Comorbidity of Eating Disorders with Suicidality and Treatment Resistant Depression

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Depressive symptoms are common during the course of AN and could have different meanings.

1) we can distinguish symptoms that are inherent to AN and which can be mistaken for depressive signs (e.g. low self-esteem, reduced social contacts)

2) long-term undernourishment can be held responsible for numerous psychological distortions, including anxiety and depression symptoms such as insomnia, impaired concentration, or social isolation.

3) natural course of AN can also lead to “depressive moments,” in particular when switching to a “purging type” AN, or when recovery mobilizes control and narcissistic issues.

MDD is also highly prevalent among AN patients and is a negative prognosis factor.

It is complex to differentiate MDD from isolated depressive symptoms that could be inherent of the AN symptomatology which raises the question of the role of antidepressant medication in treatment of depression in AN.

No significant benefit of antidepressant medication in AN has been shown in clinical trials, and according to international guidelines it should be prescribed only as a second-line treatment, after appropriate refeeding, and in case of an authentic depressive disorder.

The clinical challenge lies in the differentiation of the depressive symptoms that are transitory and likely to improve without medication from those that signal the presence of an MDD.

3 criterion could be indicative of MDD:

1) family history of mood disorder, as it is a major risk factor for MDD among relatives;

2) the chronology of appearance of both disorders, when MDD pre-exists AN;

3) a few specific symptoms cannot be attributed to undernourishment or reactive depressive signs, such as morning insomnia, daily variation of depressive symptoms, suicidal attempts or ideation and guilt ideation.

Pragmatic therapeutic strategy for the use of AD in AN during adolescence for depressive manifestations in AN:

1) therapeutic emergencies: when an obvious and severe MDD is comorbid to AN, immediate antidepressant would be required;

2) isolated and non-specific depressive sign: no medication would be relevant as they are supposed to improve with refeeding and psychotherapeutic support;

3) intermediary patterns most frequent: to abstain from prescribing medication in first line, but an AD medication should be quickly considered in the presence of one (or several) MDD criterion and its persistence despite refeeding. The general medical state of this fragile population of patients should be evaluated (standard blood test, ECG) before and during treatment.

MDD and AN

Psychological autopsy studies have found that 30%-90% of individuals who die from suicide suffered from MDD (Isometsa, 2001).

MDD is common in AN: 50-75% of individuals with AN experience lifetime MDD (Calugi et al., 2014; Fernández-Aranda et al., 2007; Mischoulon et al., 2011; Rastam, Gillberg, & Gillberg, 1995; Wade et al., 2000) which may be a risk factor for suicide in AN (Preti et al., 2011).

Individuals with an ED who attempt suicide are more likely to have a lifetime history of MDD than individuals with an ED who do not attempt suicide (Henderson et al., 2005; Bulik et al., 2006; Grilo et al., 2006; Steiger et al., 1999).

In fact, over 80% of individuals with AN who attempted suicide reported that their last attempt occurred during an episode of MDD (Bulik et al., 2006).
**MDD and ED**

- Eating disorders co-occur with depression 37% of the time and often are missed by the clinician. Patients with ED may be at risk for noncompliance because of fears of weight gain associated with some AD therapies.
- Suicide risk is a concern with severely depressed patients, up to 80% will report suicidal ideation. In two studies that compared patients with and without treatment resistance, suicide attempts were more common in the treatment-resistant group.
- Severely ill patients do tend to be less responsive to psychotherapy alone. In a meta-analysis by Thase and colleagues, patients with severe and recurrent illness reported significantly better to combination treatment with medications and psychotherapy than to psychotherapy alone.

- According to data from the NIMH Collaborative Depression Study, about 20% of patients with major depressive disorder will develop a chronic course of illness. For patients with recurrent depression, this same risk of chronicity persists with each new episode of depression.

**Prognosis**

- Only 25% of bulimics and 16% of AN where making full recovery when measured on strict criteria (Von Holle et al., 2008)
- Significant numbers of children with ED are being missed, misdiagnosed, treated too late or too weakly (BBC, 2013)
- Patients spend many years at low but medically safe weight during which time the psychopathology becomes chronic and unreachable by therapy.
- AN has to be treated vigorously early in adolescence or it is likely to become severe and enduring.

