Depression in COPD – management and quality of life considerations

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Abstract: Depression is common in COPD patients. Around 40% are affected by severe depressive symptoms or clinical depression. It is not easy to diagnose depression in COPD patients because of overlapping symptoms between COPD and depression. However, the six-item Hamilton Depression Subscale appears to be a useful screening tool. Quality of life is strongly impaired in COPD patients and patients' quality of life emerges to be more correlated with the presence of depressive symptoms than with the severity of COPD. Nortriptyline and imipramine are effective in the treatment of depression, but little is known about the usefulness of newer antidepressants. In patients with milder depression, pulmonary rehabilitation as well as cognitive-behavioral therapy are effective. Little is known about the long-term outcome in COPD patients with co-morbid depression. Preliminary data suggest that co-morbid depression may be an independent protector for mortality.

Keywords: COPD, depression, quality of life, epidemiology, survival, antidepressants

Introduction

It is recognized that many physical illnesses may have a direct link to the appearance of depressive syndromes and many studies have documented a high rate of depression and anxiety among patients suffering from COPD (Yellowlees et al 1987; Karajgi et al 1990; van Ede et al 1999; Aghanwa and Erhabor 2001; Dowson et al 2001; Mikkelsen et al. 2004). COPD is a severe treatment-resistant pulmonary disease with varying impact on the patient's general physical condition, functioning, and quality of life. It is assumed that a successful treatment of a co-morbid depression leads to improved quality of life and less restricted general functioning (Rodin et al 1991). However, the evaluation of psychopathology in medical patients, eg, those with COPD, presents special problems. Almost all self-report and clinicians' rating scales for detecting depression is biased by a large number of items dealing with somatic symptoms. For example, the Hamilton Depression Scale (Ham-D) (Hamilton 1960; Hamilton 1967) has eight or nine items reflecting somatic complaints or changes in somatic functioning. Such items are also included in the official diagnostic criteria for depression, ie, ICD-10 (WHO 1992) and DSM-IV (APA 1994). Therefore, it is difficult to decide when these somatic symptoms are secondary to depression and when they are a secondary to the somatic illness.

This review will focus on our knowledge about epidemiology, diagnostic procedures, treatment aspects, and quality of life in COPD patients with co-morbid depression. We will also summarize recent findings concerning how the interaction between depression and COPD may affect patients' survival.

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Prevalence and co-morbidity

The prevalence of depressive symptoms in COPD patients varies considerably. Two recent reviews (van Ede et al 1999; Mikkelsen et al 2004) found a prevalence of depression, ranging from 6% to 57%.

Van Ede et al (1999) found a prevalence ranging from 6% to 42%. They emphasized that only 4 out of 34 studies had a control group (McSweeny et al 1982; Prigatano et al 1984; Isoaho et al 1995; Engstrom et al 1996). However, all four studies showed that the prevalence was higher in the study group, ie, the COPD patients, but the difference was statistically significant in two of the studies only (McSweeny et al 1982; Prigatano et al 1984).

Mikkelsen et al (2004) pointed out that two of the latest prevalence studies identified clinically significant depressive symptoms in 42%–57% of COPD patients (Yohannes et al 2000; Lacasse et al 2001). The major co-morbidity studies are summarized in Table 1.

There are many possible explanations for these differing results. Many studies are performed on small samples and are lacking control groups. The way the psychiatric diagnoses are obtained also varies. Some studies utilize established diagnostic criteria, other studies only use clinical assessments or self-reported symptoms. Most studies contain no formal data analysis and only simple descriptive statistics. Finally, differences in the objective characteristics and severity of COPD may contribute to the variations in prevalence figures.

In summary, the prevalence of depression is high in COPD patients, for both occurrence of "significant symptoms" and clinical depression. Although there are large variations in prevalence figures, the latest studies point out a prevalence of more than 40% (Yohannes et al 2000; Stage et al 2003).

Quality of life

According to McSweeny et al (1982), quality of life is concerned with the following four dimensions: emotional functioning, social-role functioning, activities of daily living (ADL), and recreational pastimes.

Compared with persons without physical illness, COPD patients have impaired quality of life (McSweeny et al 1982; Prigatano et al 1984; Yohannes et al 1998).

