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A Retrospective Comparative Chart review of prescription patterns of Trazadone and Zolpidem in an Psychiatric out-patient clinic shows equal patient preference and benefit profile

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ABSTRACT:

Two commonly prescribed medications to address sleep problems, in psychiatric outpatient setting Trazodone and Zolpidem (AMBIEN) were compared in a chart review, and assessed for efficacy and patient preference. This article focused on patient preference for either medication as evidenced by either a direct patient request for that medications, and once initiated the duration of treatment time before a change in medication was requested, or the total duration of treatment for medication. The authors reviewed 101 charts, in which sleep was identified as a clinical concern and was treated with a medication option. Sleep Hygiene was routinely discussed with patients, however the charts did not track compliance with proper sleep hygiene techniques by the patients. The efficacy of the medication was noted by the time duration from when the improvement in the symptoms (sleep) had been established and maintained to the point that the patient no longer needed or desired to continue medications. The findings indicated that both medications were efficacious, and by day 270, only 7% of the patients in either cohort, continued to need to use the medications. The self-reported satisfaction and improvement was also equal with both groups. As the two medications were noted to be almost equal in preference and efficacy, then reviewing the Cost Benefit Analysis indicated that it might be beneficial to try Trazodone for sleep issues before trying a more costly option such as zolpidem (AMBIEN).

INTRODUCTION

Insomnia is a common medical complaint. It is a term which refers to difficulty initiating sleep, difficulty maintaining sleep and early morning awakening and inability to fall sleep again (American Psychiatric Association, DSM-5, 2014) It is the most prevalent sleep disorder, occurring in 19% to 50% of clinical patients seeking treatment in the outpatient setting (Katz DA, 2002), (National Sleep Foundation., 1995), (Culpepper, 2006). One of the main features of insomnia is difficulty initiating sleep, defined as subjective sleep latency of more than 20 to 30 minutes (Katz DA, 2002). A study noted the prevalence of insomnia was as high as 69% in primary care patients (Shochat T, 1999). Also, a recent national survey of non-institutionalized adults reported a 35% insomnia prevalence rate during the course of the year, with insomnia affecting women more than 50% of the time (Mellinger GD, 1985). About 20% to 36% of patients are affected by insomnia chronically which lasts for a duration of greater than 1 year (Bixler EO, 1979), (Chevalier H, 1999), (Hohagen F & 242(6):329–336., 1993), (Vollrath M, 1989; 239(2):113–124.), (Zeithofer J, 1994;). Insomnia is a symptoms of many psychiatric illnesses and can also present as a comorbidity with other psychiatric illness with a

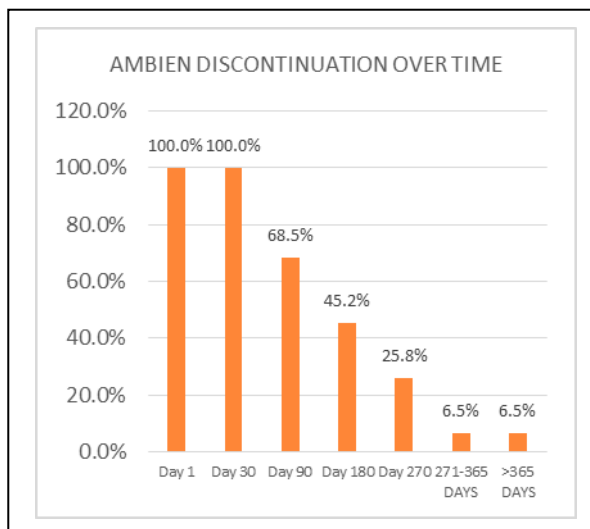
large number of patients presenting with insomnia (Becker, 2006). Although common, the importance and incidence of insomnia is often underestimated, especially in the elderly. This can be an issue as it is associated with a significant increase in morbidity and mortality in the elderly. Nursing home visits are greatly increased due to sequelae of insomnia (Ancoli-Israel, 2000; 23 (Suppl 1):S23–30 (discussion S6–8).).

In addition to its prevalent, insomnia is associated with various sequelae and quality of life issues. Moreover, not all medications are universally available, affordable or effective. Medications especially proprietary name-brand medications, can at times be cost prohibitive, the authors decided to perform a chart review to see if there is any cost justifiable benefit to one medication over the other.

The results were not surprisingly different from anecdotal observations, but the results are a good informative discussion point that can be shared with patients, in aiding them make informed decisions about the medications that they may wish to choose for their insomnia.

