Research letters

Long-term prognosis in anorexia nervosa: lessons from a 21-year follow-up study

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In a prospective long-term follow-up of 84 patients 21 years after first hospitalisation for anorexia nervosa, we found that 50·6% had achieved a full recovery, 10·4% still met full diagnostic criteria for anorexia nervosa, and 15·6% had died from causes related to anorexia nervosa. Predictors of outcome included physical, social, and psychological variables.

Anorexia nervosa is a serious illness known to be associated with a chronic course and high mortality.[1] The outcome of this disease is difficult to predict. We did a long-term study to ascertain the influence of various medical, psychological, and social variables on prognosis.

A well-documented sample of 84 female patients with anorexia[2] were followed-up after an average of 21·3 (SD 2·9) years following first inpatient treatment. This sample of patients had been previously investigated after 3·6 and 11·7 years. At follow-up, 16·7% (n=14) of the patients had died. For these patients, causes of death were obtained from the attending physician. Of the remaining patients, 90% (n=63) completed a psychiatric interview, a physical assessment, and standardised psychological questionnaires. The average age at follow-up was 41·9 (SD 6·5) years. Ordered logistic regressions were done to identify predictors of outcome. Variables included in the analyses were chosen based on findings from previous reports.

Patients for whom data were available (n=77) were classified into three outcome groups as defined by scores on the psychiatric status rating scale (PSR),[3] which is based on DSM-IV[4] diagnostic criteria for anorexia nervosa. At follow up, 50·6% (n=39) of the patients were classified as having a good outcome (PSR=1), 20·8% (n=16) had an intermediate outcome (PSR=2, 3, or 4), and 26·0% (n=20) had a poor outcome. Of the patients with a poor outcome, all met full DSM-IV criteria for anorexia nervosa (PSR=5 or 6) at follow-up (n=8, 10·4%) or at the time of death (n=12, 15·6%). Two (2·6%) additional patients died from causes unrelated to anorexia nervosa (asthmatic attack and metastatic rectal carcinoma). Causes of death for the 12 patients that seemed to be associated with anorexia nervosa included: infection (bronchial pneumonia and sepsis, n=4), complications due to dehydration and electrolyte imbalance (n=3), and suicide (n=2). One patient died from generalised peritonitis after small intestinal perforation. Two patients died in an extremely malnourished state, but the exact causes of death are not known. The standardised mortality rate was 9·8.

At follow up, most patients meeting criteria for anorexia nervosa were classified as binge-eating/purging type (n=18), compared with restricting type (n=2). No patients met diagnostic criteria for bulimia nervosa at follow-up. In terms of medical comorbidity, chronic renal failure, necessitating haemodialysis, was found to be an important complication (n=4, 5·2%). Significant psychosocial differences existed between the outcome groups. For example, the patients with a poor outcome missed significantly more days of work per year (mean days missed=99 [SD 129], p<0·01) compared with the intermediate (40 [78·7]), and good (3·6 [6·5]) outcome groups. Results from the ordered logistic regressions showed that a long duration of illness before first admission to hospital was an important predictor for a poor outcome. Moreover, a low body-mass index, an inadequate weight gain during first hospitalisation, and severe psychological or social problems (subscales of the anorexia nervosa symptoms scores ANSS)[5] were additional risk factors for a poor outcome. Patients with the binge-eating/purging type seemed to have a higher risk of developing a poor outcome than those classified as restricting-type. However, the large CI of the odds ratio of this variable restricted its statistical value. Age at onset was not clearly associated with an increased risk for a chronic course (table).

Predictor variables (assessed at first admission)	Odds ratio (95% CI)	p
Duration (years)	1·34 (1·14–1·57)	<0·01
Body-mass index (kg/m²)	0·75 (0·59–0·95)	0·020
Anorexia nervosa binge-eating/purging type	2·53 (1·05–6·10)	0·038
Severity of psychological symptoms (psychological ANSS)	1·24 (1·05–1·46)	0·010
Severity of social problems (social ANSS)	1·22 (1·08–1·38)	0·001
Weight gain during first admission (kg)	0·89 (0·79–0·99)	0·046
Age at onset (years)	1·09 (0·97–1·21)	0·146

*The odds ratio indicates the odds of being grouped in a worse (>1) or better (<1) outcome group for each one-unit increase in the predictor variables.

Ordered logistic regressions for predicting outcome group 21·3 years after first hospitalisation

Statistical significance does not necessarily equal clinical significance, however, and it is important to note that from a clinical viewpoint, the variables in our model that were statistically significant have also been found to be clinically meaningful predictors of outcome. The low attrition rate and high rate of direct follow up support the representativeness of these findings to adult patients treated in an inpatient setting. Results from our search for prognostic factors suggested several recommendations for improving prognosis. The finding that a longer duration of illness before first inpatient treatment and a low body-mass index were associated with a poor outcome, emphasises the importance of early identification and intervention. The other prognostic findings suggest that clinicians should target social and psychological symptoms as well as adequate weight gain during treatment. The subclassification of anorexic patients according to DSM-IV into binge-eating/purging type versus restricting type seemed also to correlate with the long-term outcome. Because of the complex nature of the prognostic factors, we recommend that treatment of severely ill patients be handled by an experienced and multi-disciplinary treatment team.

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Tolerability and side-effects of post-exposure prophylaxis for HIV infection

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A study of HIV post-exposure prophylaxis in 28 recipients showed that indinavir-containing regimens were poorly tolerated. This finding has implications for compliance and efficacy of the currently recommended combinations.