COPD patients with co-morbid depression have impaired quality of life compared with COPD patients without depression (Bosley et al 1996; Yohannes et al 1998; Kim et al 2000; Aydin and Ulusahin 2001; Felker et al 2001; Yohannes et al 2003). Yohannes et al (2003) also showed that COPD patients' quality of life was more correlated to the presence of depressive symptoms than to the severity of COPD as measured by FEV_1. This phenomenon was also demonstrated by Kim et al (2000). In a different study 28 patients were followed over 4 years, but even though their physical condition got better because of aggressive medical treatment, no improvement in quality of life was shown (van Schayck 1997).

In spite of this, co-morbid depression does not seem to worsen the physical aspects of COPD (Light et al 1985; Borak et al 1998). For example Light et al (1985) found no significant correlation between the level of depression or anxiety and the distance that the patient could walk in 12 minutes.

Diagnostic aspects

Today, the ICD-10 and DSM-IV criteria for depression are the most common diagnostic tools. When it comes to depression in patients with severe somatic illness, the validity of the ICD-10 and DSM-IV criteria for depression may to a certain degree be questioned because it is difficult to decide when somatic symptoms are secondary to depression and when they are secondary to somatic illness. In fact, the ICD-10 has a general exclusion criterion that the depressive episode is not attributed to any organic cause, while the DSM-III-R/IV is less restrictive on the matter. Severe COPD could lead to somatic symptoms impossible to separate from depressive symptoms. Endicott (1984) has therefore suggested replacement of the somatic symptoms in the DSM-III-R/IV criteria with alternative non-somatic depressive symptoms, ie, replace change in appetite–weight with tearfulness–depressed appearance, sleep disturbances with social withdrawal, fatigue or loss of energy with brooding–pessimism, and diminished ability to think or concentrate with lack of reactivity to environmental events. These modifications have to some extent been validated (Rapp and Vrana 1989; Kathol et al 1990) and may be they should be used when trying to identify depression in subjects with somatic illness. However, as long as there is no method for deciding whether the somatic symptoms are secondary to depression or COPD, the classification will be biased.

In a recent study, we tested the internal and external validity of the six-item Hamilton Depression subscale (HAM-D-6) in a sample of 49 COPD patients (Stage et al 2003). We found that HAM-D-6 could be used as a screening instrument for depression in COPD patients, ie, the sensitivity of the test was 0.91, the specificity was 0.88, the positive predictive value 0.87, and the negative predictive value was 0.91 when the cut-off score was set to 7 or more on HAM-D-6. The HAM-D-6 items are shown in Table 2. If the HAM-D-6 total score is 10 or more, treatment with an antidepressant is often required.

Table 1 Summary of co-morbidity studies: Prevalence of psychiatric co-morbidity in COPD patients

Author	Sample/control group	Psychiatric assessment methods	Findings
McSweeny et al 1982	203 COPD, nocturnal oxygen treatment 73 healthy controls (HC)	Self-report: MMPIPOMS, SIP	Depression 42% in COPDvs 9% in HC
Prigatano et al 1984	985 COPD outpatients 25 HC	Self report: POMS, SIP	No prevalence figures. POMS anxiety and depression score significantly higher in COPD group
Yellowlees et al 1987	50 COPD inpatients with exacerbation	Psychiatric interview: DSM-III diagnoses	Panic anxiety 24% Generalized anxiety 10% Depression 12%
Karajgi et al 1990	50 COPD outpatients	Psychiatric interview: DSM-III diagnoses	Anxiety disorders 16% Mood disorders 8%
Isoaho et al 1995	82 COPD community sample 246 HC	Self-report: Zung Depression Scale	Depression, men 26% vs 18% Depression, women 33% vs 20%, Differences non-significant
Engstrøm et al 1996	68 COPD in- and outpatients 89 HC	Self-report: HADS	Depression 7% vs 1% Anxiety 13% vs 6% Differences significant
Yohannes et al 2000	137 COPD outpatients	Psychiatric interview and self-report: MADRS Geriatric Mental Health Scale	Clinical depression in 42% 2/3 of these patients moderately depressed (MADRS)
Dowson et al 2001	79 COPD inpatients	Self-report:HADS	Depression 28% Anxiety 50%
Lacasse et al 2001	109 COPD, home care	Self-report: SF-36 GDS	Depressive symptoms 57%
Aghanwa and Erhabor 2001	30 COPD outpatients 30 hypertensive patients 30 HC	Self report and interview: GHQ-30 PSE	Depression 16.7% anxiety 10% in COPD group Significantly less in control groups
Aydin and Ulusahin 2001	38 COPD inpatients 120 tuberculosis patients	Self report: GHQ-12	Depression and/or anxiety 47.3% Prevalence 19%–26% in control group Differences significant
Stage et al 2003	49 COPD outpatients	Psychiatric interview: ICD-10 diagnoses Hamilton Rating Scales for anxiety and depression	Major depression 33% Mild depression 14%

