term mental illness and community disruption.[4] The general health questionnaire detects psychiatric disorders in community settings.[3] Of those exposed, 24% scored above the level at which a subject could be considered a case compared with 3% of controls. This was not related to potential level of exposure and may be in response to strains on the fabric of this community.

The results of this phase of the study were presented to the people of the South Mainland of Shetland at a public meeting held on 13 September 1993.

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Members of the Shetland Health Study Group were: Mr C Cumming, Gilbert Bain Hospital, Shetland; Drs P Christie, D Brewster, Common Services Agency, Scottish Health Service, Edinburgh; Dr V S G Murray, National Poisons Unit, London; Dr J S Oliver, Glasgow University, Glasgow; Dr A Proudfoot, Edinburgh Royal Infirmary, Edinburgh; Mrs M Stove, Mrs M Robertson, Miss K Hudson, Shetland Health Board, Shetland; Dr M D Hunter, Dr C M Rowlands, Mrs S Mann, Levenwick Medical Practice, Shetland; Dr A Min, Mrs S Thompson, Hillswick Medical Practice, Shetland; Mr M R Hall, Shetland Islands Council, Shetland; and Dr G I Forbes, Environmental Health (Scotland) Unit, Glasgow.

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Circadian variation in attempted suicide by deliberate self poisoning

Roberto Manfredini, Massimo Gallerani, Stefano Caracciolo, Angela Tomelli, Girolamo Calò, Carmelo Fersini

Institute of Internal Medicine, University of Ferrara Medical School, I-44100 Ferrara, Italy
Roberto Manfredini, *assistant professor*
Carmelo Fersini, *professor*

Accident and Emergency Department, St Anna Hospital, Ferrara
Massimo Gallerani, *section head*

Department of Psychology and Institute of Pharmacology, University of Ferrara Medical School, Ferrara
Stefano Caracciolo, *assistant professor in psychology*
Girolamo Calò, *assistant professor in pharmacology*

Mental Health Service, Operative Unit of World Health Organisation Parasuicide Multicentre Study, Ferrara
Angela Tomelli, *medical assistant*

Correspondence to:
Dr Manfredini.

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Circadian patterns have been shown for many physiological variables and several medical diseases.[1] Suicidal behaviours usually occur with symptoms of depression, although only a few people who attempt suicide fully satisfy diagnostic criteria for having an affective disorder. Clinical and experimental evidence suggests that affective disorders are related to disturbances in the phase or amplitude of biological rhythms—for example, sleep-wake cycles, environmental dark-light cycles, and hormonal rhythms. We determined whether a specific temporal risk exists in the occurrence of attempted suicide by deliberate self poisoning.

Patients, methods, and results

We studied prospectively all patients who attempted suicide by deliberate self poisoning and were admitted to the accident and emergency department of St Anna Hospital, Ferrara, Italy, from 1 January 1989 to 31 December 1991. This hospital alone deals with medical emergencies occurring in the city and suburban area of Ferrara (about 150 000 residents).

Attempted suicide by deliberate self poisoning was diagnosed from the clinical history (from relatives, witnesses, or the patients themselves), physical examination, and response to the benzodiazepine flumazenil. In most cases the presumptive diagnosis was then confirmed by specific toxicological assay. All patients were interviewed by a consultant psychiatrist, who recorded demographic characteristics, the nature of the drugs or substances ingested, and the time of ingestion.

Seventy one patients were men (mean age 41 (SD 18)) and 141 women (mean age 39 (17)). Ninety eight patients had taken benzodiazepines, 10 antidepressants, six neuroleptics, four barbiturates, 10 sodium hypochlorite and 29 other drugs; 32 had taken a mixture of drugs and data were not available for 22.

The time of self poisoning was categorised into 24 increments of one hour, 0600 to 0659 being classed as 6 am (table). Data in the group as a whole and by sex were analysed by cosinor analysis, in which the cosine curve best fitting the data was determined by multiple linear regression.[2] For rhythms detected by rejection of the zero amplitude hypothesis (at $P < 0.05$), the cosinor procedure yields (*a*) the rhythm adjusted mean (or mesor), which measures the extent of the rhythm; (*b*) the amplitude (the distance from the mesor to the peak or trough of the cosine curve best fitting the data); and (*c*) the acrophase (peak time of the cosine curve best fitting the data). Each of the values has an estimate of variance.

