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Review of Therapy for GAD

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Abstract: Generalized anxiety disorder (GAD), a chronic anxiety disorder characterized by persistent significant nervousness, autonomic nervous function excitement and excessive vigilance, is the most common anxiety disorder. With the deepening of research, people have a profound understanding of the causes and mechanisms of GAD and for patients with GAD, and there are systematic treatments based on series of clinical evidence and meta-analysis. This article will start with some mainstream treatment methods including CBT, DBT and medication therapy, commonly used in clinical practice, compare their feedback, and discuss their advantages and disadvantages.

Keywords: GAD, CBT, DBT, medication therapy

1. Introduction

Generalized anxiety disorder (GAD) is characterized by excessive and uncontrollable anxiety and worry about various domains, and is often accompanied by many other physical symptoms, including muscle tension, fatigue, difficulty concentrating, irritability, difficulty concentrating or difficulty sleeping [1]. GAD is a chronic disease with strong persistence, which means that patients might be affected for a long time, about 6-12 years without reasonable treatment [2]. Statistical analysis shows that the prevalence rate of GAD patients during 12 months is 1.2% - 1.9%, and the lifetime prevalence rate is 4.3% - 5.9% [3].

GAD is a common psychological disease in modern society, which has received extensive attention. Therefore, there are plenty of studies and cases related to GAD and accordingly, people have also developed some treatment methods to deal with. Among them, Cognitive behavior therapy (CBT) is one of the mainstream methods to treat GAD. It is a treatment method focusing on improving the symptoms of psychological diseases, achieving the therapeutic effect by changing views of patients on themselves and their surroundings. But at the same time, CBT therapy is not completely satisfactory, and nearly half of the GAD patients receiving psychiatric did not show effective positive feedback: no significant relief of symptoms, no response to treatment [4,5].

Dialectical Behavior Therapy (DBT) is a widely used treatment method, and its effect on treating complex and difficult mental disorders involving emotional disorders and related cognitive and behavioral dysfunction has been proven [6].Since patients with generalized anxiety disorder (GAD) cannot obtain better feedback after CBT, and many situations have not been significantly improved, Malivoire [7] believes that dialectical behavior therapy (DBT) may be an effective alternative therapy for GAD, especially DBT skill training has a significant impact on patients with complex comorbidities and mood regulation disorders.

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At present, experimental evidence and meta-analyses have shown the effectiveness of medication therapy on GAD [8]. Chen and colleagues [9] pointed out that most psychological interventions are better than self-help interventions, and most medication interventions are better than psychological interventions. However, clinicians and patients are often reluctant to adopt medication therapy, instead, being more inclined to psychotherapy [3]. Common medications include antianxiety medications (benzodiazepines, buspirone), antidepressants (tricyclic medications (TCA), selective serotonin reuptake inhibitors (SSRI), serotonin norepinephrine reuptake inhibitors, norepinephrine and specific serotonin amine antidepressants (Nassa), and β-Receptor blockers [10].

This article will discuss several mainstream treatment methods of GAD, that are CBT, DBT and medication therapy and their effects, aiming to find the most appropriate treatment scheme for GAD under the current technical conditions.

2. Cognitive Behavior Therapy (CBT)

Cognitive behavior therapy (CBT) is a structured, short-term, cognitive oriented psychotherapy. A.T. Beck, who developed this therapy measured the characteristics of mental illness in different situations, and then tried to determine beliefs, the characteristics of each disease, and the treatments that are suitable for changing maladaptive beliefs, and finally formed a theory of cognitive behavioral therapy [11]. According to this treatment, People's emotions do not come from things themselves, but from their understanding of things, such as beliefs, evaluations, and interpretations. Ellis [12] established the ABC model, one of the theoretical basis of psychotherapy to describe the process and reason of treatment of GAD patients, in which A represents the activation event, the activation experience or the activities that people disturb themselves. B represents the rational belief or realistic belief in the activation event, which usually leads to C, the corresponding consequence. IB represents an irrational belief in activation events, which usually leads to iC and improper consequences (especially emotional disorders and dysfunctional behaviors). D stands for questioning irrational beliefs. E represents effective rational beliefs to replace people's irrational beliefs, and also represents effective appropriate emotions and effective functional behaviors to replace their disturbed emotions and dysfunctional behaviors.

