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Current practices in managing acutely disturbed patients at three hospitals in Rio de Janeiro-Brazil: a prevalence study

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Abstract

Background: The medical management of aggressive and violent behaviour is a critical situation for which there is little evidence. In order to prepare for a randomised trial, due to start in the psychiatric emergency rooms of Rio de Janeiro in 2001, a survey of current practice was necessary.

Methods: A seven day survey of pharmacological management of aggressive people with psychosis in the emergency rooms of all four public psychiatric hospitals in Rio de Janeiro, Brazil.

Results: In one hospital data were not available. Of the 764 people with psychosis attending these ERs, 74 were given IM medication for rapid tranquillisation (9.7%, 2.1/week/100,000). A haloperidol-promethazine mix (with or without other drugs) was used for the majority of patients (83%).

Conclusion: The haloperidol-promethazine mix, given intramuscularly for rapid tranquilization, is prevalent in Rio, where it is considered both safe and efficient. However, scientific evaluation of all pharmacological approaches to rapid tranquilization of psychotic people is inadequate or incomplete and a randomized trial of IM haloperidol-promethazine is overdue.

Background

Agitated or violent patients constitute 10% of all emergency psychiatric treatment [8]. The majority of these people have severe psychiatric problems such as schizophrenia, affective disorder or substance abuse[8]. Less frequently, organic illness or serious psychological stresses underlie the aggression. The medical management of aggressive and violent behavior by people with schizophrenia or other serious mental illnesses is of continuing central concern to clinicians [2].

In order to gain an overview of the evidence underlying current practice, the authors first undertook a search of the Cochrane Library. The search strategies used for all data-

Table 1: Pharmacological treatments and outcomes favoured by clinicians

Study	Favored regimen	Number of Doctors
USA 1999 [15]	Haloperidol + lorazepam +/- benztropine	11/20
	Droperidol	4/20
	Benzodiazepine (unspecified) alone	3/20
	Droperidol + lorazepam + diphenhydramine	1/20
	Haloperidol + benztropine	1/20
	Use of physical restraints	
	Common	14/20
	Usually not used	6/20
	Route of administration	
	Preferred IM or IV	14/20
	Preferred IM	3/20
	Unknown	3/20
UK 1994 [4]	Chlorpromazine	14/28
	Haloperidol	8/28
	Haloperidol + chlorpromazine	2/28
	Droperidol	1/28
	'Neuroleptic'	1/28
	Haloperidol + diazepam	1/28
	Haloperidol + lorazepam	1/28
	Desired end point	
	Sedated but mobile	12/28
	Not sedated but calm	9/28
	Asleep	7/28
	Route of administration	
	Preferred IM	26/28
	Preferred IV	2/28

bases mentioned are available from the authors. Relevant randomised clinical trials seem few, small and of debatable clinical utility [19]. For example, we found only one randomised trial (n = 40) comparing haloperidol (IV) with placebo for acutely disturbed psychiatric patients [14]. Only one statistically significant difference was found (RR unimproved by 2 hours 0.19 95% CI 0.04 to 0.9). A very small (n = 12) randomised trial compared benzodiazepines with placebo for acutely disturbed people [11], and, unsurprisingly, found no clear differences. Seven trials (total n = 206), compared benzodiazepines versus typical antipsychotics[9]. Benzodiazepines are statistically significantly more likely to produce an 'improvement' by 1.5 hours (RR 1.6 95% CI 1.02 to 2.5), but patients may also be at greater risk of needing additional injections (RR 0.66 95% CI 0.42 to 1.02). On the other hand, more patients given haloperidol are asleep by three hours than those allocated to benzodiazepines (RR 1.6 95% CI 0.99 to 2.5). Ninety-six people were randomised to trials investigating the value of a benzodiazepine-haloperidol mix versus haloperidol alone for acutely disturbed people [9]. The combination, largely with lorazepam, is no better than haloperidol for all the outcomes measured (eg. unimproved by 1.5 hours RR 0.7 95% CI 0.3 to 1.7), except for being asleep by 3 hours, favouring the mix (RR 2.0 95% CI 1.1 to 3.5). A systematic review of droperidol for acutely disturbed people, now withdrawn from use because of cardiac problems with *prolonged use*, shows it to be of unclear advantage when compared with placebo (1 RCT, n = 41, RR needing additional injection by 30 minutes 0.46 95% CI 0.2 to 1.2) or haloperidol (1RCT, n = 27, RR needing additional injection by 30 minutes 0.45 95% CI 0.2 to 1.01) [5]. A systematic review of zuclopenthixol acetate (5 RCTs, total n = 413), found no statistically significant differences for outcomes such as 'not sedated by two hours' (RR 0.6 95% CI 0.3 to 1.3) and 'needing another injection' (RR 1.5 95% CI 0.8 to 2.9), when compared to haloperidol, chlorpromazine or clothiapine[6].