Distribution of attempts at suicide by time

Time	Men (n=71)	Women (n=141)	Total (n=212)
0000-0059	5	5	10
0100-0159	3	4	7
0200-0259	1	5	6
0300-0359	2	0	2
0400-0459	0	4	4
0500-0559	1	1	2
0600-0659	1	1	2
0700-0759	2	3	5
0800-0859	2	3	5
0900-0959	3	7	10
1000-1059	2	10	12
1100-1159	3	4	7
1200-1259	4	9	13
1300-1359	4	12	16
1400-1459	1	2	3
1500-1559	3	7	10
1600-1659	3	5	8
1700-1759	4	3	7
1800-1859	2	11	13
1900-1959	6	7	13
2000-2059	8	15	23
2100-2159	6	10	16
2200-2259	3	6	9
2300-2359	2	7	9

A significant circadian rhythm was found for the whole population ($P=0.007$, mesor 8·83) and for men ($P=0.007$, mesor 2·86) and women ($P=0.026$, mesor 5·87). The acrophases were respectively 1745 (95% confidence interval to 1432 to 2258), 1837 (1537 to 2148), and 1716 (1303 to 2129).

Comment

The sociodemographic data on our sample were consistent with published data. In particular, women attempting suicide outnumbered men by two to one. This might indicate women's greater demonstrative tendency as men outnumber women by two to one in studies of completed suicide.

Our results suggest that the risk of attempting suicide by self poisoning is greatest in the early evening, which is in agreement with previous studies.[3] The risk of suicide is greatest during the late morning

and early afternoon.[4] As suicide and attempted suicide have different psychological causes and epidemiological risk factors, these data support the hypothesis that chronobiologically determined changes influence suicidal behaviour. The acrophases of important biological variables such as temperature, heart rate, and cortisol secretion vary in people with affective disorders compared with control subjects and may affect behaviour in addition to diurnal changes in mood and social activities. Increased adrenergic activity and lowered serotoninergic activity[5] in the afternoon might play a part in mood changes.

It could also be argued, however, that people who attempt suicide by minor self poisoning often do not want to die and their cry for help is more likely to be heard in the hours of the day when social and psychiatric services are available.

In conclusion, a specific temporal risk, defined as the point of confluence of many factors (hormonal, environmental, and behavioural), probably plays a part in suicidal behaviour. Treatment of depressive disorders might therefore be improved by aiming for peak drug concentrations at vulnerable times.

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Postural hypotension in elderly patients given carvedilol

H Krum, E L Conway, J H Broadbear, L G Howes, W J Louis

Department of Clinical Pharmacology and Therapeutics, Austin Hospital, Heidelberg, Victoria 3084, Australia
H Krum, *senior clinical pharmacologist*
E L Conway, *senior lecturer in clinical pharmacology and therapeutics*
J H Broadbear, *research associate*
L G Howes, *senior clinical pharmacologist*
W J Louis, *professor of clinical pharmacology and therapeutics*

Correspondence to:
Dr Louis.

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First dose postural hypotension is commonly observed with antihypertensive drugs,[1,2] but its incidence may be overstated in clinical trials because of protocol requirements, which may include frequent venesection, fasting, acute withdrawal from caffeine, and frequent changes in posture.[1] The β blocker vasodilator drug carvedilol is associated with orthostatic hypotension, particularly in elderly people.[2-4] We assessed the incidence of first dose hypotension in the absence of possible confounding factors linked to protocol.

Methods and results

The study group comprised 16 elderly patients (nine men; mean (SD) age 70 (6), mean weight 73 (17) kg) with uncomplicated mild or moderate hypertension whose supine diastolic blood pressures were 90-110 mm Hg after one week's washout with placebo after antihypertensive treatment. Previous studies showed that a sample of 10-18 subjects would produce an 80% chance of detecting a difference in response of 10 mm Hg between treatments at the 95% confidence level. The protocol was approved by the Austin Hospital Ethics Committee, and consent obtained from each patient.