**Treatment SE-ED**

- Tailoring treatment (Touyz et al., 2013)
- As weight phobia is pathognomonic, any treatment that prioritizes weight gain above all else will lead to avoidance and premature termination at the first opportunity.
- Rather than recovery being basic premise, should focus more upon retention, engagement, improved quality of life with harm minimizing (Strober, 2009; Williams et al., 2010)

- Modified CBT for AN (Pike et al., 2003) has demonstrated efficacy for relapse prevention for adult AN. Active treatment aimed restoring normal eating habits by challenging underlying beliefs and through cognitive restructuring and change in behavior, planned “homework”, set clear aims.
- Modified specialist supportive clinical management (SSCM) has shown promise in adult AN (McIntosh, Jordan & Bulik, 2010). Aimed to education, advice, care, support without mandating change.
Treatment SE-ED
- CBT-AN & SSCM for SE-DE with significant emotional, social and medical problems, 34 age/17 years of illness (Touyz et al., 2013). Only 12% prematurely terminated treatment, which suggests that focus on quality of life rather than target weight was more acceptable to SE-AN patients.
- Both treatment groups significant improvement in quality of life measures, mood disorder symptoms, social adjustment.
- Improvement in areas outside the core pathology can significantly improve their quality of life, causing a domino effect on patients well-being and disease burden, which will in turn further motivate and enable them to make progress on their core ED symptoms.

Pharmacological treatment
- AD for overlapping symptoms, and possibly common neurobiological roots (e.g. serotonin dysfunction) among AN, depression (e.g. low mood, loss of interest, social isolation), and OCD (e.g. preoccupation, rituals)
- Olanzapine, a 5HT2/D2 receptor antagonist (blocks serotonin [5HT] and dopamine [D] neurotransmission at postsynaptic receptor site) – was favored for effect on reduction of ED ruminations (Mondraty et al., 2005)
- Bissada et al., 2008 reported greater reduction in obsessive symptoms, regained weight more quick and more likely to reach BMI> 18 compared with placebo for ten weeks (87.5% vs 55.6%)

Pharmacological treatment
- Lebow et al.(2013) reported improvement of mood but possible worsening of anxiety, and Kishi et al., (2012) described increased adverse effects as drowsiness and sedation with AP.
- Moore et al.,(2013) increased symptoms of binge eating have been mentioned with use of AP.

Cochrane AD for AN
- Review evaluated the evidence from RCT for the efficacy and acceptability of AD treatment in acute AN. Seven small studies were identified; four placebo-controlled trials did not find evidence of efficacy of antidepressants in improving weight gain, eating disorder or associated symptoms, as well as differences in completion rates.

Cochrane AD for AN
- A lack of quality information precludes us from drawing definite conclusions or recommendations on the use of antidepressants in acute AN. Future studies testing safer and more tolerable antidepressants in larger, well designed trials are needed to provide guidance for clinical practice.

Cochrane: Antidepressants and psychological treatments, alone or combined, for bulimia nervosa
Cochrane BN

- Psychotherapeutic approaches, mainly CBT, and AD medication are the two treatment modalities that have received most support in controlled outcome studies of bulimia nervosa. Using a more conservative statistical approach, combination treatments were superior to single psychotherapy.

- The number of trials might be insufficient to show the statistical significance of a 19% absolute risk reduction in efficacy favoring psychotherapy or combination treatments over single AD.

- Psychotherapy appeared to be more acceptable to subjects. When AD were combined with psychological treatments, acceptability of the latter was significantly reduced.

- The use of a single AD agent was clinically effective for the treatment of BN when compared to placebo, with an overall greater remission rate but a higher rate of dropouts.

- No differential effect regarding efficacy and tolerability among the various classes of antidepressants could be demonstrated.

Cochrane BN

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Zinc

- Severe malnutrition combined with excessive exercising may lead to Zinc deficiency in AN, in turn possibly serve to maintain the illness through dysregulation of serotoninergic and GABAergic neurotransmission, as these processes require zinc (Birmingham et al., 1994, Birmingham & Gritzner, 2006).

Treatment BMD

- Etiology of bone loss in AN is multifactorial. In addition to nutritional deficiencies and reduced estrogen and progesterone, relative hypercortisolism and low levels of insulin-like growth factor (IGF-1), a correlate for bone formation observed.

- Benefits seen in postmenopausal osteoporosis administering hormone replacing therapy (HRT) in AN remain controversial, no benefit of oral contraceptive (OC) on BMD.

- RCT (Misra et al.,2011) physiologic transdermal estrogen replacement (100mcg 17beta-estradiol, with cyclic progesteron) on BMD in adolescents with AN was first study to report both spine and hip BMD Z-scores increased significantly over time in patients treated with estrogen in comparison to placebo.