With such limited evidence it is understandable that doctors may differ in their choice of drugs. We then sought surveys of the opinion of clinicians in MEDLINE and PsycINFO. Groups of doctors in the UK and USA had been

asked to list their preferred pharmacological management of acutely aggressive patients. In the USA[3], medical directors of 20 psychiatric emergency rooms were asked about their management of agitated patients. In the UK[4], 28 psychiatrists were asked to give their opinion on how a violent patient with a diagnosis of acute paranoid psychosis should be pharmacologically managed. The results of these surveys are shown in Table 1 and suggest some similar patterns of drug preference but no consistent favourite regimen.

Management preferred by clinicians, however, may not reflect real-world practice. We searched MEDLINE to identify surveys of Emergency Room practice. In 1989, a prospective survey over 160 days was conducted in a major psychiatric centre located in south London[12]. Patients were included if they had received an injection as an acute treatment and during this period, 102 incidents

Table 2: Studies of clinical practice

	Ratio of means of administration IV : IM	Drug of choice	Frequency of use	mean dose in mg (range)	Second injection	Complications / comments
UK 1992[3]	1:1	Diazepam	(Most frequent)	27 (10–80)	26%	1 hypotension
		Haloperidol	▲	22 (10–60)		1 cardiorespitory arrest (60 mg haloperidol + 80 mg DZ)
		Chlorpromazine	|	162 (50–400)		1 tachycardia, 1 hypotension
		Droperidol	|	14 (10–20)	26%	
		Paraldehyde	|			1 respiratory distress
		Amytal	|			
		Lorazepam	▼			
		Nitrazepam	(Least frequent)			
France 1999 [10]	0:80	Loxapine	80%	200 mg	6%	2 with acute dystonia
		Droperidol	5%			
		Chlorazepate	5%			Mostly people with substance abuse (study in General Emergency Room)
		Cyamemazine			6%	
		Diazepam	< 2%			
		Sultopride				
		Meprobamate				

were reported. In France a similar survey was conducted during 9 months in 1997[10]. Physical restraint by nurses was used for 64% of people in the UK survey and for 86% of agitated/violent attendees at the French emergency room in Rouen. The results of these two surveys are presented in Table 2.

In the UK, intravenous treatments were common, and the doses employed, high. In France, where aggression due to intoxication was common, loxapine IM was largely used. Other less informative surveys were identified[15].

About one percent of people suffer from schizophrenia[7]. Over 80% of those people live in low to middle income countries[13]. In global terms, therefore, by far the greatest burden of care of people with schizophrenia falls to those in low and middle-income countries[20]. People whose illness precipitates aggressive or violent behavior are unlikely to be very rare in these societies, so it is reasonable to assume that most psychosis-related aggression is being managed in the developing world. Recognizing this, and that the evidence-base of management is weak, the authors undertook a survey of practice as a preliminary phase of a large, pragmatic randomised trial. This paper reports a survey of drug management of severely disturbed behavior, undertaken in one week in March 2000 in the Psychiatric Emergency Units of Rio de Janeiro, Brazil.

The county of Rio de Janeiro has about 5.8 m habitants and four public hospitals are responsible for the care of about 70% of the population (Hospital Phillippe Pinel, Centro Psiquiátrico Rio de Janeiro, Centro Psiquiátrico Pedro II, Hospital Jurandir Manfredini).

Materials and Methods

The period of the survey covered emergency consultations from Saturday 25th March 2000 to Friday 31st March 2000, inclusive.

Data collection is difficult because information is recorded differently in each institution and electronic data are not available. The principle researcher repeatedly visited the emergency rooms and short stay wards of the hospitals and collected data on everyone who had presented for an emergency consultation during the prevalence period. Emergency room notes were also inspected and medical records sought for additional information on use of emergency intramuscular sedation. The main focus of this work the management of disturbed people who were likely to suffer from a psychotic illness. Therefore, whenever a primary diagnosis of substance abuse had been made, data were not recorded.

