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Improving Outcomes in Patients Who are Prescribed Alprazolam with Concurrent Use of Opioids

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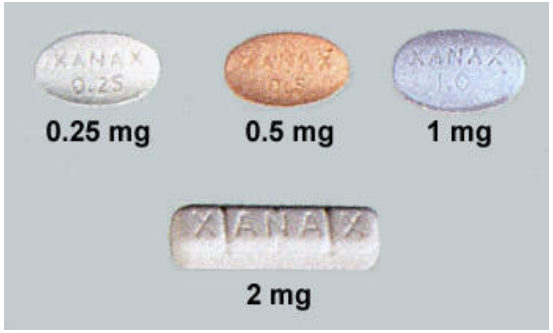
Background and Rationale

- Alprazolam is the most commonly prescribed benzodiazepine, a class of drugs that are used to treat panic and anxiety disorder in the US.[1]
- Relative to other Benzodiazepines, Alprazolam has rapid onset and offset of action resulting in high risks of adverse outcomes including dependency, withdrawal, rebound anxiety and drug overdose deaths.
- The most recent CDC Morbidity and Mortality Weekly Report found Alprazolam to be the benzodiazepine associated with the highest number of ED visits in the US [1].

Background and Rationale

- The estimated number of ED visits for alprazolam in 2008 (104,800) was more than twice the number for the next most common benzodiazepine, Clonazepam (48,400)[1].
- There is no evidence demonstrating an advantage of alprazolam over other benzodiazepines in the management of adult patients with panic disorder.[2]
- By reducing alprazolam prescription, we may reduce risks of overdose, number of ED visits, and benzodiazepine misuse/illegal sales, subsequently improving overall health outcomes.



Project Details

- **Setting**: Center for Counseling at Walton, Article 31 community mental health clinic
- **Method**: Continuous Quality Improvement Project (CQI)
- **Timeline**: Jan 2014 – Dec 2014
- **Subjects**: A total of 17 alprazolam dependent patients were identified on my case load (Jan-*Sept 2014). All of them carried a diagnosis of anxiety or panic disorder.

* A number of alprazolam dependent patients were being transferred to my caseload due to the departure of a provider in October 2014. Those patients were excluded from this study as the CQI project had already entered its final quarter.

Subjects Data

Age	Gender	Methadone	Pain Narcotic	Buprenorphine	Substance Abuse history
49	F	n/a	Oxycondone	n/a	yes
55	F	n/a	Morphine & Oxycodone	n/a	yes
38	F	n/a	Hydrocodone	n/a	yes
52	M	n/a	n/a	4mg	yes
57	F	n/a	n/a	n/a	no
46	M	n/a	UDS+opioid	n/a	yes
49	F	n/a	n/a	n/a	yes
61	F	n/a	Oxycodone	n/a	no
34	M	30mg	n/a	n/a	yes
47	F	n/a	n/a	n/a	yes
47	F	35mg	Oxycodone	n/a	yes
51	M	n/a	n/a	n/a	yes
41	F	n/a	n/a	n/a	no
47	F	n/a	n/a	n/a	yes
44	M	n/a	n/a	n/a	no
52	F	n/a	Tramadol	n/a	yes
46	M	n/a	Oxycodone	n/a	yes

Goals

1. More than 50% of alprazolam dependent patients (>8) are able to either:

   - Switch to a longer acting benzodiazepine (Lorazepam, Clonazepam, Diazepam) safely, or
   - Discontinue all benzodiazepine safely, or
   - Decrease alprazolam dosage.

2. A greater than 50% decrease in the number of patients using Alprazolam and opioids concurrently.

All without worsening of anxiety/mood symptoms based on patient self-report or relapse to illicit drug use/misuse of benzodiazepine based on results from random urine drug screen and New York State Prescription Monitoring Program Registry.

Interventions

- Conversation with patient about the risks of Alprazolam use, particularly concurrent use with opioids.

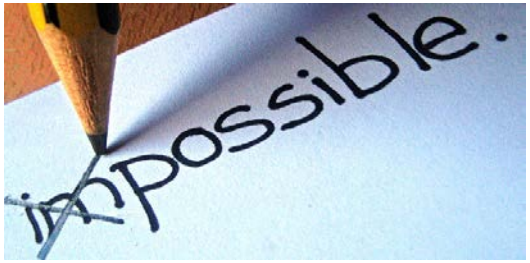
- Patients were given the following options:
  1. Alprazolam taper to lower dose
  2. Discontinue all benzodiazepines
  3. Switch to long acting benzodiazepines as tolerated - choices of long acting benzodiazepines are based on patient's history of past benzodiazepine use and tolerance
  4. Decline all options
  5. Initiate first line medications for panic/anxiety such as SSRI or SNRI if they are not already being treated with these medications.

- Random urine toxicology was utilized to screen for medication adherence and illicit drug use/relapse to illicit drug use.

