

Drug Prescribing Pattern (Generalized Anxiety Disorder) in Banyumas General Hospital

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Abstract—Generalized Anxiety Disorder (GAD) is an anxiety disorder with an estimated 6 % of Indonesia's population. The medication of anxiolytic must be administered appropriately according to the patient's clinical condition. This is due to the variability of individual responses to anxiolytic drugs. This study was aimed to explore the type of drug, the determinant of patient (age, gender, occupation), and duration of treatment. The study was conducted retrospectively since January 1st 2017 until December 31st 2018 at Polyclinic YANKESWA Banyumas Hospital. The sample of this study were 47 patients who meet the inclusion criteria, who received anti-anxiety drug therapy for 6-24 month, and had a complete list of clinical therapies. The results of the study showed that there were 47 medical record data of patients, with a range of age 22-63 years; and various job statuses. The therapy received by GAD patients was anxiolytic drug such as Benzodiazepines group including Alprazolam (41%), Clobazam (9%), and Lorazepam (11%), SSRIs include: Fluoxetine (6%), Sertraline (14%) and TCA: Amitriptyline (8%).

Keywords: GAD, prescribing pattern

I. INTRODUCTION

GAD is a chronic anxiety disorder characterized by persistent and excessive anxiety, and difficult to control which can be accompanied by psychological and somatic symptoms.

According to Prof. Zullies Ikawati. Ph.D (2013) anxiety disorders is associated with abnormalities in some parts of the brain and impaired function of several neurotransmitters including norepinephrine (NE), GABA (Gamma Amino Butyric Acid), and serotonin (5-HT), amygdala structure which is a temporal lobe in the brain that plays an important role in stimulating and responding to anxiety symptoms. Locus Ceruleus (LC) located in the bone marrow is the main part of the brain that contains NE with a wider distribution area of the brain that is responsible for anxious responses (such as: vagus, hypothalamus, lateral and paraventricular). Hippocampus is an area of the brain that is responsible for both combining trauma memory stimulus and along with entorhinal cortex involving in overgeneralizing anxious responses. Hypothalamus is the main area in the overall neuroendocrine and autonomic response to anxiety improvement.

There are 3 neurochemical theories about the pathophysiology of anxiety disorders:

1. Norepinephrine (NE) model

This theory explains that people with anxiety have an excessive level of sensitivity to anxiety and an excessive reaction to stress stimulus. In response to attack stressful situations, LC acts as an alarm, activates NE, release and stimulates sympathetic and parasympathetic

nerves. Anxiogenic medication (yohimbin, alpha 2 adrenergic receptor blocking agents) stimulates NE and causes noradrenergic activity.

NE can also excrete glutamate (excitatory neurotransmitters), which causes anxiety and panic disorder.

2. GABA Model

There are 2 GABA protein-receptors: GABA_A and GABA_B. GABA is the main inhibitory neurotransmitter in CNS that has a strong regulation or inhibitory effect on 5 HT, NE, and DOPAMIN systems. When GABA is bound to GABA_A receptor, the ion channel of Cl opens and causes negative charge influx. This condition causes hyperpolarization of cell membranes and decreases nerve cell excitability. This decreasing effect becomes an anxiolytic mechanism of GABA against drugs, such as benzodiazepine.

3. Serotonin Model

The disorders of serotonin system which are inhibitory neurotransmitters cause disruption in the release and reuptake of presynaptic auto receptors, serotonin reuptake transporters, or the effects of serotonin on synaptic central receptors. This mechanism is believed to play a role in anxiety disorders.

Broadly speaking, anxiety can be caused by 2 factors:

1. Factors of the disease or medical disorders and medication.

a. Disease factors or medical disorders.

Some diseases related to anxiety are cardiovascular disorders (angina, arrhythmias, congestive heart failure, ischemic heart disorders and cardiac infarction), endocrine and metabolic diseases (hyperthyroidism, hyperparathyroidism, hypothyroidism, hypoglycemia, hyponatremia, hyperkalemia, pheochromocytoma, vitamin B12 deficiency and folate deficiency), neurological disorders (dementia, Parkinson, migraine, seizures, strokes, and neoplasms), respiratory disorders (asthma, COPD, pulmonary embolism and pneumonia), other diseases (anemia, SLE, and vestibular dysfunction).

b. Medication.