Results

It was impossible to be confident that the records of use of intramuscular (IM) medication for the 133 people who attended the emergency room of Hospital Jurandir Manfredini were accurate, so data are not presented. Between 3% and 15% of medical notes were not available in the other hospitals, so it was not possible to know if those people were also given emergency sedation (Table 3). During the seven-day period 764 patients attended the emergency room in the three hospitals and at least 74 received emergency sedative intramuscular drugs for psychiatric conditions that were not clearly induced by abuse of substances. All 74 patients were thought to be suffering from a psychotic illness at the time of sedation but follow up was not possible to confirm the initial impression. No patient received intravenous sedation and no patient received extra doses. The total proportion of those receiving IM sedation was similar among the three hospitals (8–11%). Data on the use of physical restraints were not recorded but it is likely that a high proportion of people were subject to four-point restraint, as this is standard practice in these hospitals. Seclusion was not an option and attempts at talking down were attempted for everyone.

The drugs of choice for IM sedation in the three hospitals in Rio de Janeiro are shown in Table 4. A haloperidol-promethazine mix was the most popular combination and was used in over 60% of episodes. This proportion reached 83% if we include haloperidol-promethazine plus other drugs.

Discussion

Surveys of the emergency sedation of acutely disturbed people with serious mental illness are rare. They are difficult to undertake involve piecing together particularly fragmented records and combining these data with the recent memories of the relevant health professionals. In a Developing World environment this process may be even more problematic with vastly under-resourced services and fully paper-based record keeping of varying standards.

For a population of about 3.5 m covered by the three hospitals, we estimate that at least 74 people per week are sedated for disturbed behavior thought to be the result of

Table 3: Numbers attending for emergency care between 25th – 31st March at three hospitals in Rio de Janeiro

Hospital	H.P.Pinel			C.P.R.J.			C.P.P.II		
	Emergency consultation	Given IM	Missing Data	Emergency consultation	Given IM	Missing data	Emergency consultation	Given IM	Missing data
Sat 25th	25	9	1	16	4	0	24	3	2
Sun 26th	22	0	2	16	6	1	27	10	3
Mon 27th	56	4	3	47	3	0	46	2	6
Tue 28th	46	6	3	30	2	1	44	5	5
Wen 29th	46	4	2	20	0	1	51	3	7
Thu 30th	52	7	3	30	2	2	38	1	3
Fri 31th	46	2	3	31	1	0	61	0	18
Total	**293**	**32**	**17**	**180**	**18**	**5**	**291**	**24**	**44**

Table 4: Drugs of choice for intramuscular sedation, doses and frequency of use in the three hospitals.

Drug of choice	Frequency of use	mean dose in mg (range)
Haloperidol + promethazine	61%	5 (2.5–10) + 50 (25–100)
Haloperidol + promethazine + diazepam	15%	5 (2.5–10) + 50 (25–100) + 10
Diazepam	9%	10
Haloperidol + promethazine + chlorpromazine	7%	5 + 50 + 25
Chlorpromazine + diazepam + promethazine	1%	25 + 10 + 50
Chlorpromazine + promethanzine	1%	25 + 50
Chlorpromazine	1%	25
diazepam + promethazine	1%	10 + 50
Haloperidol + diazepam	1%	5 + 10
Promethazine	1%	50

serious mental illness. Eventually, a proportion of this group may not have been diagnosed as having had psychotic illness. The authors suspect, that however, because the emergency rooms are only used for psychiatric crises, and as the authors tried to screen out those suspected of abusing substances, the proportion not suffering from a psychotic illness would be very small.

According to these figures, acute sedation for this group in Rio de Janeiro seems to be less prevalent than in central London (Brazil 2.1/week/100,000 *vs* London 3.3/week/100,000)[12]. There may be many reasons for this discrepancy and the authors would not wish to read too much into these findings.

Emergency treatment, however, does seem more consistent in Rio de Janeiro than in London. Eighty three percent of patients receiving any drug for sedation in the emergency room of these hospitals were given promethazine in addition to haloperidol. Brazilian clinicians consider this approach both safe and efficient. The rational for this combination lies in the will to swiftly instigate antipsychotic drugs, and in the sedative and antimuscarinic properties of promethazine. Doses of promethazine are usually between 25–50 mg but, as adjunctive sedative for emergency use, could reach 100 mg IM. The onset of action is about 1–2 hours after intramuscular administration and half-life is 5–14 hours. The main adverse reactions of promethazine are gastrointestinal disturbances, dry mouth and blurred vision.[18] Paradoxical reactions such as CNS stimulation and extrapyramidal symptoms have been reported, but are exceedingly rare.

Despite the high prevalence of use in Brazil, and we have now been alerted to wide use in the Indian Sub-continent, the authors have been unable to find any randomised studies evaluating the use of haloperidol-promethazine mix IM in the psychiatric emergency.

