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RESEARCH ARTICLE

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The Profile of Pharmacological Treatment in Trigeminal Neuralgia Patients in The Period of January 2018-December 2018

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ABSTRACT

Trigeminal neuralgia is a condition that affects the trigeminal nerve, that manifests in a series of stabbing like pain, and often described like electricity. Its treatment guideline is to prioritize pharmacotherapy until patient is well. The gold standard treatment for trigeminal neuralgia is pharmacotherapy of Carbamazepine. However, carbamazepine is proven to cause allergic reaction to some patients. This research aims to describe the pharmacotherapy that is given to patients. The regiments of pharmacotherapy in trigeminal neuralgia shows that CBZ is the main pharmacotherapy given, as it is the gold standard treatment. GBP is the second most pharmacotherapy given and a concoction medication of Paracetamol, Diazepam and Amitriptyline being the third most favored therapy. Neurotropic B Vitamins plays a big role, as a support in the therapy to maintain the health of the overall nervous system. The pain scale data shows that almost all patients have significant pain relieve. The therapy of trigeminal neuralgia in this study shows that CBZ is most favored as it is the gold standard, however not all AEDs are accessible. Almost all patients have significant pain relieve eventhough not using gold standard treatment.

Keywords: trigeminal neuralgia; pharmacotherapy

INTRODUCTION

According to the European Academy of Neurology, the gold standard treatment of trigeminal neuralgia will be to approach with a pharmacologic treatment. Carbamazepine is chosen gold standard drug to be prescribed to patients with early symptoms due to its efficacy. Although carbamazepine is the gold standard approach, it still has a prevalence of allergies in patients⁽²⁾. Due to this, trigeminal neuralgia patients who are allergic must be prescribed other pharmacological drugs. Other medicines are suggested as alternatives are other AEDs, such as Oxcarbamazepine, Gabapentin, Phenytoin and Pregabalin.

The cases of trigeminal neuralgia in Dr. Soetomo Hospital are treated mainly with Carbamazepine, however some patients are allergic to it. This leads to some patients being given medicines that are not a gold standard with only medicines provided by health insurance.

METHODS

This was a cross-sectional descriptive study. The population of data were patient with trigeminal neuralgia diagnosis. Secondary data were collected from medical records consisting of pharmacotherapy and pain scale from the Outpatient Clinic of dr. Soetomo Hospital, Surabaya from January 2018 to December 2018. The data were tabulated in Ms.excel, and interpreted through tables and graph. The research started by collecting patient data from medical records. The data, consisting of patient's pharmacotherapy and pain scale were tabulated in Ms. excel. The pharmacotherapy was arranged according to its date and pain scale before and after the treatment. After tabulating the data, graphs and tables were chosen as media to interpret the data. The next step after data processing was to write the article according to the data found, with help from referencing other articles and journals to support the data shown in this research.

RESULTS

Sex Distribution

From the 19 patients fulfilling the criteria of inclusions, 12 patients were female while the rest of the 7 other patients were male. The distribution of female patients to male patients can be observed in figure 1.

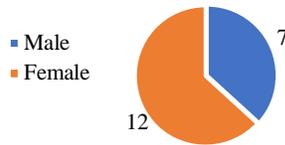


Figure 1. Distribution of sex in trigeminal neuralgia patients

Age Distribution

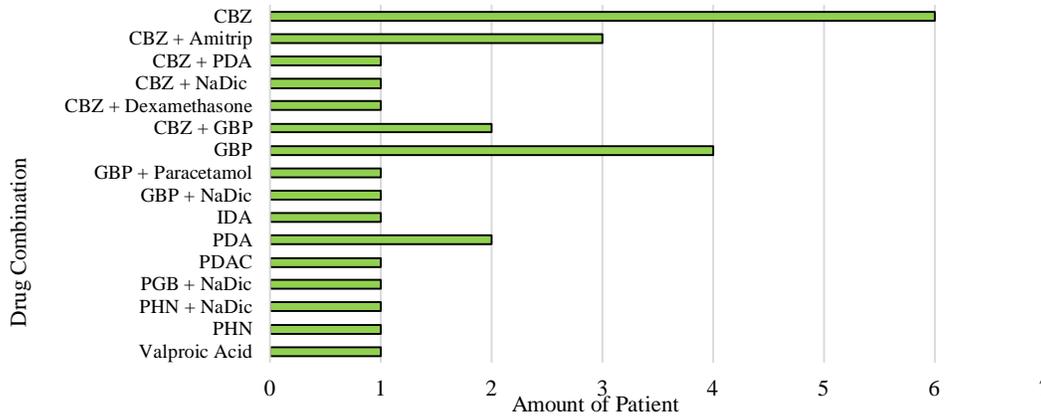
According to Bangash, age can be categorized into 6 groups (Bangash, 2011). Distribution of age group in trigeminal neuralgia patients can be observed in Table 1