Abbreviations: GDS, Geriatric Depression Scale; GHQ, General Health Questioner; HADS, Hospital Anxiety and Depression Scale; HC, healthy controls; MADRS, Montgomery-Asberg Rating Scale; MMPI, Minnesota Multiphasic Personality Intervention; POMS, Profile of Mood States; SIP, Sickness Impact Profile.

Treatment of depression in COPD patients

Antidepressants

The tricyclic antidepressants (TCAs) have been tested in a few studies (Light et al 1986; Sharma et al 1988; Borson et al 1992). Although the results are contradictory, there is some evidence that TCAs are effective. Borson et al (1998) studied 30 patients who completed a 12-week, randomized, controlled trial of nortriptyline. Nortriptyline was clearly superior to placebo for treatment of depression. Nortriptyline treatment was accompanied by marked improvements in anxiety, certain respiratory symptoms, overall physical comfort, and day-to-day function; placebo effects were negligible. Physiological measures reflecting pulmonary insufficiency were generally unaffected by treatment. It has also been shown that imipramine in combination with diazpam is effective (Sharma et al 1988), while doxepine failed in a placebo-controlled trial (Light et al 1986). Table 3 shows treatment information about imipramine and nortriptyline. Note that

Table 2 The six-item Hamilton Depression subscale (HAM-D-6)

1. Depressed mood
2. Guilt feelings
3. Work and interest
4. Retardation
5. Psychic anxiety
6. General somatic

Table 3 Treatment information about the tricyclic antidepressants (TCAs) imipramine and nortriptyline: the decision to start a TCA treatment balances the documented efficacy and the increased risk of side-effects in elderly patients

Effect	Better than placebo in randomized controlled trials
Dose in elderly patients	Imipramine: 50–100 mg/day Nortriptyline: 25–75 mg/day Start low – go slow!
Recommended plasma levels at steady state	Imipramine (plus desipramine): 175–350 ng/ml Nortriptyline: 50–150 ng/ml
Examples of common side-effects	Orthostatic hypotension (less common with nortriptyline), dizziness, tachycardia, dry mouth, blurred vision, disturbance of accommodation, constipation, and drowsiness
Examples of less common side-effects	Arrhythmias, heart block, confusional states, seizures, urinary retention, paralytic ileus, drug fever, skin rash, bone marrow depression, altered liver function, hypomania, and falls. Increased mortality in patients with ischemic heart disease. Pre-existing heart block gets worse during treatment
Pre-treatment examinations	Physical examination Measurement of orthostatic hypotension ECGBlood tests including liver enzymes

Table 3: Key points

- Around 40% of all COPD patients have severe depressive symptoms or clinical depression
- The six-item Hamilton Depression Subscale seems to be a useful screening tool
- Quality of life is strongly impaired in COPD patients and is more correlated with the presence of depressive symptoms than to the severity of COPD
- Nortriptyline, imipramine, pulmonary rehabilitation. and cognitive-behavioral therapy are effective treatment options
- Preliminary data suggest that co-morbid depression may be an independent protector for mortality
- Much more research is needed in this field

the doses of imipramine and nortriptyline are lower than in patients without co-morbid COPD, mainly because most COPD patients are elderly. Treating elderly patients with TCAs like imipramine and nortriptyline is not unproblematic due to an increased risk of severe side-effects. The decision to start a TCA treatment balances the documented efficacy and the increased risk of side-effects in elderly patients.

Little is known about the effectiveness of newer antidepressants like the selective serotonin reuptake inhibitors (SSRIs) but smaller studies and case reports suggests that SSRIs are well tolerated although the compliance may be poor (Papp et al 1995; Smoller et al 1998; Yohannes et al 2001).

Benzodiazepines and other drugs

Benzodiazepines have anxiolytic effect in COPD patients (Nutt et al 1999), but may cause respiratory depression. Therefore, benzodiazepines should be considered only if other anxiolytic agents have failed.

Buspirone has been tested in COPD patients, but the results are not conclusive (Argyropoulou et al 1993; Singh et al 1993).

