

## Venlafaxine and sexual disinhibition

### Introduction

Venlafaxine (Efexor®) was approved for marketing in the Netherlands in June 1994. The therapeutic indications of venlafaxine are *episodes of depression, short term treatment of generalised anxiety disorder, short term treatment of social anxiety/social phobia and treatment of panic disorders with or without agoraphobia*.

Venlafaxine is an antidepressant neither belonging to the tricyclic antidepressants, nor to the selective serotonin reuptake inhibitors. Venlafaxine is a Serotonin and Norepinephrine Reuptake Inhibitor, inhibiting neuronal uptake of serotonin, norepinephrine, and to a lesser extent dopamine. In doses of 75 mg daily, venlafaxine selectively inhibits the reuptake of serotonin, what makes it a selective serotonin reuptake inhibitor (SSRI). In doses of more than 75 mg daily, venlafaxine acts as a Serotonin and Norepinephrine Reuptake Inhibitor [1].

### Reports

On December 20, 2006, the database of Netherlands Pharmacovigilance Centre Lareb contained three reports concerning sexual disinhibition associated with the use of venlafaxine.

Patient A is a male aged 26 who was using venlafaxine 37.5 mg twice daily. Indication for use was not reported. After seven weeks he experienced increased libido and sexual disinhibition. It was assumed that the effects would disappear with time, but symptoms persisted and the venlafaxine dosage was reduced. At the time of reporting the patient had not recovered. No concomitant medication was reported.

Patient B is a male aged 34 who was using venlafaxine 75 mg once daily. Indication for use was not reported. After 2-3 days of treatment he reported a libido increase, which he considered to be very disturbing. Venlafaxine was withdrawn, patient outcome is unknown. No concomitant medication was reported.

Patient C is a female aged 45. She has a medical history of depression. She used venlafaxine for depression in increasing doses, first 75 mg twice daily and thereafter 75 mg three times daily. Ten days after the dose increase she experienced a libido increase which she describes as disturbing. Dose was reduced to 37.5 mg once daily. Patient outcome is unknown. No concomitant medication was reported.

### Other sources of information

#### Literature

Michael and Owen describe in a case report a patient who suffered from venlafaxine-induced libido increase and spontaneous erections. The patient, a 50-year-old male, was referred with a first episode of major depression. Before the depression, his sexual function was normal. Since becoming depressed his libido was non-existent and he had not had any sexual contact. Patient was put on treatment with a combination of venlafaxine and lithium. One week after venlafaxine dosage was increased to 375 mg daily he reported increased libido, much higher than before his depression. After six weeks on the same medication the libido increase waned and his depression improved [2].

Bolukbasi and Akyol describe a case where a 58-year-old man with Parkinson's disease presented with depressive symptoms. One month earlier the patient had undergone detailed urological and neurological investigation because of loss of penile erections and decreased libido without any yield of an organic reason for it. Patient was started on venlafaxine 37.5 mg twice daily for the depression which was increased to 150 mg twice daily during the end of the first week of treatment. Ten days later he recognized spontaneous erections and an increased libido. Mood began to improve in the third week of treatment and after a month treatment he was nearly normal in mood and level of desire for sex. When venlafaxine treatment was tapered off the patient's psychiatric and sexual status was still satisfactory [3].

Alvezizos *et al.* describe a case of a depressed woman who experienced an increase of sexual desire above premorbid levels after receiving a combination of venlafaxine and mirtazapine. The patient, a married female aged 46, had a nine year history of recurrent depressive illness. The duration of the present depressive episode was 1.5 years. Her usual sexual activity had been satisfying to her, but this was moderately decreased during the depressive episode. The depression was treated with various antidepressive agents but these had no effect on the disease. Treatment was started with venlafaxine, initially 75 mg every three days, titrated up to 225 mg daily, and mirtazapine 30 mg daily. After using venlafaxine 225 mg for two weeks the patient reported a rapid improvement of depressive symptoms. She also reported that her sex drive was greater than it had ever been. However she complained of delayed or absence of orgasm and reduced lubrication. Furthermore she experienced progressively increasing anxiety and psychomotor agitation. Venlafaxine was tapered off within 3 days. During the following days her sex drive progressively decreased to slightly above her normal level. To avoid relapse of depressive symptoms venlafaxine was started in a low dose once (75 mg daily) again. One week later her sex drive increased again to above her normal level. Venlafaxine was replaced by fluvoxamine 50 mg daily and her sex drive progressively decreased to her pre-morbid levels [4].

## Databases

On January 2, 2007, the Lareb database contained 705 reports on venlafaxine. At the end of the 2<sup>nd</sup> quarter of 2006 the WHO Collaborating Centre for International Drug Monitoring had received 17 reports of libido increase associated with the use of venlafaxine (ROR 3.9 95% CI 2.4 - 6.3).

## Mechanism

Norepinephrine facilitates libido and erections [2]. It has been reported that ephedrine, an  $\alpha$ -adrenergic and  $\beta$ -adrenergic agonist significantly can facilitate the initial stages of psychological sexual arousal in women [5]. Venlafaxine enhances norepinephrine transmission and could therefore lead to libido increase in patients treated with this drug.

The re-uptake of dopamine is inhibited while using venlafaxine [1]. It has recently been shown that drugs that increase dopaminergic transmission, i.e. drugs that are used in the treatment of Parkinson's disease, can cause sexual disinhibition [6].

## Prescription data

Prescription data for venlafaxine in the Netherlands over the last five years are presented in table 1.

Table 1. Number of patients treated with venlafaxine in the Netherlands.

	2001	2002	2003	2004	2005
venlafaxine (Efexor®)	64,749	74,064	86,584	103,660	109,170

Source: GIP/College voor zorgverzekeringen 2006 (<http://www.gipdatabank.nl>)

## Discussion

Libido decrease is associated with depression. One could argue that the sexual disinhibition during use of venlafaxine could be a result of the improvement of the depression. In two of the three reports received, the reporter states that the libido increase was considered to be disturbing, suggested that the libido was much higher than before the depression. The latency in two of the cases (2-3 days and 10 days after dose increase) is also too short to see improvement of the depressive symptoms.

## Conclusion

Lareb received three cases of sexual disinhibition associated with the use of venlafaxine. Venlafaxine induced sexual disinhibition has been described in the literature.

### References

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