Table 1. Age distribution of trigeminal neuralgia patients

Age group	Number of patient	Percentage
<40	1	5.5
40-50	3	15.5
51-60	8	42
61-70	6	31.5
71-80	0	0
>81	1	5.5
Total	19	100

Analgesic Therapy Distribution

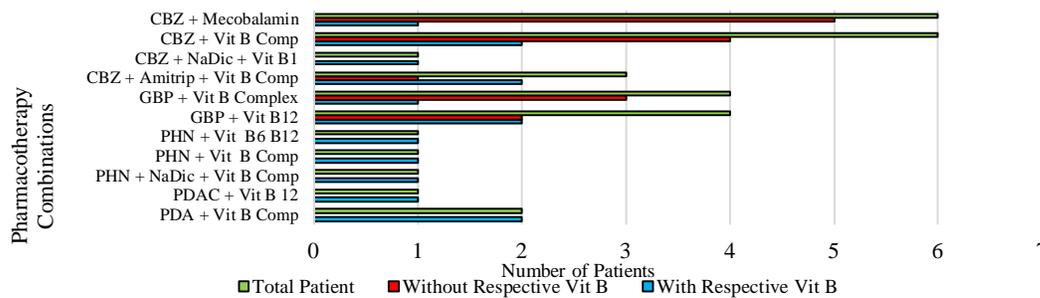
Patients receive multiple forms of therapy, and this includes single analgesic therapy and multi analgesic. The following data shows the type of analgesic is given and the amount of patients. As some treatments may not show satisfactory responses, patients may change or added analgesics, this causes some patients to be given multiple analgesics throughout the therapy.



CBZ=Carbamazepine; GBP=Gabapentin; PGB=Pregabalin; PHN=Phenytoin; NaDic=Diclofenac; Amitrip=Amitriptyline; IDA=Ibuprofen, Diazepam, Amitriptyline; PDA=Paracetamol, Diazepam, Amitriptyline; PDAC= PDA=Paracetamol, Diazepam, Amitriptyline, Caffeine

Figure 2. Distribution of analgesic therapy received by trigeminal neuralgia patients

Distribution of Vitamin B in Pharmacotherapy



CBZ=Carbamazepine; GBP=Gabapentin; PHN=Phenytoin; NaDic=Diclofenac; Amitrip=Amitriptyline; PDA=Paracetamol, Diazepam, Amitriptyline; PDAC= PDA=Paracetamol, Diazepam, Amitriptyline, Caffeine

Figure 3. Distribution of different vitamin b within total patients

Patients receives Vitamin B to support the treatment of trigeminal neuralgia. It is not the main pharmacotherapy and is not mentioned in trigeminal neuralgia treatment guidelines as a recommended therapy. The data below shows that main pharmacotherapy and the vitamin B pairing.

Pharmacotherapy Regiments and Pain Scale

The pain scale of the patients using main therapies (Carbamazepine, Gabapentin, PDA) are noted during the treatment, giving data of the pain scale before the treatment and after the treatment. Most patients have pain relieved to NRS2 of 0, meaning “no pain”, and some patients only have partial pain relieved, although in a significant amount. However, due to that it’s a cross-sectional research, it should be considered that some patient’s may not be fully healed yet.

Table 2. Distribution of pain scale before and after treatment

No	NRS1	NRS2	Δ NRS	Subjective Response	Pharmacotherapy Regiments
1	9	0	9		CBZ
2	3	0	3		GBP, CBZ, GBP+NaDic prn GBP+Paracetamol prn Vit B Complex
3	8	4	4		CBZ
4	5	0	5		CBZ+ Amitrip Vit B Complex
5	7	0	7		CBZ+ Amitrip
6	7	0	7		CBZ+NaDic Vit B1
7	7	3	4		Depakote CBZ+GBP
8					
9	8	-	-	Slight recuperation	GBP Vit B Complex
10	8	0	8		CBZ+Dexamethasone
11	7	0	7		PDAC, PHN, PHN+NaDic, GBP, PGB+NaDic Vit B Complex
12	4	0	4		PDA Vit B Complex
13	7	-	-	Complaints subside after medication	PDA Vit B Complex
14	8	0	8		CBZ+PDA
15	6	0	6		IDA CBZ