- Bisphosphonates (alendronate) increase BMD in AN, especially in adults. Miller et al. (2011) showed more favorable with risedronate, either alone or in combination with low-dose testosterone (no added effect of testosterone).
Neuromodulation in AN

- “Bottom-up” sensory-hedonic-motivational drive to consume food combined with enhanced inhibitory abilities — deep brain stimulation, rTMS
- rTMS especially with comorbid depression (high frequency 10Hz at 110-120% of the motor threshold delivered over the left DLPFC 26-8 weeks maintenance twice rTMS sessions) BMI increase by 4 points, reduction of feeling of fullness, fatness, and anxiety, depression.

Conclusions on biological interventions in SE-ED

- Reduction of comorbid psychiatric pathology that may increase resistance to treatment, or interventions that may improve general health parameters (nutritional and medical stability), with or without weight gain, and other improvements to global functioning and quality of life, should be goals of biological intervention.

Assessment data on 11,588 adult men and women presenting to specialist ED clinics in Sweden between 2008 and 2012

- 71% of the patients with ED had at least one other Axis I disorder.
- The most common type of diagnosis was anxiety disorders (53%), where generalized anxiety disorder was the most common diagnosis.
- The highest levels of comorbidity were found for women with Binge Eating Disorder (BED) and men with Bulimia Nervosa (BN). High prevalence of psychiatric comorbidity in both men and women with ED.

BD with vs. without ED

- Outpatients referred to Stanford University BD Clinic during 2000-2011 were assessed with the Systematic Treatment Enhancement Program for BD (STEP-BD) affective disorders evaluation, and while receiving naturalistic treatment for up to 2 years, were monitored with the STEP-BD clinical monitoring form. Patients with vs. without lifetime EDs were compared with respect to prevalence, demographic and unfavorable illness characteristics/current mood symptoms and psychotropic use, and longitudinal depressive severity.
Among 503 BD outpatients, 76 (15.1%) had lifetime EDs, associated with female gender, and higher rates of lifetime comorbid anxiety, alcohol/substance use, and personality disorders, childhood BD onset, episode accumulation (≥ 10 prior mood episodes), prior suicide attempt, current syndromal/subsyndromal depression, sadness, anxiety, and antidepressant use, and earlier BD onset age, and greater current overall BD severity.

Among currently depressed patients, 29 with compared to 124 without lifetime EDs had significantly delayed depressive recovery. In contrast, among currently recovered (euthymic ≥ 8 weeks) patients, 10 with compared to 95 without lifetime EDs had only non-significantly hastened depressive recurrence.

Mortality in AN is amongst the highest of all psychiatric disorders (Hoang, Anthony, & James, 2015), with suicide being one of the leading causes of death and implicated in about 20% of deaths (Acles et al., 2011). According to a recent meta-analysis, individuals with AN have an 18.1 (95% confidence interval (CI): 11.5, 28.7) times higher risk of dying from suicide than the general population of females aged 15–34 years (Keshaviah et al., 2014). Although the suicide rate in those with AN may be declining in recent decades (Prelli et al., 2011), it remains substantially elevated compared with the general population (Piseslav et al., 2013).

Behavioral genetic methods explicate the Genetic factors contribute to the liability to AN, MDD, and suicide (Bulik et al., 2010; Hawton, Saunders, & O'Connor, 2010; Kendler et al., 2006). Study by Wade et al. (Wade et al., 2015) gave a glimpse into the relation among broadly defined ED (including AN, bulimia nervosa, binge eating disorder, and purging disorder), MDD, and broadly defined suicidality (ranging from transitory thoughts to suicide attempts). Their model revealed a common genetic influence on eating disorders and suicidality (but not MDD), and no appreciable influence of common environmental factors.

Suicide and ED

Suicide is a global problem. In 2012, suicide was the second leading cause of death among 15–29 year olds (World Health Organization, 2015) and the leading cause of death among 15–19 year old females (Patton et al., 2009). The World Health Organization estimates that 800,000 people worldwide end their lives by suicide each year. 90% of individuals who commit suicide are believed to suffer from psychiatric disorders (Hawton & van Heeringen, 2009), with anorexia nervosa (AN) and major depressive disorder (MDD) among the disorders with the highest risk (Cheesney, Goodwin, & Fazel, 2014).

Additionally, the lifetime prevalence of SA in patients ranges from 3.0%–29.7% (Bulik et al., 2008; Forcano et al., 2011; Franko & Keel, 2006; Runfola et al., 2014).

According to the Interpersonal Theory of Suicide, an individual has to have both an increased fearlessness about death and an increased tolerance to pain in order to be capable of attempting suicide (Ribeiro et al., 2014). The repeated exposure to pain via restriction (Selby et al., 2010) coupled with decreased pain sensitivity (whether acquired or inborn) (Papezová, Yamamotová, & Uher, 2005) may contribute to the increased prevalence of SA in this population.

