

Prevention of suicide

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We reviewed the epidemiologic features of suicide in Canada and evaluated suicide prevention programs. Three groups were found to be at increased risk for suicide: men aged 70 years or more, women aged 65 to 69 and men aged 20 to 24. The other groups, in decreasing order of risk, were the mentally ill, people who have attempted suicide, those with a life-threatening illness, native people, people with a family history of suicide and prisoners. Studies that evaluated suicide prevention programs showed that none significantly reduced the incidence of suicide; however, the studies were found to be methodologically inadequate or used noncomparable systems of data collection. On the basis of our findings we recommend that primary care physicians routinely evaluate suicide risk among patients in high-risk groups and that intervention include counseling, follow-up and, if necessary, referral to a psychiatrist. Close follow-up is recommended for newly discharged psychiatric patients and those who recently attempted suicide.

Revue critique de l'épidémiologie du suicide au Canada et des programmes pour sa prévention. Sa fréquence est particulièrement élevée dans trois tranches d'âge: celles des hommes d'au moins 70 ans, des femmes de 65 à 69 ans, des hommes de 20 à 24 ans. En ordre de risque décroissant les plus menacés sont les malades mentaux, les personnes qui ont déjà tenté de se suicider, les malades en danger de mort, les autochtones, les personnes qui présentent des antécédents familiaux de suicide, les prisonniers. Les travaux antérieurs sur l'efficacité des programmes préventifs font croire que ceux-ci n'ont pas amené une diminution significative de la fréquence des suicides; mais ou bien leur méthodologie est insatisfaisante, ou bien le recueil des données y a été fait par des moyens non comparables. Nos trouvailles nous portent à recommander que le médecin de première ligne estime systématiquement le risque de suicide chez ses malades appartenant aux groupes précités. Son intervention comprendra les conseils, le suivi et, s'il le faut, le recours au psychiatre. Les malades psychiatriques qui viennent de quitter l'hôpital et les personnes qui ont récemment tenté de se suicider doivent surtout être suivis de près.

The National Task Force on Suicide in Canada defined suicide as "intentional self-inflicted death".¹ Suicide is one of the leading causes of death among young people in Canada. It ranks second among men aged 15 to 19 years and third among women in the same age group.^{2,3} Health care professionals are especially concerned about the increasing rate of suicide. Since 1960 not only has suicide accounted for a greater proportion of all deaths but also the rates per 100 000 population have been increasing steadily.¹ (Unless otherwise stated, the rates of death, from suicide or other causes, cited in this article refer to the number of deaths per 100 000 population.)

Successful suicide prevention depends on both the ability to define accurately the population at risk and the presence of effective prevention programs. We examined the characteristics of people in Canada

at high risk and estimated the magnitude of increased risk in each high-risk group. In addition, we reviewed the effectiveness of suicide prevention programs. Lastly, on the basis of our findings we recommended strategies for primary care physicians to help them evaluate suicide risk and implement effective prevention programs in their practices.

Suicide trends in Canada

Death from suicide may be misclassified often and be considerably underreported.^{1,4} Since 1930 the suicide rate has been increasing steadily except for a temporary decline during the Second World War.^{1,2} Between 1950 and 1986 the rate rose from 7.8 to 14.6, an overall increase of 87%.⁵ The suicide rate in Canada ranks in the upper 50th percentile of Western countries and is well above the median rate of

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10.0.⁶ Mao and associates⁷ estimated that the 3700 suicides in Canada in 1986 resulted in a loss of 122 908 potential life-years (97 613 among males, 25 295 among females).

In 1983 the suicide rate (15.1) was lower than the rate of death from cardiovascular (317.5) or respiratory (53.5) disease but higher than the rate of death from diabetes (12.4) or cirrhosis of the liver (9.5).² In 1985 the suicide rate (12.9) was lower than the rate of death from traffic (16.2) and other (14.9) accidents but higher than the rate of deaths from homicide (2.8);⁸ this indicates that the rate of death from suicide is 4.6 times higher than the rate of death from homicide.

