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Rapid Tranquillisation: An AGREEable Ground?

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Abstract

Objective: Evidence base for rapid tranquillisation is an under researched area. Guidelines on rapid tranquilisation from English speaking countries were appraised using AGREE (Appraisal of Guidelines Research and Evaluation) and differences in their recommendations were analysed. Methods: Four independent psychiatrists appraised the guidelines using the AGREE tool. AGREE is a validated instrument used to assess the quality of guideline and recommendations using six domains of which each domain captures a specific aspect of the guideline development. The content was analysed manually. Results: Seven guidelines from five English speaking countries met the inclusion criteria. All the guidelines scored well on the domain of "scope and purpose". NICE guidelines from the UK consistently scored well on all domains with the maximum possible score of 100 on the "applicability" domain. APA from the USA did well on the domain of "editorial independence". AGREE could only examine the guideline development process and not the content. The guidelines differed in their recommendations of choice of drug for rapid tranquillisation. Discussion: All guidelines scored reasonably well on AGREE. National Institute of Clinical Excellence (NICE) has used robust strategies in developing the guidelines. Guidelines failed to achieve consensus in recommendations despite using a common pool of evidence. Haloperidol-promethazine combination is not recommended by any with the exception of NICE. This suggests data is selectively interpreted depending on locally prevalent customs.

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Keywords

Tranquillisation, Guidelines, Anti-Psychotics, Psychiatric Emergencies

1. Introduction

Violent or aggressive behaviour is a psychiatric emergency that necessitates swift mobilisation of staff and resources. Commonly it is secondary to psychotic symptoms, physical illness (e.g. delirium) and substance abuse [1]. Violent behaviour in an emergency room setting elicits varied responses and inexperienced staff may be required to handle such situations. This can have an impact on care of other patients with acute medical problems. On psychiatric wards, violent behaviour is likely to provoke aggression amongst other inpatients thereby stretching staff resources. Effective management of these volatile situations can reduce risks to the patient, other service users, staff and family members who are often victims of aggression [2].

Rapid tranquillisation is the use of medication to manage agitated or aggressive behaviour [3] and is used when other psychological and behavioural approaches have failed to calm the patient. A literature search of rapid tranquillisation revealed eight surveys of clinical practice and two surveys of clinician preferences (**Table 1**). There was failure of consensus on choice of medication for rapid tranquillisation—probably reflecting local cultural influences on prescription practices. All but one survey were from the western world. Appraisal of various guidelines around the world for schizophrenia suggests that recommendations are not uniform and quality of guideline may vary [4]. We have not come across any similar appraisal of guidelines on rapid tranquillisation and this is one important piece of the puzzle that we felt needs to be solved.

Table 1. Surveys on rapid tranquillisation.

Year	Authors	Methods	Participants	Location	Response	Duration	Results
1992	**Pilowsky *et al.***	Retrospective practice-based	Doctors and nurses	South London, UK	95%	6 months	Mean doses of parenteral antipsychotics and sedatives exceeded BNF* recommendations.
1994	**Cunnane *et al.***	Retrospective vignette-based	General adult consultants	Oxford, UK	68%	**Not mentioned**	No clear consensus. Chlorpromazine preferred over haloperidol. IM route favoured.
1996	**Simpson *et al.***	Retrospective vignette-based	Consultants and registrars	Manchester, UK	67%	**Not mentioned**	Haloperidol preferred to chlorpromazine. BNF maximum doses felt to be inadequate to control severe aggression.
1997	**Mannion *et al.***	Retrospective practice-based	Psychiatry trainees	Dublin, Ireland	80%	6 months	High dose antipsychotics and IM routes preferred. Zuclopenthixol acetate used in nearly half the incidents.
1998	**Hyde *et al.***	Retrospective practice-based	Nurse-based computerised database	Manchester, UK	100%	24 months	Zuclopenthixol or haloperidol + lorazepam IM preferred. Higher doses used in disturbed or resistant cases.
1999	**Binder *et al.***	Retrospective practice-based	Medical directors of emergency settings	USA-wide	100%	1 month	Haloperidol-lorazepam combination favoured. IM route preferred.
1999	**Moritz *et al.***	Prospective practice-based	100 consecutive patients in emergency room	Rouen, France	100%	9 months	Intramuscular loxapine was the preferred drug of choice.
2002	**Huf *et al.***	Retrospective practice-based	Practitioners in psychiatric emergency room	Rio de Janeiro, Brazil	100%	1 week	Haloperidol-promethazine combination preferred by 83% of participants.
2003	**Reid *et al.***	Retrospective practice-based	Consultants	West Scotland, UK	84%	**Not mentioned**	Droperidol perceived to be more effective than haloperidol or chlorpromazine Disapproval at its withdrawal.
2005	**Pereira *et al.***	Retrospective practice-based	Consultants and trainees	UK-wide	22%	**Not mentioned**	Lorazepam and haloperidol favoured with most doses exceeding BNF limits. Chlorpromazine, zuclopenthixol and droperidol next in line.