Anorexia Nervosa, Major Depression, and Suicide Attempts: Shared Genetic Factors

Participants were women from monozygotic (MZ) and same-sex dizygotic (DZ) twin pairs who participated in the Swedish Twin Study of Adults Genes and Environment (STAGE). STAGE, a population-based prospective study of Swedish twins born 1959–1985, assessed more than 30 different health and demographic topics (Furberg et al., 2008; Lichtenstein et al., 2006). Data were collected on-line in 2005; twins were between 20 and 47 years old.
Final sample for modeling included 6,899 women from MZ and same-sex DZ twin pairs. There were 1,651 MZ and 1,109 DZ pairs with complete data, 256 MZ and 245 DZ pairs with incomplete data, and 222 MZ and 155 DZ individuals with no cotwin information. The mean (SD) age of the sample was 33.0 (7.6) years.

The prevalence of each disorder was: AN = 3.6% (n = 245), MDD = 26.2% (n = 1,659), and SA (including suicide completions) = 1.9% (n = 128). A total of 226 women (3.3%) met criteria for AN and MDD, 17 (0.2%) had AN and SA, and 90 (1.3%) had MDD and SA. Fifteen women had a lifetime history of all three phenotypes. No differences in prevalence between MZ and DZ twins were observed for AN ($\chi^2 = 1.31, p < .26$), MDD ($\chi^2 = 0.11, p < .74$), or SA ($\chi^2 = 0.53, p < .58$). The phenotypic correlations were .34 (95% CI: .27, .41), .30 (95% CI: .18, .42), and .50 (95% CI: .42, .57) for AN-MDD, AN-SA, and MDD-SA, respectively.

This study sheds light on factors that underlie the commonly observed phenomenon of comorbid AN, MDD, and SA and points to mechanisms that implicate shared genetic factors in their co-occurrence.

The authors found that ED are associated with increased risk for suicidality and the comorbid pattern appeared to be almost entirely explained by shared genetic factors.

Although results from multivariate twin modeling show that genetic factors account for a large part of the liability of the three traits, unique environmental factors (including measurement error) account for essentially all the remaining liability. Common environmental factors play a negligible role in liability to any of the three traits.

Comorbidity of AN and SA that require clinical care is largely due to genetic factors. This is in contrast to AN and MDD, where the unique environmental correlation is substantial.

Shared biology could underlie the frequency with which suicide attempts occur in individuals with AN. Clinicians should screen for a family history of SA in individuals with AN, regardless of lifetime MDD status, alert to be vigilant for signs of suicide.

Quantifying the contribution of genetic and environmental factors to AN, MDD, and SA lends evidence to explanatory models that account for their co-occurrence. This models provide valuable insight into the association among these traits and to factors that contribute to the lethality of AN.

Among 503 BD outpatients, 76 (15.1%) had lifetime EDs, which were associated with female gender, and higher rates of lifetime comorbid anxiety, alcohol/substance use, and personality disorders, childhood BD onset, episode accumulation (≥10 prior mood episodes), prior suicide attempt, current syndromal/subsyndromal depression, sadness, anxiety, and antidepressant use, and earlier BD onset age, and greater current overall BD severity.

Among currently depressed patients, 29 with compared to 124 without lifetime EDs had significantly delayed depressive recovery. In contrast, among currently recovered (euthymic ≥8 weeks) patients, 16 with compared to 95 without lifetime EDs had only non-significantly hastened depressive recurrence.

Among BD patients with vs. without comorbid lifetime EDs, those who were currently depressed had significantly delayed depressive recovery, although those who were currently recovered had only non-significantly hastened depressive recurrence.

Among BD outpatients, comorbid lifetime EDs were common, and were associated with female gender and higher rates of multiple BD unfavorable illness characteristics, including comorbid anxiety, alcohol/substance use, and personality disorders, childhood onset, episode accumulation, prior suicide attempt, and current syndromal/subsyndromal depression, sadness, anxiety, and antidepressant use, as well as earlier BD onset, and greater current overall illness severity.

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What predicts suicide attempts in women with eating disorders?

- 15% of subjects reported at least one prospective suicide attempt over the course of the study. Significantly more anorexic (22.1%) than bulimic subjects (10.9%) made a suicide attempt.

Multivariate analyses indicated that the unique predictors of suicide attempts for anorexia nervosa included the severity of both depressive symptoms and drug use over the course of the study. For bulimia nervosa, a history of drug use disorder at intake and the use of laxatives during the study significantly predicted suicide attempts.