By province

Although there were some interprovincial differences all of the provinces and the territories followed the Canadian trend of an overall increase in rates from 1960 to 1986.⁵ Before 1980 the suicide rates were higher in the western than in the eastern or central provinces, but this has changed in recent years. Large increases in Quebec (252%) and New Brunswick (193%) occurred between 1960 and 1986. Four provinces had their highest rates in 1975, three in 1980 and three in 1986. Alberta had the highest rates, 18.7 in 1980 and 17.9 in 1986. In 1986 the rates in Ontario (12.4) and the other eastern provinces were below those in British Columbia (14.7), Saskatchewan (13.7) and Manitoba (14.4). The two territories had much higher rates than the rest of Canada.

By sex and age

Men commit suicide over three times more often than women do. Between 1960 and 1986 the rates among men increased from 12.0 to 22.8 (90%), as compared with 3.0 to 6.4 among women (101%).⁵ The male:female ratio was greatest in 1960 (4:1); it was lowest in 1970 (2.5:1) and has been rising since 1975 (3.6:1 in 1986).

In 1960 the suicide rate among men was unimodal, increasing with age to a maximum of 29.9 among those 60 to 64 years of age. From 1970 to 1986 the pattern was bimodal, peaking first among men 20 to 30 years old and again among those 55 to 59. By 1986 the highest rate was among men over 70 years of age (34.9); men aged 25 to 29 accounted for the next highest rate (33.1) and men 50 to 54 for the third highest (30.0).

The suicide rate among women was much lower overall. In 1960 it was unimodal, peaking at midlife. In 1970 the rate peaked among women 45 to 49 years of age (15.1) but levelled off thereafter. By 1980 the rate began to resemble the bimodal pattern

for men. In 1986 the highest rate occurred among women aged 50 to 54 years (12.9); the rates for the other age groups were from 4.5 (among women 15 to 19 years) to 9.8 (among those 60 to 64 years).

Between 1960 and 1986 the greatest increase in the rates by age and sex occurred among men 15 to 19 years of age (281%). Women in the same age group had the second greatest increase (275%); they were followed by women aged 35 to 39 (190%) and men aged 20 to 24 (166%). In 1960 the rate among men 20 to 24 exceeded the overall national rate by 62% (12.3 v. 7.6); however, by 1986 it exceeded the national rate by 125% (32.8 v. 14.6). By contrast, the rate among women in the same age group was less than half the national average in both 1960 (2.4 v. 7.6) and 1986 (6.4 v. 14.6).

Method of suicide

Of the suicides among men in 1986, 38% involved firearms and 27% strangulation or hanging.⁵ The respective figures among women were 12% and 19%. The most common method among women was drug overdose (in 37%); only 9% of the men used this method. Gas poisoning, usually with motor vehicle exhaust, accounted for 13% of the suicides among men and 10% among women. The remaining 13% of suicides among men and 22% among women involved other methods, such as stabbing, drowning and jumping from high places.⁵

Parasuicide

Parasuicide — a nonfatal outcome of attempted suicide⁹ — covers a wide variety of self-destructive life-threatening acts that are notoriously under-reported in Canada. This is due to inconsistencies in reporting, incomplete information and pressure from communities and families against reporting.¹ Epidemiologic data on parasuicide have not been collected systematically. Suicide attempts are 30 to 100 times more frequent than completed suicide,¹⁰ and women are more than twice as likely as men to attempt suicide. The rate peaks among women aged 15 to 19 years (822.9) and among men in the same age group (493.4). The rate gradually decreases in the older groups but is higher among men (70.2) than among women (41.1) aged 65 years or more.¹

People at high risk

The prediction of suicide with the use of psychosocial risk factors has proved to be unusually difficult because of the low incidence rate and the problem of defining suicide.¹¹ Statistical methods may identify high-risk groups but cannot accurately predict which members of the groups will attempt or

commit suicide. Vulnerability to death by suicide is found at all levels of psychopathologic illness and normalcy.¹² The following are groups in Canada that are at increased risk for suicide (Table 1¹³⁻²⁰).

