ABSTRACT

Specific phobias are among the most common psychological problems both in men and women. For treatment of specific phobias, exposure-based therapy is the first choice followed by cognitive therapy, relaxation techniques and short-term pharmacotherapy. Long-term pharmacotherapy for specific phobias, is associated with adverse drug reactions and drug abuse, thus not a reasonable choice for long-term symptom control. Glucocorticoids and d-cycloserine (DCS) cause fear reduction when used in combination with exposure based therapy. Being a non-anxiolytic DCS accelerates fear reduction during exposure by facilitating memory consolidation during post-treatment phase. Adjuvant cortisol to exposure therapy also caused great reduction in fear in spider phobia.

Keywords: Specific phobia, Exposure-based therapy, DCS, Glucocorticoids

INTRODUCTION

Diagnostic and statistical manual of mental disorders (DSM-IV-TR) defines a phobia as a disruptive fear of a particular object or a situation, that is not proportional to the danger posed. The phobic symptoms are so intense that they cause distress or interfere with social or occupational activities of the person. A specific phobia is an unwanted fear caused by the presence of a specific object or situation, e.g. fear of flying, fear of snakes or fear of heights. DSM-IV-TR categorizes specific phobia according to the source of fear.\(^1\) A person with one type of specific phobia is likely to have another type of specific phobia, thus there is a high co-morbidity of specific phobias.\(^2\)
with loss of blood (traumatophobia), fear of knives, dental or medical procedures; d) situational type, e.g. fear of airplanes, driving, enclosed spaces i.e. avoiding elevators and fear of the number 13, fear of ghosts etc; and other type, e.g. phobic avoidance of situations that may lead to choking, vomiting and an illness. Persons with BII type phobias can actually faint because of excessive vasovagal reflex that causes bradycardia and orthostatic hypotension.

Phobias are not under a voluntary control, cannot be reasoned anyway, and entail an avoidance behavior which is one of the primary factors that maintains anxiety. Phobias, which are initially triggered by a very specific stimulus, can eventually become generalized. Thus, a fear of using the elevators may become extended to fear from all kinds of closed rooms. Some phobias are linked to broader circumstances from the beginning and such patients avoid anxiety provoking objects or situations. This can lead to severe impairment in their lifestyle e.g. inability to leave home. A person may be experiencing phobias about more than one object or situations.

Anxiety disorder work group (Curtis et al) shows that specific phobia types tend to differ in a variety of dimensions, including age of onset, sex composition, pattern of co-variation among phobias, focus of apprehension, timing and predictability of phobic response and type of physiological reaction during exposure to the phobic situation.

Pharmacotherapy is generally thought to be ineffective for the treatment of specific phobias. However, little research has been conducted to assess the role of the pharmacotherapy in the management of specific phobias. Therefore, this review describes many contradictory issues related to specific phobia; its prevalence, current understanding, etiopathogenesis, diagnosis and pharmacotherapy.

Prevalence

Specific phobias are among the most common psychological problems, being the most common in women and the second most common in men. Specific phobias, strike more than 1 in 10 people, all though they seem to run in families and are more prevalent in women. The NCS-R has reported a lifetime prevalence rate of 12.5% and a 12-month prevalence rate of 8.7% for specific phobias, and the lifetime prevalence to be double in women than in men. In the age above 65 years, fear of spiders and insects were the most common form of specific phobia accounting to 33.3% of the phobic fears followed by cats or dogs (27.7%); blood or injury (5.6%); and heights (5.6%). One study has found situational/environmental type specific phobias to be the most common (13.2%) followed by animal type phobias (7.9%) and BII type phobias (3.0%). Specific phobias are rarely the primary reason for seeking treatment.

Diagnostic

Based on DSM-IV-TR criteria;

The fear should be persistent and unreasonable, cued by the presence or anticipation of an object or situation. Exposure to the feared object or situation should always cause immediate anxiety which may be in the form of a panic attack. The person recognizes that the fear is excessive and unreasonable, but not always in children. The phobic situation is avoided or endured by intense anxiety or distress. Anxiety, distress or avoidance during the feared situation interferes significantly with normal routine, work or social activities or relationships of the person or there is marked distress about having the phobia.