CBZ=Carbamazepine; GBP=Gabapentin; PGB=Pregabalin; PHN=Phenytoin; NaDic=Diclofenac; Amitrip=Amitriptyline; IDA=Ibuprofen, Diazepam, Amitriptyline; PDA=Paracetamol, Diazepam, Amitriptyline; PDAC= PDA=Paracetamol, Diazepam, Amitriptyline, Caffeine

DISCUSSION

Demographics Data

This study aims to describe the pharmacological treatment of patients diagnosed with trigeminal neuralgia. Among the 19 people who are treated for trigeminal neuralgia, 12 were female and 7 are male. This data is consistent to the other studies that states women are more prone to trigeminal neuralgia^(1,3). The patients are all adults, only one patient is under 40. Most of the patients are between the group 51-60 (42%) and 61-70 (31.5%) referred to table 1 This data is also consistent to many research and studies about trigeminal neuralgia patients, where it states that most cases occur in the age above 50^(1,4). In total, there are 4 patients under the age of 50, and 14 over the age of 50.

Pharmacotherapy Profile

The success of treating the pain caused by trigeminal neuralgia mainly comprises of the use of AEDs, antidepressants and other types of drugs that are known to cause neuropathic pain relieve. These analgesics varies but the gold standard of trigeminal neuralgia treatment is CBZ^(5,6). As a gold standard, CBZ is the main utilized drug in the treatment of trigeminal neuralgia. Through out the year, CBZ is given to a total of 14 patients, in consideration that multiple analgesics may be given to a single patient. GBP, a newer form of AED is given to a total of 6 patients, PDA to a total of 3, and the rest were only give to one patient (Figure 2). These analgesics aren’t always used as a single drug therapy, but they could be combined to expect a form of synergy between 2 drugs. Monotherapy of CBZ is still dominant compared to other forms of treatment, given to 6

patients, GBP being the second dominant given to 4 patients, a combination of CBZ + Amitriptyline given to 3 patients, PDA and CBZ + Amitriptyline were given to 2 patients, and the other combinations and single drug were given to one patient (Figure 2). Pharmacotherapy of trigeminal neuralgia shows that the medication given are not only those that is specifically used to reduce the pain, but also the use of vitamin b. The types of vitamin B that is given varies; Vitamin B1, Vitamin B6, Vitamin B12, Vitamin B Complex and Mecobalamin.

Anti-Epileptic Drugs

Anti-epileptic drug is the preferred medication for trigeminal neuralgia according to from the guideline by European Academy of Neurology⁽⁷⁾. In this study, Carbamazepine, Gabapentin, Phenytoin, Pregabalin and Valproic Acid were given to patients to treat trigeminal neuralgia. The main objective of the AED's is to reduce the excitability of the nerves and these AEDs have different approaches to them. Carbamazepine and Phenytoin has the same mechanism of action, through the blocking of sodium channels. The inhibition of the sodium channels causes the suppression of hyper excitable and exaggerated responses from primary afferent neurons, leading to the suppression of pain stimulus⁽⁸⁾. Gabapentin and Pregabalin has a similar mechanism of action through Ca channels. They both interact the alpha2delta subunits Ca channels to reduce excitability, however Gabapentin also have to increase the concentrations of GABA within the brain. This property is the similar with the mechanism of Valproic Acid, which increase the GABA through enzyme systems.

Concoction Medicine

PDA, PDAC and IDA is a therapy of paracetamol, diazepam and amitriptyline (PDA) or (PDAC) with addition of caffeine in conjunction seems to be a desired therapy in the treatment of trigeminal neuralgia, and IDA uses Ibuprofen instead of Paracetamol. This medication of combined drugs are expected to work synergistically to provide its action. In this case, Paracetamol and Ibuprofen has a similar mechanism of action that reduces the PG levels in the body that leads to a reduced sensitization in the nerves⁽⁹⁾. Diazepam works by promoting the binding of GABA to GABA_A receptors, which results in the hyperpolarization of the neuronal membrane occurs due to the shift in charge thus reducing excitability of the neurons⁽¹⁰⁾. Amitriptyline's mechanism of action is thought to inhibit synaptic transmission between first and second order neurons directly⁽¹¹⁾. Caffeine's role in pain control is one of its properties that is still less considered. Its pain control properties are suggested to interact with adenosine. The antinociception in neuropathic pain, nociceptive and inflammatory models are caused by the activation of the A1 and A2A receptors⁽¹²⁾. The structure of caffeine, which is similar to adenosine competes for the inhibition of A2A receptors resulting in their inhibition. Although this concoction is not an AED, PDA and PDAC comprises of medicines that have characteristics in the reduction of neuropathic pain.