Conclusions

From the global perspective, current use of drugs in the psychiatric emergency is varied [1]. Expert consensus differs, and systematic reviews of the best evidence produce equivocal results[6]. Brazilian psychiatrists are consistent in favouring use of IM haloperidol-promethazine for people who are dangerously aggressive due to psychotic illnesses, but recognize that authority to recommend the use of this combination has to be supported by well-designed, conducted and reported randomized trials. The TREC study (Tranquilização Rápida-Ensaio Clínico), comparing haloperidol-promethazine IM with a benzodiazepine, now running in Brazil and India, is one such trial (protocol available from corresponding author).

Competing interests

None declared.

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References

1. **Treatment of schizophrenia 1999. The expert consensus guideline series.** *J Clin Psychiatry* 1999, **60**:3-80
2. Atakan Z, Davies T: **ABC of mental health. Mental health emergencies.** *BMJ* 1997, **314**:1740-1742
3. Binder RL, McNiel DE: **Emergency psychiatry: contemporary practices in managing acutely violent patients in 20 psychiatric emergency rooms.** *Psychiatr Serv* 1999, **50**:1553-1554
4. Cunnane JG: **Drug management of disturbed behaviour by psychiatrists.** *Psychiatric Bulletin* 1994, **18**:138-9
5. Cure S, Carpenter S: **Droperidol for schizophrenia and schizoaffective psychoses (protocol).** *Cochrane Database Syst Rev,* 2001
6. Fenton M, Coutinho ES, Campbell C: **Zuclopenthixol acetate in the treatment of acute schizophrenia and similar serious mental illnesses.** *Cochrane Database Syst Rev* 2000
7. Jablensky A, Sartorius N, Ernberg G, Anker M, Korten A, Cooper J, Day R, Bertelsen A: **Schizophrenia: manifestations, incidence**

and course in different cultures. A world health organization ten-country study. *Psychol Med Monogr Suppl* 19921-97
8. Kaplan HI, Sadock BJ, Grebb JA: **Kaplan and Sadock's Synopsis of Psychiatry.** *Baltimore USA: Williams & Wilkins.* 1994
9. Khorsand V, Leucht S, Kissling W: **Benzodiazepines for schizophrenia and schizoaffective psychoses (protocol).** *Cochrane Database Syst Rev* 2000
10. Moritz F, Bauer F, Boyer A, Lemarchand P, Kerleau JM, Moirot E, Navarre C, Muller JM: **Patients in a state of agitation at the admission service of a Rouen hospital emergency department.** *Presse Med.* 1999, **28**:1630-1634
11. Nestoros JN, Suranyi-Cadotte BE, Spees RC, Schwartz G, Nair NP: **Diazepam in high doses is effective in schizophrenia.** *Prog Neuropsychopharmacol Biol Psychiatry* 1982, **6**:513-516
12. Pilowsky LS, Ring H, Shine PJ, Battersby M, Lader M: **Rapid tranquillisation. A survey of emergency prescribing in a general psychiatric hospital.** *Br J Psychiatry* 1992, **160**:831-835
13. Population Reference Bureau: **Population Reference Finder (Web page).** 2002 [http://www.worldpop.org/datafinder.htm]
14. Reschke RW: **Parenteral haloperidol for rapid control of severe, disruptive symptoms of acute schizophrenia.** *Dis Nerv Syst* 1974, **35**:112-115
15. Schnyder U, Klaghofer R, Leuthold A, Buddeberg C: **Characteristics of psychiatric emergencies and the choice of intervention strategies.** *Acta Psychiatr Scand* 1999, **99**:179-187
16. The Cochrane Collaboration: **The Cochrane Library.** *Oxford, Update Software.* 2002
17. The Royal College of Psychiatrists: **Management of Imminent Violence: Clinical practice guidelines to support mental health services.** *London: Royal College of Psychiatrists.* 1998
18. The Royal Pharmaceutical Society of Great Britain: **The British National Formulary (Web page).** 2001 [http://bnf.org/]
19. Thornley B, Adams C: **Content and quality of 2000 controlled trials in schizophrenia over 50 years.** *BMJ* 1998, **317**:1181-1184
20. World Health Organization: **The World Health Report 2001: Mental Health – new understanding, new hope. Annex Table 3 Burden of disease in disability-adjusted life years (DALYs) by cause, sex and mortality stratum in WHO Regions, estimates for 2000 (Web page).** 2002 [http://www.who.int/whr/2001/main/en/annex/annex3.htm]