CONCLUSIONS:

- Women with anorexia nervosa or bulimia nervosa are at considerable risk to attempt suicide. Clinicians should be aware of this risk, particularly in anorexic patients with substantial comorbidity.

Treatment of Anorexia Nervosa and Major Depressive Disorder

- ED are complex and often begin with good intentions: The desire to lose excess weight and change eating habits. For some people, the desire to lose weight can result in anorexia nervosa. Why some people are at risk of developing eating disorders and others are not is not entirely clear, but there is evidence that heredity and depressive disorders can elevate the risk.

- One study found that AN is estimated to have a heritability rate of 58% (heritability is the variation between individuals in a given population due to their genetic variation) and that the comorbidity of AN and MDD is likely due to genetic factors that influence the risk for both disorders.

- Another study of over 2,400 females in inpatient treatment for eating disorders found that 94% of patients evidenced comorbid mood disorders, largely unipolar depression (depression without manic states).

- Given that anorexia nervosa and major depression commonly co-exist, it helps to understand the symptomology and treatment options for both.

Treatment of Anorexia Nervosa and Major Depressive Disorder

- As many as 30-40% of patients with major depressive disorder are found to be unresponsive to a trial of antidepressant medication. Many labeled with treatment-resistant depression actually have pseudoresistance (inadequately treated or are misdiagnosed).

- Others may have unrecognized comorbid psychiatric or general medical conditions that contribute to treatment resistance. Variables such as gender, family history, age of onset, severity, and chronicity have also been evaluated as possible risk factors for treatment-resistant depression.

TREATMENT RESISTANCE VERSUS PSEUDORESISTANCE

- Guscott and Grof (1) note that refractory depression is "first and foremost a sociological fact - a phenomenon of labeling." To accurately label a patient’s symptoms, the first task for the clinician is differentiating between true treatment-resistant depression and pseudoresistance.

- Ruling out pseudoresistance falls into three areas of focus in the clinical assessment: 1) physician factors, 2) patient factors, and 3) accuracy of diagnosis.

Accuracy of Diagnosis

- Physician-related factor that is a common cause of pseudoresistance is misdiagnosis - with incorrectly labeled primary diagnosis. E.g., substance-induced mood disorders secondary to alcohol, substances, or medications and depression secondary to general medical conditions, such as hypothyroidism.

- In a study by Keller et al. (6), the diagnosis of secondary depression emerged as a major predictor of chronicity of symptoms despite adequate antidepressant treatment.
FACTORS ASSOCIATED WITH TREATMENT RESISTANCE

- Presence of a comorbid psychiatric or general medical disorder. Keitner and colleagues (12) reported that 53% of patients admitted with major depression have coexisting axis I, II, or III conditions, which they termed "compound depression".
- Female gender, family history, early or late age of onset, severity of illness, and chronicity of course.

Comorbid Psychiatric Disorders

- Often comorbid disorders are missed or are suboptimally treated, and they can confound both the evaluation and treatment of the depression (12).
- Psychiatric disorders that are most often comorbid with depression include anxiety disorders, substance abuse, and personality disorders.

Anxiety

- Fawcett and Kravitz (14) screened 200 patients with DSM-III major depression and found that 29% had a history of panic attacks, 62% had experienced moderate psychic anxiety and 72% moderate worry. To address the overlap of anxiety and depressive symptoms, the ICD-10 has introduced the concept of mixed anxiety-depression to define patients who have subsyndromal states that do not meet criteria for either primary disorder (15).

- Personality disturbance has been viewed as a predisposition or vulnerability that precedes the affective disorder; as a complication or attenuated manifestation of the affective disorder; and as a modifier that influences the clinical expression of the affective disorder (the pathoplasty model) (23).
- Estimates of the prevalence of comorbid personality disorders in patients with MDD range from 14% to 85%, with a mean of about 50%. Personality disorders most frequently reported as comorbid with depression are in the anxious-fearful cluster (Cluster C), followed by the dramatic-unstable cluster (Cluster B).

- The weight of evidence indicates that depressed patients with personality disorders are less responsive to antidepressant therapy compared to patients with no Axis II pathology and have a worse prognosis for long-term outcome (23, 27, 24).

Comorbid Psychiatric Disorders

- Other psychiatric disorders that may be comorbid with depression and may easily be missed include obsessive compulsive disorder (OCD), eating disorders, and body dysmorphic disorder (BDD).
- Often, patients do not reveal such symptoms to the clinician because of shame or embarrassment. Careful direct inquiry is needed because these disorders may also contribute to treatment resistance if they go unrecognized.
There is significant overlap between OCD and depression. Kendell (28) reported a 22% incidence of obsessive-compulsive symptoms in depressed patients. More commonly, patients develop depression during the course of OCD rather than developing OCD secondary to depression (29). The overlap between these two syndromes might help explain their shared responsiveness to SSRIs.