Etiology of specific phobias

There is a considerable evidence for the familial or genetic transmission of specific phobia. Rates of specific phobia were higher among first-degree relatives of persons with a specific phobia. In the Virginia twin study concordance rates for animal phobia were 25.9% and 11.0% among monozygotic and dizygotic twins, respectively. Specific phobias have a complex etiology involving a number of factors e.g. learning histories, past experience, and biology. Specific phobias can begin following a direct learning experience, a traumatic experience, e.g. a person can develop a fear of driving following a car or bike accident or a fear of dogs after a dog bite. Also, fear may be learned by observational learning, e.g. a child whose father is afraid of heights may develop a fear of heights. Informational learning may also cause the development of a phobia e.g. a person learns fear flying after watching news footage of an air crash. Some biological factors may also cause or maintain a specific phobia. When a person encounters a fearful situation many biological changes occur in the body e.g. changes in brain activity, the release of cortisol, insulin and growth hormone; and increase in heart rate and blood pressure. Specific phobias are usually co-morbid with other anxiety disorders such as panic disorder with agoraphobia. Persons with specific phobias can get serious life impairment e.g. failing to get a necessary medical care, impaired social activities and reduced time and productivity at work. They adopt a lifestyle to avoid contact with the feared stimuli and those with severe specific phobia seek treatment. The majority of the persons with specific phobias (83.4%) experience, at least, one psychiatric disorder during their lifetime.

Management of specific phobias

Persons with specific phobias can be treated by several effective treatment methods. The chief goal of treatment is to decrease fear, the phobic avoidance, and significant distress or functional impairment.
Exposure-based therapy

Exposure is clearly the treatment of choice for specific phobia. Patients with a specific phobia are gradually exposed to their feared situations on repeated occasions until the situation no longer triggers the fear response. Prolonged and repeated in-vivo exposure to the fear stimuli is the most studied, efficacious intervention and first-line treatment for specific phobia. Many studies have shown that exposure-based treatments are effective, in helping patients, to overcome a variety of specific phobias e.g. fear of blood, BII, dental procedures, spiders, snakes, thunderstorms, flying, heights, water and choking.

Most of the patients are able to achieve clinically significant and long-lasting improvement in the exposure sessions lasting 2-3 hours. The exposure can be imaginary or real life; and the real life exposure is more effective than the imaginary one. Exposure therapy directed by a therapist is generally more effective than the self-directed treatment. Exposure should be conducted in a variety of settings to enhance exposure outside the therapeutic setting. In virtual reality exposure (VRE), the feared situation is presented in three-dimensional simulations, which may enhance efficacy of the exposure therapy. Applied tension (AT) and applied relaxation (AR) are a variation of in vivo exposure intended to counteract the vasovagal fainting response that is unique to BII phobias. Recently videotapes are commonly used to show feared object to patients during the exposure. Computer-assisted behaviour treatments, i.e. computer guided self-exposure, are in common use. More recent is the use of virtual reality to expose the patients to simulated situations that are more difficult to replicate in vivo such as flying, and heights. Emerging data on the effectiveness of virtual reality is encouraging. But some studies suggest that in vivo exposure is still superior.

Cognitive therapy (CT)

Cognitive strategies have also been used either alone or in combination with exposure therapy, providing an added benefit, in the treatment of specific phobia. By cognitive therapy, patient learns to identify their anxious thoughts and replace them with more realistic thoughts. CT alone is usually not the appropriate choice for the persons with specific phobia. CT appears to be more effective than no treatment in reducing self-reported fear and avoidance, but less effective than in-vivo exposure. It has been concluded that cognitive therapy provides little additional benefit over exposure-based therapy alone.

Progressive desensitization

This treatment approach is used in patients having great difficulty in facing the fear object or situation. This involves learning relaxation and visualization techniques. However, this is not as effective as the exposure therapy.

Relaxation

Different relaxation techniques i.e. breathing retraining and exercise can help persons with specific phobias to cope effectively with the associated stress and physical reactions.

Hypnosis (hypnotherapy)

A subconscious mind of the patient is targeted in order to implement a new belief system. The patient is convinced, in an unconscious state, that his or her fear has been eliminated, and he can operate with the same belief while awakening.