Adolescents

Suicide is particularly rare before puberty but increases in frequency with age.²¹ Both age and cohort have been found to affect the rate of suicide.²²

Using cohort analysis Solomon and Hellon²³ showed that adolescents who have experienced some form of self-injury continue to be at risk over their lifetime. Some studies have supported the notion of imitative suicide,^{24,25} but the evidence in this age group is not conclusive.²⁶ Reports of suicides committed simultaneously by two or more people or a series of suicides occurring together are rare and may account for no more than 1% to 5% of all suicides among adolescents.²⁷

Table 1: Suicide rates per 100 000 population in Canada*

Group	Year	Rate	Magnitude of increased risk†
General population	1986	14.6	—
Male	1986	22.8	1.6 (22.8/14.6)
Female	1986	6.4	0.4 (6.4/14.6)
Specific age group, yr			
15-19			
Male	1986	20.2	0.9 (20.2/22.8)
Female	1986	4.5	0.7 (4.5/6.4)
20-24			
Male	1986	32.8	1.4 (32.8/22.8)
Female	1986	6.0	0.9 (6.0/6.4)
65-69			
Male	1986	24.6	1.1 (24.6/22.8)
Female	1986	9.3	1.5 (9.3/6.4)
> 70			
Male	1986	34.9	1.5 (34.9/22.8)
Female	1986	7.1	1.1 (7.1/6.4)
Psychiatric patients in hospital ¹³			
Affective disorder	1975	695	23.0 (695/30.1)
Schizophrenia	1975	456	15.0 (456/30.1)
Drug abuse	1975	194	6.4 (194/30.1)
Alcoholism	1975	187	6.2 (187/30.1)
Personality disorder	1975	187	6.2 (187/30.1)
Neurosis	1975	150	4.9 (150/30.1)
Organic brain syndrome	1975	71	2.4 (71/30.1)
Overall	1975	279	9.3 (279/30.1)
People who have attempted suicide			
General population	1977-88	—	26.9 ¹⁴ -100 ¹⁵
Male	1971	222	7.4 (222/30.1)
Female	1971	370	12.2 (370/30.1)
People with life-threatening illness			
Cancer ¹⁶	1983	—	4.0
Acquired immune deficiency syndrome ¹⁷	1988	680	66.0
Native people	1982	36.1	> 2.0
Inuit ³	1978	62.7	2.1 (62.7/30.1)
Status Indians ³	1978	45.9	1.5 (45.9/30.1)
Men ⁵	1986	56.3	2.5 (56.3/22.8)
Women ⁵	1986	11.8	1.8 (11.8/6.4)
Youths in Alberta ¹⁸	1986	—	5.0
People with family history of suicide ¹⁹	1988	—	9.0
People in custody ²⁰	1986	60.0	4.1 (60/14.6)

*Data were obtained from the Department of National Health and Welfare, Ottawa, unless otherwise stated.

†The rate in the general population, the base rate in the same sex group or the rate of highest incidence was used to yield the most conservative estimate of increased risk.

The major determinants of suicide in this age group are psychologic problems, especially early indicators of antisocial personality,²⁸ physical illness, poor emotional control and communication skills, low self-esteem, academic problems, unemployment and multiple losses (especially parental loss at an early age).²⁹⁻³¹

According to Boldt and Solomon³² predisposing factors include a history of mental disorder, drug and alcohol problems and chronic physical disorders. Factors that trigger suicidal behaviour are mental health crises, perceived failures and loss or bereavement; however, these stressors affect most adolescents.³³ Comparative studies of suicide and parasuicide among adolescents have shown that the family environment is an important factor.³⁴ Those who attempt suicide have been found to have experienced more environmental changes (residence, school and cohabitants other than parents) than a comparison group.³²

Elderly people

In 1986 men aged 70 years had the highest suicide rate (34.9).¹ After 60 years the rates begin to increase in both sexes.¹ Blazer, Bachar and Manton³⁵ predicted that suicides among the elderly will become an increasing public health concern since this group is the most rapidly growing in Canada.