Post-exposure prophylaxis with antiretroviral drugs is offered to health-care workers exposed to HIV-1 through inoculation injuries. This practice is supported by a case-control study showing that zidovudine seemed to lower the risk of HIV transmission after needlestick injury by about 70%.[1] Although there is no evidence to support the use of combination antiretroviral therapy in prophylaxis, multidrug regimens are proven to be more effective than monotherapy in established HIV-1 infection. This finding, in addition to concerns about the increasing prevalence of antiviral resistance, led to UK guidelines in 1997 recommending a three-drug combination of zidovudine, lamivudine, and indinavir as standard post-exposure prophylaxis.[2] There are few data on the tolerability and safety of combination regimens in non-HIV-1-infected people. The consideration of provision of prophylaxis after sexual or non-occupational exposure for HIV-1 infection[3] increases the importance of reviewing experience.

We studied retrospectively the use of post-exposure prophylaxis for occupational HIV-1 exposure in three London Hospitals (St Bartholomew's, the Royal London, and Homerton) from 1996 to January, 1999. 28 people had inoculation injuries from 27 patients. 24 of the source patients were proven HIV-1 positive, two (the source of three injuries) were later shown to be HIV-1 negative, and one was not tested for HIV-1. Most known HIV-1-infected sources had advanced HIV-1 disease, with a median viral load of 77 500 copies/mL HIV-1 RNA. 16 had experience of antiretroviral drugs. All had received at least one drug in the currently recommended regimen of post-exposure-prophylaxis, seven of 16 had received two, and three of 16 had received all three drugs. Experience of these drugs increased towards the end of the study period, which reflects the more generalised use of protease inhibitors.

Side-effect	Indinavir-containing regimen (n=19)	Non-indinavir-containing regimen
Nausea and vomiting	14 (74%)	0
Fatigue	8 (42%)	1 (11%)
Influenza-like illness	2 (11%)	1 (11%)
Rash (urticaria)	2 (16%)	0
Unpleasant taste	2 (11%)	1 (11%)
Headache	2 (11%)	0
Reflux	1 (5%)	0
Retrosternal pain	1 (5%)	0
Diarrhoea	0	1 (11%)
Fever	1 (5%)	0
Galactorrhoea	1 (5%)	0
Dysuria, crystaluria, haematuria	2 (11%)	0
Hyperbilirubinaemia	1 (5%)	0
None	2 (11%)	5 (56%)

Side-effects during prophylactic treatment

18 recipients of prophylactic treatment were prescribed the recommended combination therapy with zidovudine, lamivudine, and indinavir. Other triple regimens used were: zidovudine, didanosine, and indinavir in one recipient; zidovudine and saquinavir with lamivudine (two recipients), stavudine (one), or didanosine (one); and zidovudine, lamivudine, and nelfinavir (one). Four received treatment with mono or dual nucleoside analogue regimens containing zidovudine, didanosine, or lamivudine. Regimens not following the UK guidelines either predated June, 1997, or used alternative drugs because of suspicion of drug resistance in the source of the injury, or because a three-times-daily regimen was not acceptable (one individual) during a religious fast.

15 of the 28 individuals completed the recommended course of antiretroviral therapy. 13 stopped or changed therapy: four because the injury was reassessed as low risk; nine because of intolerable side-effects. All were on regimens that included indinavir. The reasons for stopping or changing were: uncontrollable vomiting, nausea (despite antiemetics), or reflux (seven); urticaria temporally related to indinavir (one); and galactorrhoea with hyperprolactinaemia (one). These side-effects were probably associated with indinavir, since all resolved when indinavir alone was withdrawn (with the exception of reflux, in which all therapies were stopped in one case). Other side-effects were more frequent in regimens including indinavir (table). The poor tolerability of such regimens was reflected in sickness absence—30% (six) of the 19 who started with indinavir needing more than 2 weeks off work. In the other regimens only one individual required more than 7 days' leave. The reason for the increased severity of side-effects compared with those in HIV-1-infected individuals[4] is unclear, but could partly reflect the anxiety associated with innoculation injuries.

In our experience, post-exposure prophylaxis regimens that include indinavir are poorly tolerated, which affects adherence; persistent vomiting may lessen the effect of other drugs in the regimen or individuals may be forced to stop drugs because of the severity of side-effects, some of which are potentially serious. The costs of providing medical support because of staff absence due to side-effects are substantial, as are the personal costs to those who have such injuries. Although any multidrug combination is likely to cause adverse effects, it seems timely to question the routine use of indinavir in prophylaxis if our findings are common. Other protease inhibitors and non-nucleoside analogues may be better tolerated. The question of whether multiple agents are necessary in post-exposure prophylaxis remains outstanding. Viral resistance is an issue that may favour combination therapy. Our data show that the source of an HIV-1-inoculation injury is increasingly likely to have experience of antiretroviral treatment. 9% of sexually transmitted infections have been shown to be with viruses showing at least single-agent resistance.[5] However, the mechanism by which prophylactic treatment works to prevent infection may be different to that involved in controlling continuing infection, and the amount of virus involved is generally low. The balance needs to be struck between giving complex therapies that may lead to poor adherence and giving adequate therapy to protect the individual. In addition, we need to continue to monitor what further actions can be taken to prevent inoculation injuries in the first place.

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