The study was a randomised double blind crossover design with four study days with single doses—carvedilol 12·5 mg, carvedilol 25 mg, pindolol 15 mg, and placebo—each separated by a washout of ⩾7 days. The patients were randomly allocated to eight different sequences of treatment.

After sitting for 10 minutes the patients received their allocated treatment and a standard breakfast. They then sat for an hour, walked about during the second hour, and were supine during the third hour. Blood pressure and heart rate were recorded with patients sitting (supine during the third hour) then after one minute standing, at 0, 30, 60, 125, and 180 minutes after they had received the treatment.

The main outcome measures were Δ supine blood pressure (blood pressure at $time_0$ − blood pressure at $time_t$) and Δ standing blood pressure (standing blood pressure at $time_t$ − supine blood pressure at $time_t$), where $time_t$ was the time that the measurement was taken and $time_0$ the value at baseline. These variables were analysed with three way analysis of variance, with patient, treatment, and period of study as factors, and treatment differences were estimated.[5]

Although all patients receiving placebo and pindolol could stand at all time points, two patients receiving carvedilol 25 mg could not stand at 125 minutes and two others receiving carvedilol 25 mg could not stand at either 60 or 125 minutes. Of these four patients, one could not stand at 125 minutes and another could not stand at either 60 or 125 minutes when they received carvedilol 12·5 mg. The table summarises differences between treatments in Δ supine blood pressure and Δ standing blood pressure two hours after each drug was given: carvedilol produced a dose dependent fall in supine blood pressure when compared with the placebo. Carvedilol 25 mg and pindolol produced similar reductions in supine blood pressure with minimal treatment differences. Dose dependent postural falls in standing blood pressure occurred with carvedilol. This orthostatic response was significantly greater with carvedilol 25 mg than with pindolol despite similar reductions in supine blood pressure.

Estimated mean differences (95% confidence interval) in Δ supine blood pressure and Δ standing blood pressure between treatments two hours after they had been given to 16 elderly patients*

	Systolic		Diastolic	
	Difference in blood pressure (mm Hg)	P value	Difference in blood pressure (mm Hg)	P value
Δ Supine blood pressure:				
Carvedilol 12·5 mg *v* placebo	17·2 (8·8 to 25·6)	<0·001	3·6 (−2·4 to 9·5)	0·233
Carvedilol 25 mg *v* placebo	22·0 (13·7 to 30·3)	<0·001	9·4 (3·5 to 15·2)	0·003
Carvedilol 25 mg *v* 12·5 mg	4·9 (−3·5 to 13·3)	0·246	5·8 (−0·1 to 11·7)	0·055
Carvedilol 25 mg *v* pindolol 15 mg	1·8 (−6·8 to 10·4)	0·668	0·3 (−5·8 to 6·3)	0·922
Δ Standing blood pressure†:				
Carvedilol 12·5 mg *v* placebo	4·6 (−8·7 to 17·9)	0·489	7·3 (0·4 to 14·2)	0·038
Carvedilol 25 mg *v* placebo	20·4 (7·3 to 33·5)	0·003	14·9 (8·1 to 21·7)	<0·001
Carvedilol 25 mg *v* 12·5 mg	15·9 (2·7 to 29·1)	0·020	7·5 (0·7 to 14·4)	0·003
Carvedilol 25 mg *v* pindolol 15 mg	22·0 (8·5 to 33·5)	0·002	10·1 (3·1 to 17·2)	0·006

*Determined with the SAS statistical package.
†In subjects unable to stand, standing blood pressure was assumed to be 65/45 mm Hg.

Comment

The incidence of first dose postural hypotension has been reported in pharmacokinetic studies as being as high as 40% with carvedilol.[2,4] To avoid potential aggravating factors we did not take blood samples, the patients received their drugs with food, and each patient began the study seated.

Despite these precautions some patients could not stand after a single dose of carvedilol, and all patients had significantly greater falls in systolic and diastolic blood pressure in the standing position with carvedilol 25 mg than with the placebo, carvedilol 12·5 mg, and pindolol. Symptoms were obvious 60 and 125 minutes after carvedilol had been given, corresponding to the times of maximum hypotensive response to carvedilol (at 1-2 h).[3] No symptoms of postural effects occurred, however, with pindolol.