Lepine³⁶ reported that the major determinants are physical illness, mental deterioration, social isolation, depression, inadequate income, and alcohol and drug dependence. Studies have found rates of clinical depression of 90% on average.³⁷ Changing roles (e.g., because of retirement, the "empty nest" syndrome and the loss of a spouse) contribute to the lack of identity, social isolation and severe depression and have been linked to increases in vulnerability to stress and disease among the elderly.³⁸

The mentally ill

Suicide rates among psychiatric patients in a veterans' hospital have been found to vary by diagnostic category,¹³ as do the rates among psychiatric patients in other health care facilities.³⁹ Mentally ill people have significantly higher rates of suicidal behaviour than healthy people.^{13,39,40} In North America the reported prevalence of mental disorders among those who commit suicide is 50% to 90%.⁴¹ In a review of studies involving patients with affective disorders Guze and Robins⁴² found that in nine of the studies suicide accounted for 12% to 19% of deaths and in eight for 35% to 60%. In another study suicide accounted for 10.6%, 10% and 8.5% of the deaths among people with depression, schizophrenia

and mania respectively;⁴³ none of the control subjects committed suicide.

Specific mental disorders common among people who commit suicide and associated with a high risk of suicide are neurosis, schizophrenia, major affective disorders, adjustment disorders and alcoholism.^{44,45} The risk of suicide has been found to increase directly with age among depressed people and those with alcoholism, and social isolation is more prevalent among depressed people than among people with other mental disorders.^{44,45} For people admitted to hospital because of mental illness the risk of suicide is greatest immediately after discharge.⁴³

In a prospective study involving 4800 patients consecutively admitted to the inpatient psychiatric service of a US veterans' hospital Pokorny¹³ attempted without success to identify people who would subsequently commit or attempt suicide. He concluded that the prediction of suicide in a particular person is not feasible.

Alcohol and drug abusers

Alcohol abuse has been found to be associated with 50% of suicides and with increased risk of suicidal behaviour.¹ The relation between alcoholism and suicide appears stronger among men than among women.⁴⁶ For both sexes the risk of suicide increases as the duration of alcohol dependence lengthens.¹²

People who attempted or committed suicide have been found to use sedatives and tranquillizers on a daily basis more frequently than those who died of natural causes. Women more than men abuse drugs alone or with alcohol.⁴⁷ A retrospective study in San Diego compared the characteristics of 133 young people (under 30 years of age) who committed suicide with those of 150 older people (30 years or more) who committed suicide.⁴⁸ Significantly more young people than older people had a principal psychiatric diagnosis of substance abuse and a secondary diagnosis of depression.

There is a trend toward an increasing frequency of suicide and attempted suicide through the use of benzodiazepines, antidepressants and neuroleptics.^{49,50} Since 1970 antidepressants have accounted for 4% to 50% of the annual hospital admissions because of acute drug overdose.⁵¹⁻⁵³ Several studies have shown that in a substantial number of cases the drug was prescribed by a physician who was contacted by the patient shortly before the act.⁵²⁻⁵⁴

People who have attempted suicide

Adults with psychiatric problems and adolescents who have attempted suicide are at high risk of

suicide. Between 13% and 35% of patients who have attempted suicide will try again within 2 years after the first attempt.¹⁵ In this group the annual rate of completed suicide is 0.9% to 2.5%.^{55,56} Among adults a history of suicidal behaviour has been shown to be associated with antisocial personality, poor physical health, alcoholism, borderline personality disorder, psychiatric disorder and future attempts.^{1,14,39,56}

In pediatric and adolescent psychiatric practice attempted suicide is one of the most common emergencies.⁵⁷ Adolescents are much more likely to make nonlethal attempts and even more likely to express suicidal ideation than to commit suicide.²¹ In a study involving a community sample of Ontario youths aged 12 to 16 years 5% to 10% of the boys and 10% to 20% of the girls reported suicidal behaviour (suicidal ideation and attempts) within a 6-month period.⁵⁸ Suicidal behaviour appeared to be related to psychiatric disorder in general, as well as to family dysfunction and parental arrest.

