Changes in birth – cohort pattern of peptic ulcer mortality in England and Wales

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Summary: Previous epidemiological studies have described the secular trends in peptic ulcer mortality in England and Wales as being characteristic of a cohort phenomenon. The most recent data on ulcer mortality, however, show increasing mortality rates from duodenal ulcer in women over 65 and from gastric ulcer in women over 75 years. While the rise in mortality rates in the oldest age groups is partly explained by their greater life expectancy, the increase in mortality from duodenal ulcer in older women shows evidence of an environmental (period) effect being superimposed on female cohorts born between 1895 and 1925. This effect could partly be due to the increasing consumption of non-steroidal anti-inflammatory drugs which coincides with the rise in mortality rates.

Introduction

Previous birth cohort analysis of peptic ulcer mortality for England and Wales suggested that mortality would decline during the latter part of this century.^{1,2} It was postulated that mortality from peptic ulceration would rise for successive cohorts born up to 1885/95 and then decrease in subsequent generations. However, an analysis of hospital discharges in England and Wales shows that rates of peptic ulcer perforation in elderly men are not declining and that the rates in elderly women are increasing.³ Such phenomena are not readily explained by the concept of the high-risk cohorts described in previous studies.

It is the purpose of the present study to examine whether recent trends in mortality follow the predicted cohort pattern. Age- and sex-specific mortality rates are examined in terms of age, period (environmental factors acting at a given time period), and cohort effect (environmental effects to which a generation is exposed).

Methods

Mortality data for gastric and duodenal ulcer for England and Wales were obtained from the reports of the Registrar General and the Office of Population Censuses and Surveys and cover the time period from 1900 to 1989. The figures for 1989 are provisional figures and may change a small amount in the final published version.

The eighth and ninth revisions of the ICD code provide a rubric for peptic ulcer of unspecified site besides gastric and duodenal ulcer. To provide continuity with previous data the figures for gastric ulcer and for peptic ulcer of unspecified site were combined.

Using population estimates of the time period under consideration age- and sex-specific death rates were calculated for 10 year age-groups and 10-year-periods. For the cohort analysis the age-specific death rates were plotted against the year of birth (Figure 1). Persons belonging to the same cohort can be identified by drawing a line parallel to the y-axis above the year of birth under review so that the age-specific curves are joint.

The presentation of curves was chosen in such a way that comparison with the previously published mortality curves (until 1977) by Susser is possible.¹

Information on national smoking habits for 1972 to 1982 was obtained from the General Household Survey.⁴ Prescription data for non-steroidal anti-inflammatory drugs (NSAIDs) from 1967 to 1985 were obtained from Intercontinental Medical Statistics.

Results

For males, trends suggest a peak of mortality in duodenal ulcer for generations born about 1885/95 and in gastric ulcer for generations of both sexes born about 1875/85 as it was previously described (Figure 1). In women, duodenal ulcer mortality shows no clear evidence of a cohort effect. The mortality patterns for the most recent time period, however, indicate deviations from the cohort shape

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Figure 1 Age-specific death rates from peptic ulcer, England and Wales, 1900–1989. Cohort age contours refer to average death rates for 10 year periods plotted versus central year of birth. (a) Duodenal ulcer: males; (b) duodenal ulcer: females; (c) gastric ulcer: males; (d) gastric ulcer: females.

within the older age groups. Alterations in peptic ulcer mortality were particularly marked in females, dying from duodenal ulcer, in whom 513 deaths occurred in 1959, but 1088 deaths in 1989. By contrast, mortality figures in males dying from gastric ulcer declined from 1454 deaths in 1959 to 890 deaths in 1989.

Gastric ulcer mortality

A comparison of mortality rates between 1955–59 and 1985–89 reveals that gastric ulcer mortality declined in all age-groups except in women over 75 years (Table I).

As the cohort curve makes apparent, the risk of death peaked in the over 75 year old age group in both sexes for individuals born about 1875 and fell from that time onwards for subsequent male cohorts (Figure 1c,d). The curve in women over 75, however, shows a plateau between 1875 and 1895 before starting to rise in women born between 1895 and 1905.

Duodenal ulcer mortality

In duodenal ulcer disease the age-specific death rates have decreased for men in all age-groups and for women under 65 years since the mid 1950s (Table II). The fall becomes steeper with later years of birth, particularly in men (Figure 1a,b). While

Table I Mortality rates of gastric ulcer by age-group per million population

Age group (years)	Males			Females		
	1955–59	1985–89	% change	1955–59	1985–89	% change
15–24	1.3	0.60	– 54	0.90	0.40	– 56
25–34	4.3	0.60	– 86	2.2	0.35	– 84
35–44	12.6	3.3	– 74	4.6	2.1	– 54
45–54	46.1	11.8	– 74	14.9	7.4	– 50
55–64	145.8	418.0	– 71	38.5	28.5	– 26
65–74	345.1	125.0	– 64	126.3	89.0	– 30
75 +	741.8	463.0	– 38	416.6	450.5	+ 8

Table II Mortality rates of duodenal ulcer by age-group per million population

Age group (years)	Males			Females		
	1955–59	1985–89	% change	1955–59	1985–89	% change
15–24	1.6	0.18	– 89	–	0.20	–
25–34	6.2	1.4	– 77	2.4	0.30	– 88
35–44	21.3	4.6	– 78	5.0	2.5	– 50
45–54	60.5	15.5	– 74	13.1	7.1	– 46
55–64	167.6	60.0	– 64	29.1	27.3	– 6
65–74	378.7	176.5	– 53	68.7	85.0	+ 24
75 +	764.7	520.0	– 32	189.9	359.3	+ 89

death rates have stayed constant in the last decade in the over 75 year old age group in men, death rates in women over the age of 65 have risen from 1955 onwards, this trend being most obvious in the very elderly (Table II). As a result, the curves for the cohorts, for which declining mortality was expected, show an increase in mortality for females born between 1895 and 1925 (Figure 1b).