Homeopathy

Homeopathy can also be useful in the treatment of social anxiety, restlessness, and phobias.

Herbal remedies

Many people with anxiety and fears opt for herbal supplements as a means of treatment. Common natural remedies for anxiety and phobia include Valerian root, Chamomile, and Ginseng.

Pharmacotherapy

Drug treatment for specific phobias has been shown to be less efficacious than behavioral treatments. Little research work has been there in drug treatment of specific phobia.

Pharmacotherapy of phobic disorders includes benzodiazepines (BZDs); antidepressants-selective serotonin reuptake inhibitors (SSRIs) paroxetine and sertraline; serotonin nor-adrenaline reuptake inhibitors (SNRIs) venlafaxine; monoamine oxidase inhibitors (MAOIs) phenelzine, moclobemide; β-adrenergic blockers, buspirone, gabapentin, pregabalin and D-cycloserine.

Short-acting BZDs e.g. diazepam is commonly prescribed, on the as-needed basis, to patients in specific situations e.g. before boarding a plane for patients with a fear of flying. But BZDs and β-blockers, alone or in combination with behavioral treatments, do not contribute much to the treatment of specific phobias. Also, situational type specific phobias share more features with panic disorder than other types of specific phobia. Thus, medication effective in panic disorder (e.g. imipramine, alprazolam) may also be effective in situational phobias. Few studies report that BZDs may be helpful in the short term but lead to greater relapse in the long-term; and may interfere with the therapeutic effects of exposure to sessions. One study had reported that CBT and BZDs caused fear reduction during dental surgery, and benzodiazepine treatment was associated with a greater relapse during the follow-up. Relapse is common upon discontinuation of the anxiolytics.
Antianxiety drugs or SSRIs are usually prescribed for the acute treatment of situational type specific phobias before confronting the feared situation. β-adrenergic blockers reduce symptoms of sympathetic arousal during exposure to feared stimuli but fail to decrease the subjective fear. Propranolol is efficacious on as and when required basis, in a dose 10-40 mg/d, for performance-related anxiety. Short-term therapy with BZDs (e.g. lorazepam 0.5-1.0 mg, p.o.) or a beta-blocker (e.g. propranolol 10-40 mg, p.o.) is preferred, ideally 1-2 hours before the exposure, when exposure to the object or situations can’t be avoided e.g. stage fright, fear of flying.

For short-term control of specific phobias BZDs (clonazepam, alprazolam, lorazepam) are a better choice than MAOIs and CBT; and offer a rapid onset of effect, good tolerability and minimal side effects. BZDs are contraindicated in patients with drug abuse or mood disorders. These drugs may be helpful to people with a specific phobia, interfering with their ability to function in day to day life e.g. riding a train to work or speaking in front of a gathering.

In a randomized controlled trial (RCT) use of an antidepressant agent, escitalopram for the treatment of specific phobia showed only a modest treatment benefit compared to placebo. A combination of psychotherapy and clomipramine has been reported to be effective. In a 12-week placebo-controlled study, escitalopram 17 mg/d was shown to be strongly antidepressant, but the study was under powered to yield statistical significance over placebo. In another 4 weeks double-blind, placebo-controlled study, paroxetine 20mg/d has been reported to show significant improvement. In both the studies phobias were varied and included heights, flying, specific animals, confined spaces, driving, storms and dentists. No long-term placebo-controlled studies are available for antidepressants in the treatment of specific phobia.

Drugs with a potential to enhance extinction process, d-cycloserine (DCS) and glucocorticoids, are the promising candidates for enhancing exposure therapy. Glucocorticoids are the stress hormones that affect the memory process. Animal and human studies show that glucocorticoids can inhibit memory retrieval and memory arousing information and facilitate the memory extinction processes. DCS, a partial agonist of N-methyl-D-aspartate (NMDA) glutamatergic receptor, has been shown to accelerate fear reduction during exposure, in several animal and human clinical studies.