Major determinants of parasuicide appear to be depressive disorders, borderline personality disorders and substance abuse.^{21,31,32,47} Personality characteristics of adolescents who attempt suicide are a tendency to react severely to a loss, poor control of rage and impulsivity.^{33,59}

People with life-threatening illness

People with a life-threatening illness¹⁷ and those with physical illness⁶⁰ are at increased risk of suicide. Suicide rates associated with disorders of the central nervous system seem to be higher than those associated with other disorders.⁶¹ The rate is 4 times higher among cancer patients,¹⁶ 3 to 23 times higher among those with Huntington's disease⁶² and 66 times higher among those with AIDS (acquired immune deficiency syndrome)¹⁷ than in the general population.

Both biologic factors and psychosocial stressors explain the increased risk among those with life-threatening illness.⁶¹ Many illnesses share stressors such as reduced physical functioning, long-term dependence, hopelessness and uncertainty about the future. Psychosocial stressors include the social stigma of illness, diminished or lost occupational functioning and long-term dependence. The high suicide rate among medical patients may be due in part to the greater frequency of depression in this population than in the general population.⁶¹

Native people

Suicide accounts for 15% to 20% of all violent deaths among native people.⁶³ In 1986 the suicide rates were 11.8 among women and 56.3 among men;

the rate was over 100.0 among men aged 15 to 29 years.⁵ These rates are two to three times higher than the rates among non-native Canadians. In 1985 in Alberta the suicide rate was over five times higher in the native youth than in the general youth population.¹⁸

Of natives who committed suicide 62.5% had a history of alcohol abuse, 85.7% had been drinking immediately before the act but had a blood alcohol level below the legal limit, and 53.0% were "under the influence of alcohol at the time of suicide" (blood alcohol level above the legal limit).^{64,65} Other major determinants of suicide are depression,⁶⁶ loss of employment,⁶⁶ social isolation⁶⁶ and loss of a spouse or "significant other".⁶⁷

People with a family history of suicide

A family history of suicide has been shown to be associated with a significantly increased risk of attempted suicide.^{1,39,45} Those who have a family member who committed suicide are nine times more likely than others to kill themselves.¹⁹ The National Task Force on Suicide in Canada has estimated that at least 40 000 to 50 000 Canadians are affected by the suicide of a family member each year.¹ Factors associated with suicide of a family member are feelings of guilt, identification with the deceased and a desire for self-punishment.¹ Studies of children's reactions to suicide by a parent or sibling have shown that guilt and consequent distortions of communication may be very severe, resulting in the children being at high risk of suicide.⁶⁸

People in custody

The number of suicides among inmates in federal and provincial prisons increased from 10 deaths in 1973²⁰ to 17 in 1986,⁵ an increase of 70%. The overall rate of suicide is about four times higher in the prison population than in the general population.

Key factors associated with suicidal behaviour are detention in maximum and medium security institutions and in isolation areas, high and low levels of education and crimes against other people.²⁰ The typical suicidal inmate comes from a deprived family background, which is characterized by abuse, criminal behaviour or both, a history of violence, psychiatric disturbance and drug and alcohol abuse.²⁰

Conclusion

It is not possible to predict which members of high-risk groups will commit suicide. However, the fact that a person is a member of one of these groups should alert primary care physicians to the possibili-

ty of increased suicide risk. The factors that contribute to an increased risk among people already at high risk must be determined.

Review of intervention strategies

The medical and mental health care systems and the social services are responsible for providing suicide intervention services in Canada. In addition, there are about 100 crisis or suicide intervention centres.¹

Very few suicide intervention programs in Canada have been formally evaluated. Most studies of the effectiveness of treatment programs have been found to be methodologically deficient or used noncomparable systems of data collection.⁶⁹ The effectiveness of Canadian crisis centres in suicide prevention has not been evaluated in any adequately designed studies.

Studies in the United States and England have provided no firm evidence that suicide rates in the general population are reduced after the introduction of community psychiatric services.⁷⁰ School-based educational programs have not been shown to be effective in reducing suicide rates.⁷⁰ The effectiveness of suicide hot lines in decreasing the rate is inconclusive. One study⁷¹ demonstrated no reduction; however, a more recent study⁷² showed a small but significant reduction among young white women, who are the most frequent users of such services, although there was no evidence that the hot lines were directly responsible.