Eating disorders co-occur with depression 37% of the time (30) and often are missed by the clinician. Patients with eating disorders may be at risk for noncompliance because of fears of weight gain associated with some antidepressant therapies.

Many patients labeled with treatment-resistant depression have an organic cause that may be uncovered during the evaluation process. Endocrine disorders, such as hypothyroidism, Cushing’s disease, and Addison’s disease, have received the most attention.

In addition, there is medications used to treat general medical conditions, which may cause mood symptoms themselves, as in the case of antihypertensives or steroids.

Disorders at the interface of psychiatry and medicine, including fibromyalgia, chronic fatigue syndrome, irritable bowel syndrome, can also complicate the evaluation and management of treatment-resistant depression (36).

Hypothyroidism. A review of studies of refractory depression and thyroid disease (37) found that 52% of patients show evidence of subclinical hypothyroidism (range 29-100%). This estimate compares with a prevalence of 8-17% in unselected populations of depressed patients.

Conditions such as fibromyalgia, chronic fatigue syndrome, and irritable bowel syndrome exist at the interface between medicine and psychiatry and are often associated with depressive symptoms. As they tend to be under-recognized and undertreated, they are important diagnoses to consider in the evaluation of treatment-resistant depression.

When the associated depression is treated with a psychotropic drug, there is usually improvement in the somatic symptoms as well. This observation suggests a common etiological step in these disorders that is addressed by the antidepressant (36).

In any sample of depressed patients, including patients with treatment-resistant depression, there will always tend to be a preponderance of women because of the gender difference in prevalence rates of depression (41).
• There are studies showing that a positive family history is associated with early onset of depression and with chronicity, both of which have been linked to treatment resistance (46, 47).

• Scott et al. (48) reported that chronic treatment-resistant depressives showed a significantly greater family history of affective illness in first-degree relatives than non-chronic depressives.

• There is evidence that early onset of depression is associated with higher rates of comorbid personality disorders and substance abuse, and also a greater family history of mood disorders (47).

• Akiskal et al. (49) have also shown that early onset of depression together with a positive family history are associated with a chronic course of illness, which tends to result in lower response rates and an incomplete remission of symptoms.

• Suicide risk is a concern with severely depressed patients; up to 80% will report suicidal ideation. In two studies that compared patients with and without treatment resistance, suicide attempts were more common in the treatment-resistant group (45, 54).

• Severely ill patients do tend to be less responsive to psychotherapy alone. In a meta-analysis by Thase and colleagues (56), patients with severe and recurrent illness responded significantly better to combination treatment with medications and psychotherapy than to psychotherapy alone.

• Chronic depressions are associated with substantial comorbidity, particularly anxiety disorders, alcoholism, and personality disorders, all of which tend to worsen treatment outcome.

• Lower level of psychosocial functioning is associated with a worse prognosis for recovery (63, 64).

• Patients with chronic depression also show a greater frequency of suicide attempts and hospitalizations, and an earlier age of onset of their illness (65), which also increases the risk for treatment resistance.
Study compared nefazodone, psychotherapy, and the combination in patients with chronic major depression, double depression, or recurrent MDD with incomplete inter-episode recovery. The type of psychotherapy used in the study was Cognitive-Behavioral Analysis System of Psychotherapy (CBASP), which is a therapy method developed specifically to treat chronic depression (71).

Response rate to combination treatment was markedly better than to either treatment alone. Thus, chronic depression may represent the type of situation in which if one chooses the right treatment, the patients will be less likely to be classified as treatment-resistant.

Duloxetine off label

Duloxetine, a serotonin norepinephrine reuptake inhibitor (SNRI), is indicated for the treatment of depression, generalized anxiety disorder, and certain forms of pain. It has also been used for off-label purposes such treatment-resistant obsessive compulsive disorder (OCD), bulimia, and binge eating disorder.