DCS has no anxiolytic properties but it facilitates memory consolidation that takes place in the post-treatment period. The use of DCS as an adjunct treatment to exposure for acrophobia has been shown to produce great improvements on cognitive, subjective and behavioural outcome measures compared to placebo. Other studies also have shown positive results when DCS was used to augment exposure-based treatment for the specific phobias. DCS appears to be a promising therapeutic approach to facilitate the effects of behavioural treatments, but much more work is required with larger samples. Addition of cortisol to exposure therapy, in subjects with spider phobia, has been reported to cause a greater reduction in fear of spiders as compared to placebo. Repeated oral cortisol 1 hour before exposure to a spider photograph caused a progressive reduction of stimulus induced fear ; and the effect was maintained two days after the last dose of cortisol indicating that cortisol facilitated the extinction of phobic fear. However the

| Treatment                  | Advantages                                      | Disadvantages                      | Remarks               |
|----------------------------|-------------------------------------------------|------------------------------------|-----------------------|
| Exposure-based therapy     | *Highly effective                               | *May cause temporary increase in discomfort or fear | *Treatment of choice. |
|                            | *An early response                              |                                    |                       |
| Applied tension (AT)       | *Highly effective for patients with BII type SP who faint. | *Treatment is relevant to BII type SP only. | *Very effective.      |
|                            | *An early response                              |                                    |                       |
| Applied relaxation (AR)    | *Effective in patients with BII type SP.        | *Treatment has not been much studied in SP. | *May be helpful in some patients. |
| Cognitive therapy (CT)     | *May decrease anxiety about conducting exposure exercises. | *Probably not effective alone. | *May be helpful in some patients. |
|                            | *Decreases relapse rate when combined with exposure therapy | *Treatment has not been much studied in SP. |                       |
| Benzodiazepines            | *May decrease anticipatory anxiety before patient enters a phobic situation. | *Probably not effective alone. | *May be helpful in some patients. |
|                            | *ADRs are common.                               | *Relapse on discontinuation        |                       |
|                            | *Not extensively studied in SP.                 |                                    |                       |
| SSRIs                      | May decrease panic sensations similar to panic disorder, in persons with situational SP. | *Only a few studies with promising results | May be helpful in some patients. |
|                            |                                                 | *Not extensively studied in SP.     |                       |
|                            |                                                 | *Relapse on stopping the drug.      |                       |

SP= Specific phobia.
beneficial effects were not immediate post-treatment. Anxiety was significantly less during standardized exposure to living spiders at follow-up compared to the placebo treated subjects.\(^{41}\)

The initial assessment is a most critical component of the treatment approach for specific phobias. The initial assessment should select goals for treatment on a priority basis. In the subjects having more than one problem, the most distressing or impairing problem should be addressed first. This will improve patient compliance and possibly the treatment outcomes.

As is generally accepted pharmacotherapy is not a necessary or suitable treatment for specific phobias. Psychological treatments that incorporate exposure to the feared substance or situation are the treatment of choice for most of the specific phobias. Additional elements of treatment, e.g. applied tension and applied relaxation for BII phobias or symptom induction exercise for phobias including a fear of internal physical sensations can be added as needed. Treatment should start by socializing the person to treatment, stressing that goal of treatment is not to completely eliminate anxiety, but to minimize the associated distress and avoidance by systematically confronting the feared stimuli.\(^{43}\)

The use of self- report measures e.g. subjective units of distress scale (SUDS) ratings and questionnaire-based measures should be collected in the initial assessment and throughout the treatment to the track session. A post-treatment assessment by a clinical interview and behavioral approach task (BAT) can provide an objective measure of treatment outcome and provide reassurance to the patient for the therapeutic gains.\(^{43}\)

CONCLUSION

Specific phobias are very common in both men and women and impairing their quality of life in the community or at the work place. Most efficacious treatment for specific phobias is exposure-based therapy followed by cognitive behavioural therapy. However conventional drugs like BZDs, SSRIs, \(\beta\)- blockers are also useful to prevent physiological symptoms of fear and anxiety because of a specific phobia. Complementary and alternative methods of treatment for specific phobia include hypnosis, herbal remedies, and homeopathy. It can be concluded that more research work is required in the pharmacotherapeutic approach of the specific phobias.