: Surveys of clinicians' preferred choices; *BNF: British National Formulary.

2. The Instrument and Its Scope

The Appraisal of Guidelines Research and Evaluation (AGREE) is an instrument used to assess the methodological rigour and potential biases involved in guideline development. It also checks for the internal and external validity of the recommendations [5]. It can assess any new, existing or updated guideline. It consists of 23 key items organised in six domains each of which rates a separate dimension of guideline. Domain 1 is "Scope and Purpose" which captures the overall aim of the guideline and its target group. Domain 2 is "Stakeholder Involvement" which captures the extent to which appropriate stakeholders were involved in developing the guideline and also represents the views of its intended users. Domain 3 is "Rigour of Development" which looks at the process of gathering and summarizing the evidence used and the methods used to develop its recommendations. Domain 4 is "Clarity of Presentation" capturing the language, structure and format of the guideline. Domain 5 is "Applicability" looking at the potential barriers and facilitators to implementation, strategies to improve uptake and resources needed to implement the guideline. Domain 6 is "Editorial Independence" which captures biases caused by any other competing interests.

Four independent raters rate the guidelines on these domains using a four point scale. The scores on the six domains are independent and cannot be aggregated. These scores help to compare the different guidelines and to decide whether or not to recommend a particular guideline over others. However it is not possible to set thresholds for the domain scores to demarcate a good guideline from a bad one.

3. Method

Guidelines on rapid tranquillisation from all English speaking countries were appraised using AGREE, with special emphasis on the NICE guidelines [6]. An English-speaking country was defined as a country with English as one of the official languages and with more than 50% residents speaking English. The 50% mark was arbitrarily chosen as a cut off figure. This was because countries where the majority of the population spoke a language other than English as first language were likely to have guidelines in local languages. This meant that there would be innumerable guidelines to assess, which would have been difficult to achieve given the language barrier.

Major databases were searched through the electronic database OVID. The databases included EMBASE (1980 to October week 3 2008), CINAHL (1982 to October week 3 2008), MEDLINE (1950 to October week 3 2008) and PsycINFO (1806 to October week 3 2008).The search terms used were "rapid tranquillisation" "tranquillisation" "behavioural emergencies", "aggression", "psychiatry emergencies", "guidelines in psychiatry" and "expert consensus guidelines". After dropping the duplicates and hand searching the abstracts seven guidelines in English language were obtained from five countries: UK, USA, Canada, Australia and New Zealand which met our inclusion criteria. The eighth guideline from Singapore was excluded as it did not meet the criterion of an English-speaking country.

Four raters used the AGREE tool to objectively assess potential biases of guidelines. The assessors were trainee psychiatrists at different levels of their training. Two of them were senior house officers: one in his first year of training and the second in his second year of training. A specialist registrar (one of the authors) and a staff grade psychiatrist both in their fourth year of training formed the team of assessors. The raters had received prior instructions regarding the scoring process. The guidelines were scored on six domains mentioned above. The scores were then standardised according to validated recommendations which could range from 0 to 100%. The content of the guidelines was analysed separately as it was not rated by the AGREE tool.

4. Results

Seven guidelines identified as above were compared for their pharmacological recommendations (**Table 2**).

Their methodological quality was evaluated using AGREE (**Table 3**). The scores from the four raters on the AGREE instrument ranged from a minimum of 33 on the domain of applicability for APA guidelines to the maximum of 100 on the applicability domain of NICE guidelines and editorial independence domain of the APA guidance. All guidelines scored well on the domain of scope and purpose. The NICE guidelines consistently scored well on all domains with the exception of editorial independence on which it performed mode rately with a score of 63.

Table 2. Guideline recommendations for rapid tranquillisation.

