should be given periodic training by preparing guidelines on agitation management, and the interventions applied should be supervised. There is a need for studies with large participation in order to better analyze the current practice regarding rapid tranquilization in Turkey.

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