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REFERENCES

1. Diagnostic and Statistical Manual of Mental Disorders (DSM).2000. Available at https://www.psychiatry.org/psychiatrists/practice/dsm. Accessed on 21 December 2015.
2. Kendlar KS, Myers J, Prescott CA, Neale MC. The genetic epidemiology of irrational fears and phobias in men. Archives General Psychology. 2001;58:257-67.
3. Mayo Clinic Staff. Phobias. Available at http://www.mayoclinic.org/diseases-conditions/phobias/basics/treatment/con-20023478/?p. Accessed on 21 December 2015.
4. Specific phobias. Available at http://www.med.upenn.edu/csta/phobias_treatment.html. Accessed on 26 December 2015.
5. Page AC. Blood-injury phobia. Clinical Psychology Rev. 1994;14:443-61.
6. Curtis GC, Hill EM, Lewis JA. Heterogeneity of DSM-III-R simple phobia the simple phobia/agoraphobia boundary: evidence from the ECA study. Report to DSM-IV anxiety disorders work group. University of Michigan. Ann Arbor, MI. 1990.
7. Phobias, Part 2: Specific and social phobias. Available at https://www.mdhll/phobias-part-2-specific-and-social-phobias. Accessed on 23 December 2015.
8. Psych Central Staff. Specific Phobia Symptoms. Available at: http://www.psychcentral.com/disorders/specific-phobia-symptoms. Accessed on 23 December 2015.
9. Kessler RC, Chiu WT, Demler O. Prevalence, severity and co-morbidity of 12 month DSM-IV disorders in the National Comorbidity Survey Replication. Archives of General Psychiatry 2005;62:617-27.
10. Lindesay J, Briggs K, Murphy E. The guys/age concern survey: prevalence rate of cognitive impairment, depression and anxiety in an urban elderly community. British Journal of Psychiatry. 1989;155:317-29.
11. Fredrikson M, Annas P, Fischer H. Gender and age differences in the prevalence of specific fears and phobias. Behaviour research and therapy. 1996;34:33-9.
12. Fyer AJ, Mannuzza S, Chapman TF. Specificity in familial aggregation of phobic disorders. Arch General Psych. 1995;52:564-73.
13. Kendler KS, Neale MC, Kessler RC. The genetic epidemiology of phobias in women: the interrelationship of agoraphobia, social phobia, situational phobia, and simple phobia. Arch General Psych. 1992;49:273-81.
14. Brown TA, Campbell LA, Lehman CL, Grisham JR, Mancill RB. Current and life comorbidity of the DSM-IV anxiety and mood disorders in a large clinical sample. Journal Abnormal Psych. 2001;110:585-99.
15. Wittchen HU, Nelson CB, Lachner G. Prevalence of mental disorders and psychosocial impairments in adolescents and young adults. Psychological Medicine. 1998;28:109-26.
16. Magee WJ, Eaton WW, Wittchen HU. Agoraphobia, simple phobia, and social phobia in the national comorbidity survey. Arch General Psych. 1996;53:59-68.

17. Marks IM. Fears, phobias, and rituals: panic, anxiety, and their disorders. Oxford University Press, London; 1987.

18. Ost LG, Salkovskis PM, Hellstrom K. One-session therapist-directed exposure vs self-exposure in treatment of spider phobia. Behavior Therapy. 1991;22:407-22.

19. Carlin AS, Hoffman HG, Weghorst H. Virtual reality and tactile augmentation in the treatment of spider phobia: a case report. Behaviour Research and Therapy. 1997;35:153-8.

20. Rothbaum BO, Anderson P, Zimand P, Hodges L, Lang D, Wilson J. Virtual reality exposure therapy and standard in vivo exposure therapy in the treatment of fear of flying. Behavioral Therapy. 2006;37(1):80-90.

21. Craske MG, Rowe MK. A comparison of behavioral and cognitive treatments for phobias. In GCL Davey (ed.). Phobias: A handbook of theory, research and treatment. Chichester: Wiley; 1997:247-280.

22. Choy Y, Fyer AJ, Lipsitz JD. Treatment of specific phobias in adults. Clinical Psychology Review. 2007;27:266-86.

23. Wolitzky-Taylor KB, Horowitz JD, Powers MB, Telch MJ. Psychological approaches in the treatment of specific phobias: A meta-analysis. Clinical Psychology Reviews 2008; 28: 1021-37.