Date	Source	Guideline	Drugs recommended		Route of admin	Comments
2004	USA	American Psychiatric Association (APA)	Dissolvable olanzapine/risperidone OR Concentrate formulation of risperidone/haloperidol		PO	Droperidol: in selected clinical situations of extreme emergency or in highly agitated patients.
			Haloperidol/ziprasidone/ olanzapine +/− lorazepam		IM	
2005	Canada	Canadian Psychiatric Association (CPA)	Dissolvable SGAs		PO	Zuclopenthixol acetate: recommended to avoid repeated injections, except in drug naïve patients.
			Haloperidol 5 mg + lorazepam 2 mg OR olanzapine (2.5 - 10 mg)		IM	
2005	USA	Expert Consensus Guidelines (ECG)	Personality disorder/ Intoxication/ No data	Benzodiazepines	PO	Medication and patient characteristics govern the choice of psychotropic used
			Schizophrenia/ Mania	Olanzapine/risperidone +/−BNZ/ haloperidol + BNZ/valproex + antipsychotic	PO	
				Ziprasidone/quetiapine	PO	
				Olanzapine/ziprasidone +/− BNZ/haloperidol + BNZ	IM	
2005	UK	National Institute for Clinical Excellence Guidelines (NICE)	Haloperidol/lorazepam/ olanzapine/risperidone		PO	Olanzapine/risperidone: avoid in dementia. IV benzodiazepine/haloperidol: exceptional cases Oral or IM lorazepam alone: non-psychotic behavioural disturbance IM (haloperiodol + promethazine) /IM midazolam: very exceptional cases. Zuclopenthixol acetate: recommended in few, other than drug naïve patients. Chlorpromazine: not recommended at all.
			Haloperidol + lorazepam OR Olanzapine		IM	
2003	USA	Patient Outcomes Research Team (PORT)	Antipsychotic + benzodiazepine		Not specified	No details explained.
2004	Australia & New Zealand	Royal Australian & New Zealand College of Psychiatrists (RANZP)	Lorazepam (1 - 2 mg)/diazepam (5 - 10 mg)		PO	Typical antipsychotics: recommended as a last resort owing to risk of EPS. Haloperidol: least effective strategy. Alternative options: chlorpromazine (50 - 100 mg PO)/clonazepam (0.5 - 2 mg IM)/olanzapine(IM). Droperidol (IM): in nonresponsive cases. Zuclopenthixol acetate: recommended to avoid frequent injections even in drug naïve patients. IV midazolam may be used for rapid onset of action.
			Olanzapine wafers (5 - 10 mg)/ quetiapine (50 - 100 mg)		PO	
			Midazolam 5 mg		IM	
2003	USA	Texas Implementation of Medication Algorithms (TIMA)	Benzodiazepine/FGA		PO/IM	Benzodiazepines (lorazepam 1 - 8 mg/day, clonazepam 0.5 - 2 mg/day) & FGAs: preferred over SGAs irrespective of route. SGAs seem less effective for agitation/ excitement of an acute exacerbation.
			Risperidone solution		PO	
			Olanzapine/ziprasidone		IM	

FGA = first generation antipsychotic; SGA = second generation antipsychotic; BNZ = benzodiazepine. Colour code: Yellow = 1st choice, Green = 2nd choice, Red = 3rd choice.

5. Discussion

Common themes in clinical practice can be identified. For instance, benzodiazepines are chosen when little background information about the patient is available. This is in keeping with the Expert Consensus Guidelines [7]. Benzodiazepines are administered in psychiatric emergencies more frequently than other agents especially when the diagnosis is unknown [8]. Haloperidol plus promethazine combination is prevalent in Brazil [9] and India [10]. Its use is supported by high quality evidence showing its consistent superiority over olanzapine, lorazepam and haloperidol [10]. However this combination does not find a place in most guidelines with the exception of NICE. Lack of uniformity in recommendations despite using a common evidence pool is indeed intriguing. This could be a result of having only small trials with methodological inadequacies in this area. The

Table 3. Methodological quality of guidelines.