Methodologically sound studies to evaluate the effectiveness in preventing suicide of programs that combine identification of high-risk patients and subsequent intervention should be performed.

Recommendations for primary care physicians

Studies have indicated that many adolescents,⁵² adults,⁷³ including physicians,⁷⁴ and elderly people⁷⁵ who commit suicide contact their family physician shortly before the event. Therefore, physicians should routinely evaluate suicidal risk among patients at high risk, particularly if there is evidence of current psychiatric disorder, especially psychosis, depression or substance abuse. Successful evaluation relies on the adequate recognition of psychiatric disorder and an accurate evaluation of the risk status of the patient. Unfortunately, there is some evidence that primary care physicians have a low rate of recognition of psychiatric disorder and suicide potential.^{54,76,77} There are no scales or semistructured interviews to estimate the risk of suicide that have been validated in the general population. However, detailed guidelines exist for eliciting the information

necessary to estimate the risk among adolescents⁵⁷ and elderly people.⁷⁵

Effective strategies are available to treat people who have been identified as being at high risk. Reduction in risk has been reported to occur among people with psychiatric disorders — for instance, patients with affective disorder who have received prophylaxis with lithium carbonate^{78,79} or have undergone electroconvulsive treatment followed by lithium therapy for 6 to 12 months.⁸⁰ Reduction has also been reported after provision of social support for isolated and depressed people, especially the elderly,⁷⁵ and for those having attempted suicide.⁸¹ A retrospective comparison⁸¹ of no intervention and two types of psychiatric intervention (two brief interviews and longer, unspecified psychiatric treatment) showed that suicide was attempted or committed significantly more often in the untreated group than in the two treatment groups. A more recent study⁸² reported an increase in the rate of suicide among patients for whom 1 month had elapsed since their last contact with a psychiatrist and no increase among those treated with neuroleptic drugs.

Despite methodologic weaknesses in these studies counselling and follow-up by primary care physicians, and referral to a psychiatrist if necessary, apparently constitute part of an adequate treatment plan to reduce suicide risk. Close follow-up is recommended for recently discharged psychiatric patients⁴³ and those who attempted suicide within the previous 6 months.¹⁰

Finally, physicians should be aware of the danger of prescribing drugs in other than small amounts to patients at risk for suicide. Methods to determine the accuracy of primary care physicians in both identifying psychiatric disorders and evaluating suicide risk should be developed and rigorously tested.

Conclusions

From 1950 to 1986 the overall rate of suicide in Canada increased. Although it is not possible to predict accurately which people at high risk will attempt or commit suicide, membership in a high-risk group should alert primary care physicians to evaluate the risk of suicide. Strategies for determining the accuracy of primary care physicians in evaluating this risk should be developed. Programs that combine identification of patients at high risk and subsequent intervention should be evaluated in terms of their effectiveness in preventing suicide.

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Pr AXID® Lilly - Nizatidine Histamine H₂ Receptor Antagonist