As one of the mainstream therapies of GAD, the efficacy of CBT can be supported by some previous studies. In many well controlled randomized clinical trials, CBT is not only better than the waiting group and the placebo control group, but also better than other psychotherapy, apart from which, it is also relatively easy to implement, and patients have good tolerance [13]. However, in a controlled, actual clinical environment, Durham and colleagues [14] interviewed GAD patients in CBT through structured interviews and found that barely 50% of the subjects improved significantly, and 30-40% of them recovered. Moreover, after the treatment, the effect of CBT can last for more than one year [15]. At the same time, the follow-up study also emphasized that compared with primary care patients, the treatment effect of CBT on secondary care patients was significantly worse, indicating that the severity of patients would also affect the therapeutic effect of CBT [14]. In addition, the efficacy of CBT was related to the age of patients receiving treatment. Compared with young people, the improvement degree of elderly GAD patients treated with CBT is lower than that of young people, which may be due to the fact that the elderly is unlikely to perceive the need for mental health services [16] or have less positive expectations for psychological treatment, and it is difficult to understand some abstract concepts outlined in the treatment [17]. In the comparison between individual therapy and group therapy, individual therapy can usually produce greater efficacy, but it is worth noting that the effect of group therapy can often be maintained for a longer time [17].

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CBT for GAD usually has two advanced forms: rational emotional behavior therapy (REBT); Acceptance and commitment therapy/acceptance-based behavior therapy (ACT/ABBT) [18]. Stefan and colleagues [19] found in the study that there was no significant difference among the different CBT forms in reducing generalized anxiety symptoms. Therefore, appropriate CBT forms can be selected according to the preferences of patients or the judgment of psychotherapists on operability.

2.1. Rational Emotional Behavior Therapy (REBT)

Rational emotional behavior therapy (REBT) is the first form of cognitive behavior therapy (CBT), founded by Albert Ellis in 1960s. REBT believes that irrational beliefs (IB) are the main core of psychological disorders. Changing a person's irrational beliefs about events will lead to significant changes in positive emotions and behavior.

In a study comparing the relative efficacy of REBT and drug therapy in 170 patients with GAD, David and colleagues [20] found that when REBT and drug therapy were fully implemented, there was no significant difference in short-term efficacy, but in the follow-up after 6 months, REBT was superior to drug therapy.

2.2. Acceptance and Commitment Therapy (ACT)

Transdiagnostic therapies have some advantages over single disease protocol (SDP), such as being able to treat multiple diseases with only one method and be able to deal with complex cases caused by comorbidity [21]. Another disadvantage of the measurement of general and specific diagnostic symptoms is that they cannot indicate whether the common higher-order structure in the disease is changing, or whether the change is limited to the symptom level, but in fact, compared with the interventions that only aim at diagnosing specific symptoms and processes, the interventions that aim at common factors of the disease are more likely to achieve remission and prevent recurrence [22].

The representative treatment is ACT. The treatment process includes contact with the present, separation, acceptance, self-regard, value and commitment. In the study, Treanor and colleagues [23] found that the patients receiving ACT treatment had less difficulty in emotion regulation and pain in emotional response, and their tolerance to uncertainty and sense of control over anxiety had improved compared with placebo group.

3. Dialectical Behavior Therapy (DBT)

Although CBT has been generally proved to have a significant effect on GAD, there is considerable evidence that some individuals need to be further intervened. A considerable number of studies found that only 42% of GAD patients showed significant clinical improvement after CBT [7]. In addition, researchers found that about 40% – 50% of GAD patients did not achieve high-end state function or relapse after CBT [5].

Linehan [24] developed DBT as the treatment of borderline personality disorder in response to the high suicide rate in the 1970s and 1980s. Based on the bio social theory, DBT believes that emotional disorder is caused by the interaction between emotional vulnerability and ineffective childhood environment [25]. The emotional and physiological arousal level of some individuals in similar situations is stronger and faster than that of the general population. Therefore, compared with other cognitive and behavioral therapies, DBT emphasizes the role of emotion in dysfunctional behavior [6,25].