Some medications can also cause anxiety disorders, such as carbamazepine, antidepressants SSRI, felodipine, quinolone, antibiotic, isoniazid, theophylline, prednisone, levodopa, ibuprofen, and others. Herbal medicines such as ginseng and ephedra, and some stimulant agents that can cause anxiety (amphetamine, cocaine, caffeine), sympathomimetic

drugs (pseudoephedrine), and thyroid hormone (levothyroxine) can also trigger anxiety. Moreover, the toxicity of some drugs can also cause anxiety (digoxin, anticholinergic and antihistamines), due to withdrawal of sedative drugs, and alcohol.

2. Factors of Mental Health Disorder

Anxiety is a clinical manifestation in a number of psychiatric disorders, a marked symptom occurs in patients with mood disorders, schizophrenia, delirium, dementia, and drug abuse.

- a. This Scientific Papers was aimed to determine the pattern of drug prescription of GAD (Generalized Anxiety Disorder) at Banyumas General Hospital in 2017 – 2018 and to find out the types of GAD drugs that are widely used for GAD therapy.
- b. Knowing the factors of Generalized Anxiety Disorder (GAD) patients based on age, gender and occupation of GAD patients.
- c. Knowing the duration of treatment in Generalized Anxiety Disorder (GAD) patients.

II. METHOD

This study used a descriptive method with a quantitative approach to a population or sample. Data collection using research instruments, data analysis performed using quantitative data.

This study conducted to determine the value of an independent variable, either one variable or more (independent) without making comparisons or connecting with other variables.

Based on this theory, descriptive approach in this study is intended to get an overview of the types of GAD drugs, GAD patient determinants (age, sex, occupation) and treatment duration of GAD.

III. RESULTS AND DISCUSSION

1. Types of Medication

Based on the study in the medical records of patients, the types of drugs used in the treatment of patients with GAD in Banyumas Regional Hospital from January 2017 to December 2018 can be seen in table 1.

TABLE 1. TYPES OF DRUGS USED IN GAD PATIENTS IN BANYUMAS REGIONAL HOSPITAL FROM JANUARY 2017 TO DECEMBER 2018

No	Class of Drugs	Drugs Name		Total of Item	Percentage
		Generic	Patent		
1	Benzodiazepin	Alprazolam	Alganax, Zypraz	26	41%
		Clobazam	Proclozam	6	9%
		Lorazepam	Merlopam	7	11%
2	SSRI	Fluoxetine	Kalxetin, Nopres	6	9%
		Sertraline	Fridep	14	22%
3	TCA	Amitriptyllin		5	8%
Total				64	100%

Table 1 shows that there are 3 types of anxiolytic drugs used in the treatment of GAD patients in Banyumas Regional Hospital including Benzodiazepines which consists of Alprazolam (41%), Clobazam (9%), Lorazepam (11%); SSRI class including Sertraline (22%), Fluoxetine (9%); and TCA class anxiety drug which is Amitriptyline (8%).

Based on the assessment of the patient's medical record data, SSRI (Sertraline / Fluoxetine) drugs were used in the case of GAD patients who have just undergone subsequent GAD drug therapy if the patient

did not respond adequately then added Benzodiazepine drugs, and in patients who have been stable it was used only Benzodiazepines (Alprazolam / lorazepam / Clobazam) medication with reference to taper dose until the patient was completely healed. The choice of drugs type was based on the patient's responses toward the side effects of anxiety drugs, for example Clobazam was given to patients who could still recover activities due to mild sedation, while Lorazepam was given to patients with liver disorders.

The most common Benzodiazepine used is Alprazolam (41%). It is usually prescribed in cases of GAD patients with concomitant chronic diseases (for example: in the case of cardiovascular patients, diabetes mellitus, hyperthyroid), whereas TCA class (Amitriptyline, 5%) was not the first line-drug, but as an adjuvant to Benzodiazepine or SSRIs class.