Pharmacology: Nizatidine is a competitive, reversible inhibitor of the binding of histamine to the histamine H₂ receptor of the gastric-acid secreting cells. Nizatidine is not an anticholinergic agent. It inhibits nocturnal gastric acid secretion and gastric-acid secretion stimulated by food, caffeine, betazole and pentagastrin. Pepsin output is reduced in proportion to the reduced volume of gastric secretions. Nizatidine has little or no effect on basal serum gastrin or food induced hypergastrinemia. Nizatidine is absorbed rapidly after oral administration. Peak plasma concentrations occur from 0.5 to 3 hours after the dose. Absorption is unaffected by food or propantheline. However, antacids decrease the absorption of nizatidine by about 10%. The absolute oral bioavailability of nizatidine exceeds 90%. Approximately 35% of nizatidine is bound to plasma protein, primarily α -1-glyco-protein. This binding is not influenced by other drugs such as warfarin, diazepam, acetaminophen, propranolol, or phenobarbital. Approximately 90% of an oral dose of nizatidine is excreted in the urine within 12 hours. About 60% of an oral dose and 77% of an iv. dose of nizatidine is excreted as unchanged drug. The elimination half-life is 1 to 2 hours and the systemic plasma clearance is about 50 L/hour. The volume of distribution is 0.8 to 1.5 L/kg. Since nizatidine is primarily excreted in the urine, renal impairment significantly prolongs the half-life and decreases the clearance of nizatidine. In anephric individuals with creatinine clearance less than 10 mL/min, the half-life is 3.5 to 11 hours, and the plasma clearance is 7 to 14 L/hour. The dose should be adjusted in patients with moderate or severe impairment of renal function (see Dosage). The pharmacokinetic profile for nizatidine in the elderly was not significantly different from the profile in younger normal subjects. Gastric acid suppression correlates directly with nizatidine doses from 75 to 350 mg. Oral doses of 100 mg or 1.3 mg/kg suppressed gastric acid secretion in sham fed volunteers for 3 hours after the dose. The duration of acid suppression directly correlates with the nizatidine dose. 300 mg nizatidine suppressed acid secretion almost entirely early in the day, and the suppression persisted about 10 hours. Nocturnal acid was suppressed for 10 to 12 hours after 300 mg nizatidine. Treatment for up to 2 weeks with nizatidine 600 mg daily did not influence the serum concentrations of gonadotropins, prolactin, growth hormone, antidiuretic hormone, cortisol, triiodothyronine, thyroxine, testosterone, 5 α -dihydrotestosterone, androstenedione or estradiol. **Indications:** 'Axid' is indicated in the treatment of conditions where a controlled reduction of gastric acid secretion is required for ulcer healing and/or pain relief: acute duodenal ulcer, acute benign gastric ulcer, and prophylactic use in duodenal ulcer. **Contraindications:** Nizatidine is contraindicated for patients with known hypersensitivity to the drug and should be used with caution in patients with hypersensitivity to other H₂-receptor antagonists. **Precautions: Gastric ulcer:** Where gastric ulcer is suspected the possibility of malignancy should be excluded before therapy with nizatidine is instituted. **Pregnancy and Lactation:** The safety of nizatidine during pregnancy has not been established. Reproduction studies performed in rats and rabbits at doses up to 300 times the human dose have revealed no evidence of impaired fertility or teratogenicity. If the administration of nizatidine is considered to be necessary, its use requires that the potential benefits be weighed against possible hazards to the patient and to the fetus. Nizatidine is secreted in human breast milk in proportion to maternal plasma concentrations (<0.1%), and caution should be exercised when nizatidine is administered to nursing mothers. **Impaired Renal Function:** As nizatidine is excreted via the kidney, dosage should be adjusted in patients with moderately or severely impaired renal function (see Dosage and Administration). **Hepatic Dysfunction:** Nizatidine is partially metabolized in the liver; however, in patients with mild to moderate hepatic dysfunction, disposition of nizatidine is similar to that of normal subjects. **Geriatrics:** Ulcer healing rates in elderly patients are similar to those in younger age groups. The incidence rates of adverse events and laboratory test abnormalities are also similar to those seen in other age groups. Age alone is not an important factor in the disposition of nizatidine. Elderly patients may have reduced renal function (see Dosage). **Children:** Safety and effectiveness of nizatidine in children has not been established. **Drug Interactions:** No interactions have been observed between nizatidine and theophylline, chlordiazepoxide, lorazepam, lidocaine, phenytoin, warfarin, aminophylline, diazepam, and