Discussion

In a study of hospital discharge rates for peptic ulcer perforations in the United Kingdom it was reported that ulcer perforation rates had increased in elderly women over a 25-year period until 1982, remained stable in elderly men and had fallen in younger individuals in both sexes over the same time.^{3,5} A similar pattern is evident for peptic ulcer mortality until 1989 in England and Wales. The present data show a rise in mortality in elderly women for duodenal ulcer and a rise in mortality rates in the oldest age group for gastric ulcer in women, whereas the rates for men declined in all age groups except the very elderly in whom mortality showed little change. It seems unlikely that the discordant trend in mortality rates in both sexes can be explained by alterations in coding practices, hospitalization criteria and diagnostic procedures, because they would have affected both ulcer types and all age groups. It is also unlikely that improved surgical and anaesthetic techniques have influenced mortality trends only in elderly males. There are plenty of examples of diseases for which diagnostic changes have had different effects at different ages when more refined techniques are applied to older people. This is, however, less likely to produce changes in sex trends.

People born at the end of the last century were shown to be at particular risk of ulcer death.¹ The increase in life expectancy in women has increased the proportion of very elderly women born at the end of the 19th century thus still belonging to the high risk cohorts at present. This possibility might in part explain the marked increase in peptic ulcer deaths in very elderly women.

The increase in mortality in women beyond 75 years, however, cannot be due to the risk experienced by generations born at the end of the last century because the rise in death rates now affects women born in the first three decades of this century. This risk is also too rapid to be only explained on the basis of increasing life expectancy in females. Therefore, changes in exposures to environmental factors have to be considered to have brought about this trend; among those are cigarette smoking and ulcerogenic drugs.

The time pattern of cigarette smoking, for example, cannot be responsible for the rise in mortality

Table III Prevalence of cigarette smoking by sex and age (%)

Age-group (years)	Males		Females	
	1972	1982	1972	1982
16-19	43	31	39	30
20-24	55	41	48	40
25-34	56	40	49	37
35-49	55	40	48	38
50-59	54	42	47	40
60 +	47	33	25	23

observed. Cigarette smoking fell steadily during the last decade (Table III) in both sexes and all age groups which could, in part, account for the fall in death rates in the younger age groups. Smoking habits in elderly women, however, have remained nearly unchanged during the last decade. An analysis by Sonnenberg showed that smoking habits were not responsible for the birth cohort pattern of peptic ulcer mortality in England and Wales during this century.⁶

Epidemiological evidence suggests that there is an association between chronic peptic ulcer,^{7,8} ulcer complications,⁹⁻¹¹ in particular bleeding,^{9,10} and ulcer death¹² in relation to NSAID-intake with a 2- to 4-fold increase in risk of takers of such a treatment. Estimation of the risk attributable to NSAID-intake can be derived from a surveillance study by Carson *et al.*¹⁰ comparing the rates of ulcer bleeding in patients treated with NSAIDs with unexposed patients. There was an excess of 0.44 episodes of bleeding over the expected rate for every 10,000 person-months of treatment. Similarly, in a case-control study by Somerville,⁹ 22% of bleeding ulcers could be attributed to NSAID-intake in patients aged over 60 years. An extrapolation of this figure to the number of ulcer deaths in the United Kingdom allows an estimate of about 2000 cases of ulcer bleeding per year in persons aged over 60 years. Given an estimation of 11 million prescriptions of NSAIDs per year for this age-group it can be calculated that 2 cases of haemorrhage occur for every 11,000 person-months of NSAID treatment, assuming a duration of one prescription for one month.¹³ When applying these estimates to ulcer deaths, 2 deaths associated with ulcer haemorrhage might be found among 110,000 person-months of NSAID treatment. Though the risk of complications and deaths seems to be low for a taker of NSAID, the total number of complications and deaths is considerable because of the widespread drug use.

In the UK the number of prescriptions of NSAID more than doubled from 1967 to 1985 in both sexes and all age groups (Table IV). At the same time the number of female ulcer deaths due to duodenal ulcer rose by more than a 100% in those

Table IV Age-specific prescription rates for men and women receiving non-steroidal anti-inflammatory drugs (Prescriptions/1000)

Age-group (years)	Males		Females	
	1967	1985	1967	1985
20–39	76	177	89	229
40–64	202	535	307	804
65 +	289	961	490	1384

aged 55 and over. This trend coincides with the age-dependent increase in NSAID consumption which, as described earlier³ may in part account for the rise in perforation rates. The interpretation of this trend is, however, complicated, as NSAID consumption has also increased in males and in the young age-groups of both sexes in whom the frequency of ulcer deaths has fallen or remained stable. One could argue that elderly women are, in particular, affected by lethal ulcer complications

associated with NSAID-intake, because female prescription rates exceed those of males by more than 50%. This implies that women might receive a higher dosage of NSAID for a longer time period compared with males. We are, however, not in a position to examine this. The higher number of prescriptions issued to women is also obvious for the young age groups in females compared with males and does not explain the discrepancy of findings.

The rising ulcer mortality in elderly people has also been observed in Holland¹⁴ and West Germany,¹⁵ but not in the United States.¹⁶ The reason for these differences is unknown.

In summary, the trend in peptic ulcer mortality in relation to NSAID-intake suggests that the main proportion of ulcer deaths is not due to NSAID-intake. It remains unknown why elderly people, in particular older women, are more susceptible to the development of lethal ulcer complications which might, in part, be explained by the increased use of NSAID.

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