2. Age

Based on the study results, the age of patients with GAD in Banyumas Regional Hospital from January 2017 to December 2018 with a total of 47 data patients' medical records showed in table 2:

TABLE 2. AGE OF GAD PATIENTS IN BANYUMAS REGIONAL HOSPITAL IN THE PERIOD JANUARY 2017 TO DECEMBER 2018

No	Age (Years)	Number	Percentage (%)
1	22 – 27	2	4%
2	28 – 33	7	15%
3	34 – 39	11	23%
4	40 – 45	3	6%
5	46 – 51	15	32%
6	52 – 57	4	9%
7	58 – 63	5	11%
Total		47	100%

The results showed that GAD patients in Banyumas Regional Hospital in the period January 2017 to December 2018 were dominated by adult patients aged 22-27 years as many as 2 patients (4%), aged 28-33 years as many as 7 patients (15%), aged 34-39 years as many as 11 patients (23%), age 40-45 as many as 3 patients (6%), age 45-51 as many as 15 patients (32%), age 52-57 as many as 4 patients (9%), and age 58-63 years as 5 patients (11%).

Based on observation on their medical record, it shows that the most common age of GAD patients, aged 46-51 years (32%) are caused by disease factors or other medical disorders, according to Prof. Zullies (2013), it is stated that anxiety disorders are caused by 2 factors, including disease factors or medical disorders and medication factors. Moreover, at the age of 45-51% years, patients had the impairment of body function.

Study conducted by Rusyani (2016) suggests that factor affecting a person's anxiety disorder at the age of 45-59 years is due to the loss of the tissue ability to repair or replace itself and slowly maintain its normal function and the psychological changes that occurs (for example: phenomenon of taboo / shame on sexual aspect), and psychosocial changes (decreased cognitive and psychomotor functions, for example: the slower response to understand or react).

According to Ifdil (2017), anxiety experienced by someone between the ages of 30-39 years occurs due to many factors, for example social factors (lifestyle),

environmental factors (having teenager children), material factors (not yet economically stable) and others.

According to the results of Suherman's study (2016), it shows that there is no significant difference between age and GAD patients, this is because GAD can be caused by various factors, for example alcoholics / drug addicts, environmental factors (family and community), post trauma factors, and others.

3. Gender

Data of GAD patients' gender amounting to 47 medical record data in Banyumas Regional Hospital from January 2017 to December 2018 are as follows:

TABLE 3. DATA OF GAD PATIENTS' GENDER IN BANYUMAS REGIONAL HOSPITAL FROM JANUARY 2017 TO DECEMBER 2018

Gender	Number	Percentage (%)
Male	18	38%
Female	29	62%
Total	47	100%

Based on data taken by gender shows that the number of patients with GAD in Banyumas Regional Hospital from January 2017 to December 2018 from 47 medical record data samples were 18 male patients (38%) and 29 female patients 29 (62%). From the study result, females affected by GAD was more than males because females use more emotions in dealing with problems (Fitrikasari, 2016). According to the result of Rahmawati's study (2017), women tend to have sensitive feelings so that they have higher risk of GAD than male.

Based on the observation, female gender is more affected by GAD especially at the age of 50 years due to menopause and other diseases that can cause GAD, for example: hyperthyroidism (known from the history of patient's medication). This results in excessive anxiety disorders, so it needs to treat.

Suhaidah (2013) stated that at the age of 40-50 years, women will experience menopause naturally, which causes anxiety disorders in women such as insomnia, anxiety, excessive sweating, fear, dry face, discomfort, irritability, and others, because menopausal women will experience the changes of reproductive organs (ovaries and uterus will gradually shrink, endometrium atrophy, vaginal epithelium thinning, the breast become soggy), hormonal changes (decreased ovarian function, reduced excitatory against gonadotropins), vasomotor changes (headaches, sweating, changes in blood pressure, intestinal disorders, etc.), and emotional changes (irritability, diminished morale, insomnia, etc.).