How to develop Eating Disorders Services in regular psychiatric settings: lessons from practice in a country in transformation

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Расстройства питания

- Нарушения Питания (НП) влияют на Общее здоровье в широком смысле этого слова и все системы органов: физическое, психическое и социальное
- Расследованиями подтверждено, что Нарушенная анеорексия, булимия и другие НП не поддаются обычному лечению
- Во многих центрах применяется интер-дисциплинарный командный подход и континуум лечения, замечено, что так достигаются более хорошие результаты и меньше рецидивов
- Среднее время лечения от 2 до 6 лет разной интенсивности и этапами

Создание центра

- ИНГО 2001, поддержка из разных фондов, проекты «День без дiets», школы, конференции для семейных врачей
- Создание программы, протоколов, подготовка специалистов
- Внедрение в больницы, измерение потребности и стоимости сервиса, регистрация карт, дневной стационар (оплачивалось из других отделений, более рентабельных)
Стационар 5 мест и описание услуг и финансовых растрат на законодательном уровне для подтверждения в министерстве здравоохранения 2008
10 мест в стационаре и 20 дневного, переход на австралийскую систему оплаты (DRG) случаи по коэффициентам, регистрация всех дополнительных услуг – полностью рентабельные и покрывает убыточные амбулаторные консультации

Распространение НП
- НП в год болеют 19 из 100 000 женщин и 2 из 100 000 мужчин
- В возрасте 13-19 лет 50,8 случаев из 100 000 в год
- Соотношение мужчин и женщин, болеющих НА 1:8-9

Распространённость:
- 6,5-1,0% болеют анорексией НА
- 2-3% болеют булимиеи НБ
- 5-8% болеют перееданием
- 90 % всех пациентов

Расстройства питания
- Необоснованная боязнь потолстеть или прибавить в весе
- Чрезмерные усилия контролировать вес (строгая диета несмотря на очень маленький вес, рвота, употребление диуретиков, средств для похудения, слишком большая физическая нагрузка)
- Отрещание того, что вес или привычки в питании являются проблемой, изменение представление о фигуре
- Для детей и подростков соответственно недостаточный прирост массы тела по возрасту
- У пациентов могут быть симптомы булимии и анорексии, НА болеют в возрасте 12-16 лет, НБ в возрасте 17-19 лет, НБ иногда развивается у пациента, страдающего НА.

Расстройства питания
- НП (нарушение питания) может осложняться депрессией, апатией, нарушением сна, беспокойством, паническими расстройствами, ОКР, эмоциональной нестабильностью
- НП вызывает соматические нарушения: аменорею, гипогликемию, сердечную аритмию, остеопороз, запоры, здёмы, эрозию зубной эмали, увеличение слоновых желез, замедление роста, уменьшение объёма мозга, бесплодие
- Отклонения и ЭКГ, нарушения равновесия жидкости и электролитов

Синдром восстановления веса
- У истощенных пациентов, при восстановлении веса, происходят сильные жидкостные и электролитные сдвиги и связанные с этим метаболические последствия
- Гипофосфатемия, Гипокалиемия, Гипоматериемия, Изменение глюкозного обмена, Нарушения жидкостного баланса
- Может привести к сердечным, респираторным, нервно-мышечным, почечным, метаболическим, печёночным заболеваниям
- Может привести к внезапной смерти
Энтеральное кормление:

- Назо-дуоденальное кормление лучше, чем назо-гастральное
- Непрерывное кормление предпочтительнее болюсного

Дневник питания

<table>
<thead>
<tr>
<th>Время</th>
<th>Съеденная пища, количество</th>
<th>Где</th>
<th>Шкала стресса 0-100</th>
<th>Рвота / Были позывы</th>
<th>Масляных ощущений</th>
</tr>
</thead>
</table>

Этиология

- Предрасполагающие факторы
- “Толкающие” факторы
- Факторы, поддерживающие болезнь

Предрасполагающие факторы (индивидуальные)

- Генетически унаследованная склонность
- Биологические особенности
- Личностные особенности:
  - Перфекционизм (НА)
  - Пограничная структура личности (НВ)

Предрасполагающие факторы (социальные)

- Нарушение правил питания в семье
- В семье преобладает позиция, акцентирующая внешний вид
- Навязывание образа в печати

«Толкающие» факторы

- Сексуальное насилие
- Лишение и др.
- Строгая диета !!!!
- Смена школы, издевательства
Поддерживающие факторы

- “Вторичная польза”
- Физиологические изменения
- Неизменные отношения в семье

Предрасполагающие факторы

- Насилие
- Слабость
- Семейные отношения
- Поддерживающие факторы
- Нарушения питания

Пациенты

- Диетолог
- Терапевт
- Медсестры
- Кинезиотерапевт
- Психиатр
- Психолог
- Консультанты
- Социальный работник

Потребность в Вильнюсе (~400 000 жит.)