To study the effectiveness of medications used

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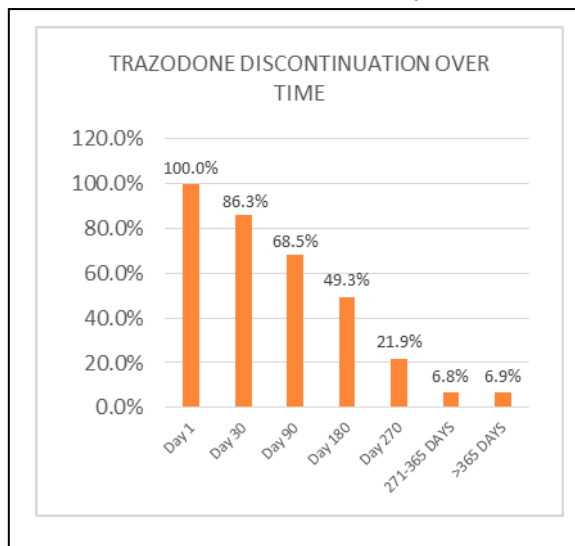
to treat insomnia, and to note the preferences of the patients, the authors identified TRAZODONE and AMBIEN as the two medications to compare. This was also based on the preponderance of the prescription written for these two medications in the out-patient clinic.

METHOD:

A total of 101 charts from outpatient clinic were reviewed. Those charts were included in the review, which listed Insomnia as an identified concern and either TRAZODONE or AMBIEN were prescribed for Insomnia issues.

The factors that were studied, included the total duration of time that the medication was used in days, and frequency of prescription of each medication and rates of discontinuation.

Duration on trazodone and/or zolpidem was cal-



culated in days from first day of treatment till the last day of treatment or up to the arbitrary date 365 days from start of treatment.

Subjective improvement in sleep (Quality and Duration as well as general Satisfaction by the patient) were inferred from chart records during the follow-up visits.

Of the 101 charts reviewed, 63% were of female and 37% were male patients. Amongst the male patients, 71 % had prescriptions for AMBIEN and 29% had prescriptions for TRAZODONE. In contrast 69% of female patients were on TRAZODONE and 31% were on AMBIEN.

It was also noted that of all total prescriptions written for insomnia in both male and female patients, TRAZODONE was prescribed almost twice as often than AMBIEN. Patients who took either TRAZODONE or AMBIEN both reportedly continued with medications, noticing improvement with adequate tolerability to their respective medications. In both group of patient it was noted that by Day 270 from the date of the initial prescription less than 7% of the patients (Male or Female) were still using any medication (AMBIEN or TRAZODONE), this ratio remained fairly constant till the end of the observation period of 365 days.

When the discontinuation data of the two medications was compared, it was noted that in the first thirty days of commencement of treatment there were no drop outs from the group taking AMBIEN, whereas almost 14% of patient who started TRAZODONE had stopped taking their medication. Although the exact reason that TRAZODONE was discontinued was not captured in the charts, it appears that the assumption was that the medication was no longer needed to address insomnia. However of those subjects who continued to take their medications, within 90 days, the discontinuation rates of both medications (TRAZODONE and AMBIEN) were almost similar.

No Adverse Events or Side Effects were noted in the charts, therefore the reason for termination of treatment with medications at various time points was assumed to be resolution of the initial insomnia.

DISCUSSION

Many pharmacological agents are used to treat insomnia, some of these medications are used "Off Label".

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Zolpidem, a non-benzodiazepine compound is one of the most common medications for treatment of insomnia. Zolpidem has been shown to cause minimal risk of withdrawal or abuse. It can be used for symptoms of initiation of sleep and middle of the night awakening. However, the drawbacks include rebound insomnia, next-day residual effects (after middle-of-the-night dosing) and complex sleep-related behaviors such as on ability to drive, memory, and psychomotor performance (Lichtenwalner M, 1997). Various studies support the efficacy, safety and tolerability of zolpidem, in adults including the elderly (Katz DA, 2002), (National Sleep Foundation., 1995), (Culpepper, 2006), (Mellinger GD, 1985), (Zeitlhofer J, 1994;). There is minimal risk of abuse or dependence with administration of zolpidem in this population (Aragona, 2000), (Morinan A, 2010), (Sadock BJ, 2007.), (Perrault G, 1992), (Liappas IA, 2003;)

Trazodone is a serotonin antagonist and reuptake inhibitor (SARI) that has been used for the treatment of MDD with or without anxiety since as early as the 1970s (Feighner JP, 1988). At lower doses than those used for the treatment of depression, trazodone is thought to be act primarily by antagonizing 5-HT_{2A} receptors, H₁ receptors and α ₁-adrenergic receptors (Stahl, 2009). Trazodone has efficacy similar to other second generation anti-depression medications. Trazodone is not FDA approved for insomnia or sleep disorders, however it is used as part of standard practice in many outpatient settings (Stahl, 2009), (Brogden RN, 1981). It is tolerated well and has fewer anticholinergic effects than TCAs (Tri cyclic antidepressants) such as imipramine and amitriptyline.

BENZODIAZEPINE group of medications are effective as hypnotic agents, however they do have certain drawbacks, including their propensity to be habit forming. They can also lead to dependency and even abuse if not monitored and used judiciously. In addition, Benzodiazepines can also cause central nervous system side effects like ataxia, anterograde amnesia, falls leading to potential complications such as motor vehicle accidents.