The essence of DBT can also be considered as teaching patients the skills to manage emotions. Therefore, the article will discuss the treatment of GAD by introducing the four skills of DBT

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Mindfulness: Developing self-awareness of negative thinking and emotions, as well as rational thinking, emotional thinking and intelligent thinking. Mindfulness is the basis for effective implementation of subsequent DBT steps. GAD patients tend to avoid the current situation, and shift their attention to the current negative emotions by worrying about the future [26]. Mindfulness guides patients to correctly understand and experience anxiety, change their negative interpretation of anxiety, and thus reduce anxiety as a whole [6]. Evans and colleagues [27] conducted an 8-week Mindfulness course for GAD patients, and found that their anxiety, tension, worry and depression symptoms were significantly reduced. Craigie and colleagues [28] found that after receiving MBCT (mindfulness based cognitive therapy), more than 60% of the intended treatment samples had a reliable improvement in their pathological worry level, and the effect was sustainable during follow-up.

Personal effectiveness: About how individuals establish and maintain positive relationships, that is, how to avoid hurting interpersonal relationships while protecting their own interests, and develop healthy relationships. The interpersonal relationship of GAD patients is more likely to be rigid and stressful than that of ordinary people [29], and the failure of interpersonal communication may further aggravate their anxiety. In the follow-up study, with less controlled, the anxiety of patients receiving interpersonal effectiveness skills was significantly reduced, whereas, in the controlled trial, no significant difference showed between the interpersonal effectiveness skills group and the supportive listening group [30]. When analyzing the study again, Newman and colleagues [31] believed that, Patients with disruptive attachment styles are better treated with interpersonal effectiveness skills.

Emotion regulation: Based on the basic cognitive behavior model, it helps the visitors better understand and cope with violent emotions. Through psychological education, we can help clients understand “how emotions work”, emotions and corresponding behaviors induced by individual explanations of things. Compared with ordinary individuals, GAD patients have a lower tolerance for negative emotions, usually can’t fully understand their own emotional changes, their emotional intensity is higher than that of ordinary people, and often can’t take reasonable and effective ways to regulate their emotions [32]. Therefore, it is essential to teach them reasonable ways to regulate their emotions so that they can correctly understand and understand their own emotional problems.

Distress tolerance: The skills to endure pain include the skills to improve a person’s tolerance for difficult situations, and the skills to accept the status quo when it is impossible to change the status quo to reduce pain. As the low tolerance to pain of GAD patients might leading them taking persistent anxiety or even increase suicide intention, distress tolerance skills can help patients increase their tolerance for pain and avoid extreme situations. Afshari and Hasani [33] found that patients’ emotion regulation strategies were improved after receiving DBT and CBT treatment, and the improvement degree of all subscales after DBT intervention was higher than that of CBT group, but CBT could better alleviate depression and anxiety symptoms than DBT.

4. Medication Therapy

GAD psychological intervention, such as cognitive behavioral therapy, is generally more acceptable than anti-anxiety drugs because of its effectiveness and harmlessness. However, due to limited medical resources, it is difficult for some patients to obtain opportunities for psychotherapy and there is no sufficient evidence to show that psychotherapy is superior to medication therapy [3]. Therefore, drug therapy may still be the main clinical treatment method for GAD. Common drugs for GAD include SSRIs, SNRIs and Benzene diazepine, and the next essay will explain the action mechanism of these drugs and their therapeutic effects on GAD.

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4.1. SSRIs

The main mechanism of selective serotonin reuptake inhibitors (SSRIs) is to selectively combine with the serotonin reuptake pump (SERT) on the presynaptic membrane, thereby inhibiting SERT's reuptake of serotonin in the synaptic space and increasing the concentration of serotonin in the synaptic space, so as to achieve the follow-up pharmacological effect.

A large amount of experimental and clinical evidence shows that SSRIs can achieve similar effects in anti-anxiety and anti-depression. Moreover, the anti-anxiety effect of SSRI seems to be independent of the baseline level of depression, and its improvement occurs simultaneously with the previous improvement of depressive symptoms, rather than mediated by it [34].

Some studies have found that the immune system is active in the acute phase of some GADs, which indicates that anxiety symptoms are related to inflammation [35], and SSRIs can produce anti-inflammatory effects by affecting glucocorticoid receptors and hypothalamus pituitary adrenal axis, based on which, Hou and colleagues [36] believed that anti-inflammatory effects are the basis of SSRIs' anti-anxiety effects.