24. Natural treatment for phobia and anxiety. Available at http://www.phobicssociety.org.uk/naturaltreatmentforphobiasandanxiety/ Accessed on 24 December 2015.

25. Adrian P. Phobic disorders treatment and management. Available at http://www.emedicine.medscape.com/article/288016-treatment. Accessed on 24 December 2015.

26. Antony MM, Barlow DH. Specific phobias. In anxiety and its disorders: The nature and treatment of anxiety and panic. 2nd edition. Barlow DH (eds.). Guilford Press, New York; 2002.

27. Wilhelm FH, Roth WT. Acute and delayed effects of alprazolam on flight phobics during exposure. Behav Res Ther. 1997;35(9):831-41.

28. Thom A, Sartory G, Johren P. Comparison between one-session psychological treatment and benzodiazepine in dental phobia. Journal of Consulting Clinical Psychology. 2000;68(3):378-87.

29. Moscovitch DA, Antony MM, Swinson RP. Exposure based treatments for anxiety disorders: theory and process. Antony MM, Stein MB (eds.), Oxford handbook of anxiety and related disorders. New York: Oxford University Press;2009:461-475.

30. Campos PE, Solyom L, Koelinka A. The effects of timolol maleate on subjective and physiological components of air travel phobia. Canadian Journal of Psychiatry. 1984;29:570-74.

31. Almay S, Zhang W, Varia I, Davidson JRT, Connor KM. Escitalopram in specific phobia: Results of a placebo controlled pilot trial. Journal of Psychopharmacology. 2008;22:157-61.

32. Waxman D. The management of phobic disorders using clomipramine (Anafranil). J Int Med Res. 1977;5(1):24-31.

33. Benjamin J, Ben-Zion IZ, Karbofsky E, Dannon P. Double blind placebo controlled pilot study of paroxetine for specific phobia. Psychopharmacology. 2000;149:194-96.

34. Norberg MM, Krystal JH, Tolin DF. A meta-analysis of D-cycloserine and the facilitation of fear extinction and exposure therapy. Biological Psychiatry. 2008;63:1118-26.

35. Quervian DJ, Bentz D, Michael T. Glucocorticoids enhance extinction-based psychotherapy. Proc Natl Acad Sci. 2011;108:662-25.

36. Quervian DJ, Aerni A, Shelling G. Glucocorticoids and the regulation of memory in health and disease. Frontiers Neuroendocrinol. 2009;30:358-70.

37. Buchanan TW, Lovallo WR. Enhanced memory for emotional material following stress-level cortisol treatment in humans. Psycho Neuroendocrinology. 2001;26:307-17.

38. Cadyce DT, Pamela RH, Lindsey BD, David R, Mark HP, Stefan GH. Augmentation of exposure therapy with post-session administration of D-cycloserine. J Psychiatr Res. 2013;47(2):168-74.

39. Smits JA, Rosenfield D, Otto MW, Powers MB, Hofmann SG, Telch MJ, Pollack MH, Tart CD. D-cycloserine enhancement of fear extinction is specific to successful exposure sessions: evidence from the treatment of height phobia. Biological Psychiatry. 2013;73(11):1054-8.

40. Helga R, Ivan F, Alessandra L, Raquel G, Mauro MV, Evandro SFC, Paula V. Does D-cycloserine enhance exposure therapy for anxiety disorders in humans? A meta-analysis. Plos One. 2014;9(7):e93519.

41. Liela MS, Markus H, Livia W, Melanie F, Wolfgang S, Helge H. Glucocorticoids enhance in vivo exposure-based therapy of spider phobia. Depression and anxiety. 2014;31(5):429-35.

42. Quervian DJ, Jurgen M. Glucocorticoids for the treatment of post-traumatic stress disorder and phobias: A novel therapeutic approach. European Journal of Pharmacology. 2008;583:365-71.

43. Hood KH, Antony MM. In Intensive One-session treatment of specific phobias, Autism and Child Psychopathology Series, TE Davis III.Springer Science+Bussiness Media LLC; 2012:19-42.