- 12 мест стационарного отделения
- 16-20 мест дневного стационара
- 2 консультирующие психотерапевта в поликлинике
- 1 подростковый психиатр-психотерапевт в поликлинике
- Планы на будущее: Детское-подростковое подразделение 6-12 стационарных мест и 8-10 мест дневного стационара, с программой для подростков 16-17 лет.
- Отдельное отделение для детей младше 15 лет уже есть, неспециализированное в общем детском психиатрическом
Организация непрерывного лечения 1-2 года

- КС Консультация психиатра (1-4)
- Стационар (2 недели-2 месяца)
- Поддерживающая терапия (3-6 месяцев)
- Группы самопомощи
- Индивидуальная психотерапия (1-2 года)

Лечение непрерывное 1-2 года до 6 лет

- отношение с акцентом на Общее здоровье: физическое, восстановление веса, психическое и социальное
- Индивидуальный подход: нет одного подходящего лечения для всех НП
- Чем раньше интервенция тем лучше результаты
- Коморбидность ожидаемая
- Семья должна быть включена в лечение
- Пациент активный в своем лечении, обсуждает и принимает вместе решения
- Прогрессирует пациент - прогрессирует лечение
- Континуум лечения на разных уровнях относительно «где находится» пациент (Prochaska model of change), по его индивидуальным потребностям

Лечение

- Мотивация лечением (позитивная)
- Медикаментозное (болезнене и осложнений)
- Психотерапия (когнитивная, интер-персональная, диалектическая, психо-динамическая, интер-субъективная, семейная, ментализация)
- После программы мониторинг состояния - семейный врач
- Сотрудничество служб и международное сотрудничество чтобы искать более эффективного метода лечения, делится опытом

Континуум Лечения - ИМЛ

- Интенсивное Леч. Лечение (изменения в ЕГТ, гипотензия <80 систол. при 10, пульс >20, темп <35)
- Серьезные лаб изменения: Na <125, K <3, Cl <86, CO2 <20 или >35, AST >50, ALT >55, album <3, P<3,4 молек 20 и <2,5 если старше; Mg <1,5, Ca <8 или >10,7, глюкоза <3,5
- Серьезные аритмии, любые блокады, синус брадикардия <50 или пролонгирование QTc при потребности в антителепиков
- Депрессия (снижение 5-10% гургера, респирация повышена, концентрирована мочи, замедленное заполнение капилляров от 1,5c до 3,0c)
- Атония кишечника, обструкция, альментарная анемия, осложнена работа почек, задержка жидкости - оттеки, травмы из за через мерных упражнений
- Беременность, сахарный диабет

Континуум Лечения - ИМЛ

- коморбидность: тяжелая депрессия, тревожность, обесценное компulsionальное расстройство, суицидальные идеи
- Ежедневная рита, отказ от пищи, за 2-3 нед не начинает восстанавливаться вес или продолжает падать
- Типично KMT <16
- Синдром рефлюкса
- Субстанция: алкоголь, наркотики
- Мотивированный пациент через 1-2 нед обычно стабилизируется
- Врач каждый день, витальные измерения 2-3 раза в день

Континуум Лечения - ИМЛ

- Интенсивное Леч. Поведения (ИЛП) после мед стабилизации: не нужно больше наос-гастрин вмешательства, может самостоятельно есть 1800 килокал/ед, но еще суицидализация еда;
- Врач 2 раза/ед, витальные измерения ежедневно
- Цель восстановить регулярное питание и вес, начинается психотерапия, интенсивная терапия, консультации диетолога, психо-эдукация, терапия принятия тела, стресс-менеджмент, культурные разницы, семейные проблемы, СВТ, и тд
Континуум Лечения - ИМЛ

☒ Интенсивное Лечение Поведения (ИЛП) после мед стабилизации: не нужно больше насо-гастрик кормления, может самостоятельно есть 1800 килокал/день, но еще супервизирование еды;
☒ Врач 2 раза/нед, витальные измерения ежедневно
☒ Цель восстановить регулярное питание и вес, начинается психотерапия, кинезитерапия, консультации диетолога, психо-эдукация, терапия принятия тела, стресс менеджмент, культурные разницы, семейные проблемы, СВТ, и тд

Континуум Лечения - Консультационная поликлиника
☒ может самостоятельно структурировать день, есть 1800 килокал/день расположив через 5 раз в день; есть мотивация
☒ Мед лаб норма
☒ ИМТ обычно >17-18
☒ Цель восстановить регулярное питание самостоятельно и вес и его поддерживать, продолжается психотерапия индив и групповая, кинезитерапия, консультации диетолога, психоэдукация, терапия принятия тела, стресс менеджмент, культурные разницы, семейные проблемы, СВТ, и тд
☒ Постепенное возвращение в учебу, работу
☒ Превенция отпада (релапса)
☒ И опять по кругу 😊