Paroxetine: Paroxetine is a representative medication for the treatment of GAD. Most clinical evidence show that paroxetine is the most effective and suitable SSRI for quite a number of anxiety disorders, such as GAD, and it has therefore been widely used [37]. Due to the consideration of the co morbid depression of GAD and the long-term efficacy of antidepressants, paroxetine is often used as the main medication to treat GAD [38].

Paroxetine is generally well tolerated in adults, the elderly and comorbid patients, and the tolerance is like other SSRIs. The most common adverse events of paroxetine were nausea, sexual dysfunction, somnolence, fatigue, headache, constipation, dizziness, sweating, trembling and loss of appetite [39]. Because the safety of paroxetine in pregnancy is not clear, the drug can be used only when the benefit to the mother is greater than the possible risk to the fetus [37]. Zohar and Westenberg 40] designed a test to explore the improvement effect and recurrence rate of paroxetine on GAD, and compared with placebo, it was found that in the paroxetine group, the anxiety symptoms were significantly improved, while the recurrence rate of GAD was significantly lower; Moreover, the recurrence rate of GAD in the paroxetine group was significantly lower than that in the placebo group. Besides, for withdrawal symptoms that may occur when using the drug, gradually reducing the dosage within a few weeks can effectively reduce the risk [41].

4.2. SNRIs

The main mechanism of 5-hydroxytryptamine noradrenaline reuptake inhibitors (SNRIs) is to combine with the 5-hydroxytryptamine reuptake pump (SERT) and noradrenaline reuptake pump on the presynaptic membrane, so as to inhibit the reuptake of 5-hydroxytryptamine and noradrenaline in the synaptic space by the presynaptic membrane and increase the concentration of 5-hydroxytryptamine and noradrenaline in the synaptic space, so as to achieve the follow-up pharmacological effect.

Duloxetine: Duloxetine, an SNRI, was approved by the Food Administration (FDA) as an effective and well tolerated first-line treatment plan for GAD in 2007 [42]. It is also the only antidepressant approved by FDA for children's GAD and effective for elderly patients (≥ 65 years) [43].

In the placebo-controlled trial for adults, duloxetine treatment can significantly improve the psychological anxiety symptoms of GAD patients compared with the placebo group, and the change of physical anxiety symptoms is small, and its tolerance is acceptable [44]. But at the same time, the incidence of nausea in the GAD treatment group was significantly higher than that in the placebo group. Due to adverse reactions, the drug withdrawal rate of patients receiving duloxetine was

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higher, but there was no evidence that the drug could significantly increase the incidence of serious adverse events [42,43]. Duloxetine currently belongs to category C of pregnancy, and its possible impact on delivery, delivery and fetal development is still unclear. Therefore, prior to the use of duloxetine, it is necessary to carefully assess the risks and ensure that the patients are informed and agree, and require the supervision of experts [45].

4.3. Benzodiazepines

Benzodiazepines are derivatives of 1,4-benzenediazepines, which mainly act on the reticular structure of the brain stem and the limbic system of the brain and can increase the level of 5-hydroxytryptamine in the brain γ- Activity of aminobutyric acid (GABA). Benzodiazepine is a common anti-anxiety drug, which is often used to treat anxiety disorders such as GAD [46]. However, due to possible tolerance and dependence, it is recommended to use this drug cautiously in clinical practice [47].

5. Conclusions

In general, people have made in-depth research on the internal factors and principles of GAD, and the clinical treatment can also achieve good results, but no treatment plan that can satisfy everyone has been found. CBT is currently the most widely used and most popular treatment method in clinical practice. Its effectiveness has been supported by a large number of randomized trials/meta-analysis and clinical experience, but it failed to experiment with a sufficiently high recovery rate. Some patients' long-term efficacy is not optimistic, and its effectiveness is also affected by the patient's age and severity of symptoms. DBT is a psychotherapy that is mainly used in BPD itself. When treating GAD, it is usually a supplement or alternate program of CBT, which cannot deal with the symptoms of GAD more comprehensively, but in some cases, it can achieve more satisfactory results than other psychotherapy. medication therapy can effectively reduce anxiety symptoms, but it cannot affect anxiety itself. It is usually used in combination with other psychotherapy. Therefore, at present, it seems that it is impossible to find an efficient and widely applicable treatment scheme, and the treatment of some severe GAD patients still needs an uneconomic and complex treatment scheme with multiple treatments at the same time.

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