Supporting Drug

Diclofenac and Amitriptyline are given in conjunction with AEDs, to support the role of pain alleviation. Diclofenac is generally used to its high specificity for the arachidonic acid-degrading enzyme, COX-2. In the human body, prostaglandins (PG) acts as an important chemical mediator that excite and sensitize nociceptors. Its mechanism of action towards neuropathic pain is suggested due to its inhibition of COX1 and COX2, leading to the decrease of PG⁽¹³⁾. However, this medicine might also be given to patients to relieve possible inflammations that may cause trigeminal neuralgia. Amitriptyline, a tricyclic antidepressant is known to be given to trigeminal neuralgia patients in the past. TCAs may directly interfere with central sensitization by blocking NMDA receptors in the spinal cord hence its effectiveness on neuropathic pain⁽¹⁴⁾. The use of TCA is considered supportive as it is not given as a sole medication to patient, and given with other AEDs to help with patients that have drug resistance. Amitriptyline is chosen than other AEDs due to that other AEDs is not as accessible and have limited quota from the national health insurance (BPJS).

Role of Vitamin B

Vitamin B plays a huge role in the treatment of trigeminal neuralgia. As a supporting component, it does not affect in pain relieve directly but helps in the overall health of the nervous system. The neurotropic B vitamins B1, B6 and B12 have different roles in the health of the nervous system and are not replaceable between them. The synergistic role of vitamin B1 B6 and B12 should be stressed, as vitamin B1 is most needed in its role as antioxidant⁽¹⁵⁾, B6 as a neuroprotective role through glutamatergic system regulation⁽¹⁶⁾ and B12 in myelin regenerating role⁽¹⁷⁾, using them synergistically as vitamin b complex might use them in its maximum potential. As seen in Table 2, patients that receive vitamin B complex are more likely to recover to NRS2 of 0.

Pain Scale

In this study, the pain scale of each patients are observed. Patients who are using CBZ, GBP and PDA are observed. Overall, the pharmacotherapies of the patients could be called a success, even though not every patient is using the gold standard treatment, it still shows that other alternative medication can still relieve the pain up to 0. There are some patients that is not fully recovered from the pain, one patient uses CBZ and another CBZ + GBP. Although not fully recovered, the patient have a significant decrease of pain. Although not a direct effect, vitamin B can play a role in pain relieve, in this case, the most used vitamin B is Vitamin B complex. The patients with vitamin B complex have their pain decrease, some to 0 but some still have pain.

Adverse Effects

There are no significant amount of remarks regarding adverse effects. One patient is prone towards SJS, an adverse effect of using CBZ. Although AEDs are notorious with adverse effects such as fatigue, dizziness and sleepiness, these are not noted in the medical record. According to a study done regarding adverse effects on patients using AED, 91% of patients develop adverse effects, where most reported are tiredness (67.8%), sleepiness (66.7%), memory problems (62.2%) and difficulty concentrating (56.7%)⁽¹⁸⁾. The reason behind this may be due to that some patients are not undergoing long term treatment; thus adverse effects has time to develop. Alternatively, minor effects as such may not be a significant concern for patients to report, as the patient themselves are experiencing severe pain that may have reduce the quality of life significantly. Compared to the minor adverse effects mentioned, patients may have thought that it is not of importance as long as the medicine alleviates the pain.

CONCLUSION

The pharmacotherapy of trigeminal neuralgia uses Anti-Epileptic Drugs, Antidepressants, and other combination drug to relieve its main complaint, pain. The use of combination therapy has also been done to help treat the pain, by using multiple AEDs or other analgesic type drugs in synergy. An example of this could be seen on the use of Carbamazepine and Gabapentin in the same time, as they have different mechanism of action to provide. Vitamin B plays a huge role in supporting the therapy of the patients, however the use of neurotropic B vitamins together must still be stressed. The regiments of medication relies on the health insurance system, as there are some drugs that is not accessible for trigeminal neuralgia patients or limited in its quota. However, observations of pain scale proves that treatments are successful despite the limitations.

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