Outcome measures

- Mood and anxiety are monitored based on patient's presentation and self-report.
- Random urine drug screen to look for medication adherence/illicit drug use/relapse.
- Tracking for ER visits and hospitalization associated with benzodiazepine use.

Results



First goal achieved!!

More than 50% of alprazolam dependent patients (9/17 = 52%) are able to either:

- Switch to long acting benzodiazepine safely (6/17 = 35%) at equivalent dose of Alprazolam,
  - 2 patients are on Clonazapam
  - 2 patients are on Diazepam
  - 2 patients are on Lorazepam
- Discontinue all benzodiazepine safely (1/17 = 6%), or
- Take a lower dosage of Alprazolam (2/17 = 11.8%)

without worsening of anxiety/mood/psychotic symptoms/ER visit/hospitalization.

Less than 50% 8/17 (47.7%) opted for:

- Declined all options (6/17 = 35%)
- Agreed to switch to long acting medications but has not initiated taper (2/17 = 11.8%) due to unstable mental state and loss to follow up

Results

Age	Gender	Methadone	Pain Narcotic	Buprenorphine	Substance Abuse history	Switched to longer acting Benzo	Declined	Agreed switching*	Discontinued Xanax	Reduced Xanax dose
49	F	n/a	Oxycondone	n/a	yes	Lorazepam				
55	F	n/a	Morphine & Oxycodone	n/a	yes	Diazepam				
38	F	n/a	Hydrocodone	n/a	yes	Clonazepam				
52	M	n/a	n/a	4mg	yes					from 6mg to 4mg
57	F	n/a	n/a	n/a	no				x	
46	M	UDS+	UDS+opioid**	n/a	yes		x **			
49	F	n/a	n/a	n/a	yes	Lorazepam				
61	F	n/a	Oxycodone	n/a	no		x			
34	M	30mg	n/a	n/a	yes			x		
47	F	n/a	n/a	n/a	yes					from 6mg to 4mg
47	F	35mg	Oxycodone	n/a	yes	Clonazepam				
51	M	n/a	n/a	n/a	yes	Clonazepam				
41	F	n/a	n/a	n/a	no		x			
47	F	n/a	n/a	n/a	yes		x			
44	M	n/a	n/a	n/a	no		x			
52	F	n/a	Tramadol	n/a	yes		x			
46	M	n/a	Oxycodone	n/a	yes			x		

Results

Second goal achieved!!

- 50% decrease in concurrent use of opioids in patients receiving prescription for Alprazolam

	Total # of patients using Alprazolam and Opioids concurrently	Alprazolam + Methadone	Alprazolam + narcotic pain medications (such as percocet)	Alprazolam + Buprenorphine
Before intervention	10	2	7	1
After intervention	5	1	3	1*

*Alprazolam dose decreased by 1/3 from 6mg to 4mg.

Results

- Among the 6 patients who declined, one was found positive for illicit methadone and opioids on the random urine drug screen. Patient was counseled and was engaged in substance abuse treatment briefly. Patient was unable to tolerate long acting benzodiazepine and relapsed. Patient declined detox and rehab. Patient has not been responding to outreach, and is pending discharge. The remaining 5 patients are stable without changes in anxiety level or positive urine toxicology.

- Two patients who previously agreed to switch to long acting benzodiazepine remain on Alprazolam.
  - one patient has continued to receive Alprazolam from primary care doctor
  - one patient has unstable mental status, changing medication may worsen patient's psychotic symptoms.

Discussion

- Conversation about risks of Alprazolam should be extended to other prescribers, i.e. PCP, who may provide medication for patients
- Some of the challenges faced when initiating conversation with patients include:
  - Allow extra time to address their concerns and fear
  - Be ready for resistance or hostility
- Factors contributing to successful changing and tapering:
  - strong therapeutic relationship
  - not currently under acute psychosocial stress
  - long history of sobriety
  - some type of social support
  - psychiatrically stable without acute mood or psychotic symptoms
- Random urine drug screen and controlled substance agreement are essential tools to monitor and reinforce treatment adherence

Limitations

- Small sample size
- Mostly established patients, recent transfers (after Oct 2014) were excluded.
- Most patients are still using Benzodiazepine chronically and using opioids concurrently.
- Random urine drug screen was not done consistently.
- Standard anxiety metric was not used to measure level of anxiety quantitatively. Anxiety metric may help to identify subtle changes in anxiety level and allow the practitioner to address it promptly.

Recommendation for Future Practice

- Use first line medications, i.e. antidepressants, for anxiety disorders.
- Educate patients about risks of long term benzodiazepine use prior to prescribing the medication.
- If possible, limit Alprazolam to short term use at lowest effective dose.
- Utilize controlled substance agreement.
- Discuss substance abuse with patients, and offer early intervention such as Alcoholics Anonymous/Narcotics Anonymous, detox and rehabilitation.

References

[1] CDC MMWR Morbidity and Mortality Weekly Report Vol. 59/No.23 June 18, 2010
[2] Journal of clinical Psychopharmacology Volume31(5), October 2011, pp647-652

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