metoprolol. Nizatidine does not inhibit the cytochrome P-450-linked drug-metabolizing enzyme system; therefore, drug interactions mediated by inhibition of hepatic metabolism are not expected to occur. In patients given very high doses (3,900 mg) of ASA daily, increases in serum salicylate levels were seen when nizatidine, 150 mg b.i.d., was administered concurrently. **Adverse Reactions:** Clinical trials of nizatidine included almost 5,000 patients given nizatidine in studies of varying durations. North American placebo-controlled trials included over 1,900 patients given nizatidine and over 1,300 given placebo. Among the more common adverse events in these placebo-controlled trials, sweating (1% vs. 0.2%), urticaria (0.5% vs. less than 0.01%), and somnolence (2.4% vs. 1.3%) were significantly more common in the nizatidine group. A variety of less common events were also reported; it was not possible to determine whether these were caused by nizatidine. **Hepatic:** Hepatocellular injury, evidenced by elevated liver enzyme tests (SGOT[AST], SGPT[ALT], or alkaline phosphatase), occurred in some patients possibly or probably related to nizatidine. In some cases there was marked elevation of SGOT, SGPT enzymes (greater than 500 IU/L). The overall rate of occurrences of elevated liver enzymes and elevations to 3 times the upper limit of normal, however, did not significantly differ from the rate of liver enzyme abnormalities in placebo treated patients. All abnormalities were reversible after discontinuation of nizatidine. **Cardiovascular:** In clinical pharmacology studies, short episodes of asymptomatic ventricular tachycardia occurred in 2 individuals administered nizatidine and in 3 untreated subjects. **Central Nervous System:** Rare cases of reversible mental confusion have been reported. **Endocrine:** Clinical pharmacology studies and controlled clinical trials showed no evidence of antiandrogenic activity due to nizatidine. Impotence and decreased libido were reported with equal frequency by patients who received nizatidine and by those given placebo. Rare reports of gynecomastia occurred. **Hematologic:** Fatal thrombocytopenia was reported in a patient who was treated with nizatidine and another H₂ receptor antagonist. On previous occasions, this patient had experienced thrombocytopenia while taking other drugs. Rare cases of thrombocytopenic purpura have been reported. **Integumental:** Sweating and urticaria were reported significantly more frequently in nizatidine than in placebo patients. Rash and exfoliative dermatitis were also reported. **Hypersensitivity:** As with other H₂ receptor antagonists, rare cases of anaphylaxis following administration of nizatidine have been reported. Because cross sensitivity in this class of compounds has been observed, H₂ receptor antagonists should not be administered to individuals with a history of previous hypersensitivity to these agents. Rare episodes of hypersensitivity reactions (eg. bronchospasm, laryngeal edema, rash, and eosinophilia) have been reported. Other: Hyperuricemia unassociated with gout or nephrolithiasis was reported. Eosinophilia, fever and nausea related to nizatidine administration have been reported. **Laboratory Tests:** False-positive tests for urobilinogen with Multistix® may occur during therapy with nizatidine. **Symptoms and Treatment of Overdosage:** There is little clinical experience with deliberate overdosage of nizatidine in humans. Test animals that received large doses of nizatidine have exhibited cholinergic-type effects, including lacrimation, salivation, emesis, miosis, and diarrhea. Should overdosage occur, use of activated charcoal, emesis, or gavage should be considered along with clinical monitoring and supportive therapy. Renal dialysis for 4 to 6 hours increased plasma clearance by approximately 84%. **Dosage and administration:** Duodenal or Gastric Ulcer: One 300 mg capsule or two 150 mg capsules once daily at bedtime. Alternatively 150 mg twice daily may be used. Healing occurs within 4 weeks in most cases of duodenal ulcer; but if healing is not documented or has not occurred, therapy should be given for 7 weeks. Maintenance Therapy in Duodenal Ulcer: One 150 mg capsule once daily at bedtime for 6 to 12 months depending on the severity of the condition. Antacids may be given concomitantly if needed.

Dosage Adjustment in Renal Impairment:

Renal Function	Creatinine Clearance (mL/min)	Dosage	
		Acute	Maintenance
Normal	> 50	300 mg/day	150 mg/day
Moderate Impairment	20 - 50	150 mg/day	150 mg/2nd day
Severe Impairment	< 20	150 mg/2nd day	150 mg/3rd day

Supplied: 300 mg: Each pale yellow and brown Pulvule 3145 contains: nizatidine 300 mg. Bottles of 100. **150 mg:** Each pale yellow and dark yellow Pulvule 3144 contains: nizatidine 150 mg. Bottles of 30. Reviewed 1989. Product monograph available on request.

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