Based on study conducted by Lusiana (2014), there is a correlation between physical changes occur in menopausal women with anxiety. This is caused by increasing age in women will result the decreased of estrogen which disrupt the reproductive system in menopausal women. In addition, the decrease of estrogen causes physical changes in menopausal women such as: the skin becomes loose, the feeling of heat at night, and others.

The study of Amin, et al (2014) states that women are more often diagnosed with generalized anxiety disorders compared to men. This is based on the fact that women are more likely to admit having anxiety. Women

from various backgrounds are subjects with a variety of social conditions which can predispose to a psychiatric condition mainly due to marital problems. In men, generalized anxiety disorder is diagnosed along with a history of alcohol abuse.

4. Occupation

Occupational data of patients with GAD based on the medical records at Banyumas Regional Hospital from January 2017 to December 2018 is as follows.

TABLE 4. OCCUPATIONAL DATA OF PATIENTS WITH GAD IN BANYUMAS REGIONAL HOSPITAL FROM JANUARY 2017 TO DECEMBER 2018

Occupation	Number	Percentage (%)
Jobless	12	26%
Civil servant	13	28%
Private sector	22	47%
Total	47	100%

From the data above, it shows that the highest percentage of GAD patients is at private sector by 47%, this result shows that GAD patients who mostly undergo pharmacotherapy are patients who work in the private sector. Work environment can trigger anxiety disorders directly or indirectly, depending on how the person solves the problems and adjusts to their environment (Fitrikasari, 2016).

Based on the result of observational data, private workers are more susceptible to GAD, especially in industrial sector, and other private workers, demands for high work targets and termination of work that can occur at any time and in facing retirement (Fitrikasari, 2016).

5. Duration of Treatment

The time needed for the treatment of GAD patients in Banyumas Regional Hospital was investigated based on the patient's medical record data from January 2017 to December 2018 with the number of GAD patients until the patient was completely stable and off the drug was 47.

TABLE 5. DATA OF THE TIME REQUIRED FOR GAD PATIENTS TO UNDERGO PHARMACOTHERAPY AT BANYUMAS HOSPITAL

Duration of Treatment (Month)	Number	Percentage (%)
7 - 9 months	6	13%
10 - 13 months	10	21%
14 - 17 months	13	28%
18 - 20 months	9	19%
21 - 24 months	9	19%
Total	47	100%

From the data about the time needed to treat GAD patients, duration of the treatment of 7-9 months were found in 6 patients (13%), 10-13 months in 10 patients (21%), 14-17 months in 13 patients (28%), 18-20 months in 9 patients (19%), and 21-24 months in 9 patients (19%).

The mean of treatment duration of GAD patients in Banyumas Regional Hospital is 7.8 months, and the most stable drug off patients are in the range of 14-17 months and the least time of treatment can be stable to take off the drug is 7-9 months.

GAD patients could not stop the medication at will while pharmacotherapy is in progress. They need healing time to be completely recovered from the symptoms of GAD. The duration of treatment in GAD patients is 6 to

24 months until the symptoms is resolved either only with pharmacotherapy or with the additional of non-pharmacotherapy (Theresia, 2016).

According to Hastuti (2012) that the time needed for the healing process of GAD patients with pharmacotherapy is 6 months to 18 months with or without the addition of CBT, ET, ACT or other therapies. However, it does not rule out the possibility that GAD patients recover before 6 months and can be even longer than 2 years due to the healing and success of treatment for GAD patients is strongly affected by family support and a conducive environment.

IV. CONCLUSION

1. Patient factors affecting GAD: The age of most GAD sufferers is between 46-51 years, the sex most affected by GAD are women, factors of the types of work that mostly affected by GAD are private sector workers.
2. Types of drugs that are widely used for GAD therapy are Benzodiazepines including Alprazolam (41%), Clobazam (9%), and Lorazepam (11%).
3. The duration of treatment of GAD patients with the shortest treatment time is 7-9 months, and the longest treatment time is 21-24 months.

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