ANTI-HISTAMINES are effective Hypnotic agents, histamine blockade causes sedation. However, Anti-Histamines can cause central and peripheral anticholinergic side effects, and the sedative/hypnotic effects are relatively short-lived. Furthermore, in younger patients, Anti-Histamines can lead to paradoxical symptoms

which may negatively effect insomnia treatment. In the chart review it was noted that of the two medications (AMBIEN and TRAZODONE), TRAZODONE was prescribed twice as much as AMBIEN for females. However irrespective of which medication was used initially for treatment of insomnia, by DAY 270, less than 7% of people needed to continue either medication for insomnia, reporting a resolution to their sleep problems.

The authors did note that both groups of patients tolerated the medications without any discontinuations because of Adverse Effects.

The authors also pondered over the reason why trazodone was prescribed more than Ambien, and more for female patients. Prescriber bias was taken into consideration and ruled out. Prescriber preference for one medication over another, usually is an indication of that medications past positive performance in similar patients. Another reason is usually patient request for a specific medication. Trazodone being in the family of Anti-Depressants, it was also considered that some patients may have been preferentially prescribed TRAZODONE to address sub-clinical manifestation of anxiety of depression.

The authors acknowledge that there may have been many reasons for the prescriptions of trazodone outnumbering the prescriptions of zolpidem in the psychiatric outpatient setting for patients, regardless of patient psychiatric diagnosis. However the true reason for such a discrepancy was not noted in the charts, therefore the reason can only be speculated and is beyond the scope of discussion of this article.

Trazodone is commonly used as a sleep aid and an anti-depressant medication (Stahl, 2009), (Brogden RN, 1981). Psychiatrists use trazodone for both indications (Scharf MB, 1990;), (Thase, 1999), (Evans SM, 1990; 255:1246– 1255.). Also, in psychiatric patients, both conditions coexist in many individuals (Passarella S, 2008), (Weyerer S, 1991), (Scharf MB, 1990;), (Thase, 1999), (Evans SM, 1990; 255:1246– 1255.) making trazodone an attractive option.

Another reason for Trazodone being prescribed more than Ambien, could be that patients choose to take trazodone over zolpidem because of its dual nature as a sleep aid and antidepressant (Stahl, 2009), (Brogden RN, 1981), thus making it seem more reasonable to take than to add another sleep medication.

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Thirdly, AMBIEN is considered by many to have habit forming potential (Rush CR B. R., Acute behavioral effects and abuse potential of trazodone, zolpidem and triazolam in humans., 1999), (Caroline Victorri-Vigneau PhD, (2014)), which could have contributed to a hesitancy by the prescriber to initiate insomnia therapy with AMBIEN, or the patient/patient's family asking for an alternative medication. Trazodone does not seem to have the habit forming properties that Zolpidem does. This may well have played a noticeable role in patients either choosing or physicians prescribing trazodone over zolpidem.

Another consideration is the Cost Benefit Analysis perspective, TRAZODONE is a more affordable option than ZOLPIDEM. According to Epocrates, generic TRAZODONE 50 mg Tablet costs \$34.84 for 60 tablets and the cost for 100mg Tablet is \$48.75 for 60 tablets; whereas name brand AMBIEN 10 mg costs \$241.99 for 30 tablets and AMBIEN CR 12.5 mg is \$287.99 for 30 tablets.

CONCLUSION:

Both zolpidem and trazodone are commonly prescribed medications for insomnia and have never been compared in such a manner in an outpatient clinical setting. Through chart review and analysis of the data, it is evident that both AMBIEN and TRAZODONE are effective medications. Overall both medications were well tolerated, and their duration of use and discontinuation patterns were also very similar. However the cost differential is between the two medications is considerable.

Currently TRAZODONE appears to be a more cost effective first line option for insomnia. It is also equally important to emphasize the importance of behavior modification and implementation of good sleep hygiene.

The authors acknowledge that this report is by no means exhaustive in its learning objectives, the one fact that has become clear is that further investigation is warranted. Further studies would be beneficial to probe the reasons why some patient prefer one medication over another.

There are various levels of practitioners (Specialist Physicians, General Practice Physicians, as well as med-level practitioners) who prescribe medications used for insomnia. On numerous occasions, patients request that their physicians prescribe a certain medication to them. As responsible physicians it is our duty to

provide our patients with the best information available about the medications, their efficacy as well as their comparative benefits; which should also include a Cost Benefit Analysis.

Trazodone showed similar results to zolpidem for treatment for insomnia. At the end of the day, it is cheaper and is more commonly used than zolpidem, an accepted FDA approved medication for insomnia. More evidence for its efficacy may help patients and physicians alike, to feel more comfortable to use it as treatment for insomnia.

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