Non-pharmacological treatment

In general the non-pharmocological treatment of depression in COPD is limited to patients with milder depression and here multidisciplinary pulmonary rehabilitation as well as cognitive-behavioral therapy (CBT) appears effective (Borson et al 1998).

CBT for this group of patients includes increasing the patients' body-awareness by exercises in relaxation and breathing. The cognitive elements of the treatment are aimed at identifying automatic thoughts and promote a more adaptive cognitive style. Graduated exposure and desensitizing is then attempted to reduce fears of symptoms as well as alleviating the panic reactions. Eiser et al (1997) found that six sessions of CBT resulted in sustained improvement in exercise tolerance in patients suffering from severe COPD and anxiety. In a recent randomized clinical trial (Kunik et al 2001), a single 2-hour session of group CBT and weekly calls over 6 weeks reduced both depressed mood and anxiety. The effect was significantly better than in the control group (2-hour education and weekly calls). There were no improvements in physical functioning in either group.

Pulmonary rehabilitation programs have also been described for COPD patients for co-morbid anxiety and depression. By means of progressive exercise, training of respiratory function, and psycho-education, patients obtained better exercise tolerance, less dyspnea, and better quality of life (Ries et al 1995; Emery et al 1998; Withers et al 1999; de Godoy and de Godoy 2003; Garuti et al 2003).

Does depression affect the long-term outcome in COPD patients?

Few studies have examined the long-term outcome of depressed COPD patients. Yet we recently published a study focusing on the survival in COPD patients (Stage et al 2005). We found that co-morbid depression significantly reduced the mortality risk at follow-up. The impact of depression remained after control for FEV_1, the only multivariate significant predictor of mortality in the data set (hazard ratio, 0.27; 95% confidence interval, 0.09–0.84; p=0.024). The cumulative mortality for depressed and non-depressed COPD patients is shown in Figure 1. We concluded that depression appears to be an independent protector for mortality, although we have no clues about the underlying mechanism. However, the study included only 49 patients and it should be replicated in a larger sample.

Conclusion

Depression is very common in COPD patients. Around 40% are affected by severe depressive symptoms or clinical depressions. It is not easy to diagnose depression in COPD patients because of the overlapping symptoms between COPD and depression. However, the six-item Hamilton Depression Subscale (HAM-D-6) appears to be a useful screening tool. Quality of life is strongly impaired in COPD patients and patients' quality of life emerges to be more correlated with the presence of depressive symptoms than with the severity of COPD. Nortriptyline and imipramine are effective in the treatment of depression, but little is known about the usefulness of newer antidepressants. In patients with milder depressionm, pulmonary rehabilitation as well as cognitive-behavioral therapy seem effective. Little is known about the long-term outcome in COPD patients with co-morbid depression. Preliminary data suggest that co-morbid depression may be an independent protector for mortality.

Much more research is needed concerning epidemiology, psychopathology, quality of life, treatment, and long-term outcome.

The key points of this review are shown in Table 3.

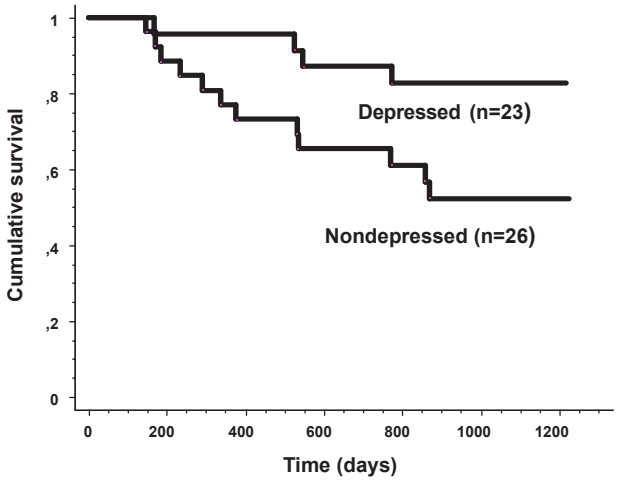

Figure 1 Cumulative mortality for depressed and non-depressed COPD patients. Reprinted from Stage KB, Middelboe T, Pisinger C. 2005. Depression and chronic obstructive pulmonary disease (COPD). Impact on survival. *Acta Psychiatr Scand*, 111:320–3. Copyright © 2005 with permission from Blackwell Publishing.

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