Guideline	Standardised AGREE Scores for each Domain (Percentage of maximum available score)					
	Domain 1 Scope & Purpose	Domain 2 Stakeholder involvement	Domain 3 Rigour of development	Domain 4 Clarity & presentation	Domain 5 Applicability	Domain 6 Editorial independence
APA	94	63	90	83	33	100
CPA	94	54	93	75	50	96
ECG	94	73	65	83	61	79
NICE	97	79	74	96	100	63
PORT	78	44	85	50	42	58
RANZP	89	73	79	67	47	83
TIMA	92	54	71	71	67	46

lack of good quality evidence necessitates those drawing up guidance to draw conclusions that are not founded on best possible evidence. For instance the only existing trial of zuclopenthixol acetate has a sample size of 40 patients [11] yet Australian and New Zealand guidelines [12] recommend it for rapid tranquillisation unlike the NICE and Canadian guidelines [13]. However even the NICE and Canadian guidelines have used equally thin evidence base for their recommendations. They differ on their inclusion of first and second generation anti psychotics thereby suggesting that guidelines are a combination of personal preferences and evidence base that is in turn influenced by selective interpretation of data.

Consensus on rapid tranquillisation guidelines is the need of the hour. Whether better quality clinical trials can help us reach an AGREEment remains to be seen.

Declaration of Interest

None.

References

[1] Atakan, Z.D. (1997) ABC of Mental Health. Mental Health Emergencies. *BMJ*, **314**, 1740-1742. http://dx.doi.org/10.1136/bmj.314.7096.1740

[2] Macpherson, R., Dix, R. and Morgan, S. (2005) A Growing Evidence Base for Management Guidelines. *Advances in Psychiatric Treatment*, **11**, 404-415. http://dx.doi.org/10.1192/apt.11.6.404

[3] Pereira, S., Paton, C., Walkert, L., *et al.* (2005) Treatment of Acute Behavioural Disturbance: A UK National Survey of Rapid Tranquillisation. *Journal of Psychiatric Intensive Care*, **1**, 84-88. http://dx.doi.org/10.1017/S1742646406000148

[4] Gaebel, W., Weinmann, S., Sartorius, N., Rutz, W. and McIntyre, J.S. (2005) Schizophrenia Practice Guidelines: International Survey and Comparison. *The British Journal of Psychiatry*, **187**, 248-255. http://dx.doi.org/10.1192/bjp.187.3.248

[5] The AGREE Collaboration. Appraisal of Guidelines for Research and Evaluation (AGREE) Instrument (Accessed 21 March 2008). http://www.agreecollaboration.org

[6] National Institute for Clinical Excellence: Clinical Guideline 25. Violence: The Short-Term Management of Disturbed/Violent Behaviour in In-Patient Psychiatric Settings and Emergency Departments. *London: NICE* 2005.

[7] Expert Consensus Panel for Behavioural Emergencies: Expert Consensus Guideline Series. Treatment of Behavioural Emergencies. *Journal of Psychiatric Practice*, 2005, **11**, 5-108.

[8] Macpherson, R., Dix, R. and Morgan, S. (2005) A Growing Evidence Base for Management Guidelines. *Advances in Psychiatric Treatment*, **11**, 404-415. http://dx.doi.org/10.1192/apt.11.6.404

[9] Huf, G., Coutinho, E., Fagundes Jr., H., Oliveira, E., Lopez, J., Gewandszajder, M., Carvalho, A., Keusen, A. and Adams, C. (2002) Current Practices in Managing Acutely Disturbed Patients at Three Hospitals in Rio de Janeiro-Brazil: A Prevalence Study. *BMC Psychiatry*, **2**, 4. http://dx.doi.org/10.1186/1471-244X-2-4

[10] TREC, Collaborative, Group (2003) Rapid Tranquillisation for Agitated Patients in Emergency Psychiatric Rooms: A Randomised Trial of Midazolam versus Haloperidol plus Promethazine. *BMJ*, **327**, 708-713.

http://dx.doi.org/10.1136/bmj.327.7417.708

[11] Gibson, R., Fenton, M., Coutinho, E. and Campbell, C. (2005) Zuclopenthixol Acetate in the Treatment of Acute Schizophrenia and Similar Serious Mental Illnesses. *Cochrane Database of Systematic Reviews*, Article No: CD000525. http://dx.doi.org/10.1002/14651858.CD000525.pub2

[12] McGorry, P. (2004) Royal Australian and New Zealand College of Psychiatrists: Clinical Practice Guidelines for the Treatment of Schizophrenia and Related Disorders. *Australian and New Zealand Journal of Psychiatry*, **39**, 1-30

[13] Canadian Psychiatric Association (2005) Clinical Practice Guidelines: Treatment of Schizophrenia. *The Canadian Journal of Psychiatry*, **50**, 1-56.

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