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Profile of drug use in Guillain Barre Syndrome (GBS) patients at "X" private hospital

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ABSTRACT

Centers of Disease Control and Prevention / CDC (2012), Guillain Barre Syndrome (GBS) is a rare disease in which a person's immune system attacks the peripheral nervous system and, if severe, paralysis can occur. The treatment the patient receives is not a cheap treatment, even if treatment is carried out too late it will cause death. This research was conducted to look at the patient profile and treatment profile of GBS patients at the "X" Private Hospital. Method: This research is observational with secondary sampling and a retrospective study on Guillain Barre Syndrome (GBS) patients in the period 1 January 2019-31 December 2022. The total population in this study was 6 patients. The profile of drug use in GBS patients that was most commonly used was specific/etiological therapy in the form of immunotherapy in 6 patients (100%); privigen (67%) and gammaras (33%). Supportive (symptomatic) therapy is in the form of 100% of neurotropics and 100% of analgesics, and 17% of complicative therapy is in the form of antibiotics. Corticosteroids used are Methylprednisolone (3x2.5 mg – 3x75 mg) IV (50%) and dexamethasone IV (4x 5 mg – 3 x 5 mg) 50%. The most common analgesics used by patients were paracetamol (3x1g) IV (100%), muscle relaxants 16% and GABA analogues 33%. The most commonly used neurotropic is Mecobalamin (3x500µg) IV 100%. GBS treatment follows therapy guidelines, and research needs to be carried out regarding the prevalence of recurrence in GBS sufferers.

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INTRODUCTION

Centers of Disease Control and Prevention / CDC (2012), Guillain Barre Syndrome (GBS) is a rare disease in which a person's immune system attacks the peripheral nervous system and causes muscle weakness, even if severe, paralysis can occur.(Tria, 2023) (Nining, 2020). This happens because the peripheral nervous system that connects the brain and spinal cord with all parts of our body is damaged. Damage to the peripheral nervous system makes it difficult for this system to

transmit stimuli so that there is a decrease in the response of the muscle system to the work of the nervous system(Maria, 2021) (Hasanah et al., 2023).

Guillain–Barré syndrome (GBS) is a collection of symptoms with an acute onset which is an immune system-mediated disease that attacks the peripheral nervous system.(KOAS, nd),(Kurniawan, Husna, & Nurlaela, 2020). Guillain–Barré syndrome was proposed in 1916 by Guillain and Barre who described the characteristic findings of cerebrospinal fluid (CSS) where an increase in protein concentration was found but without an increase in the number of cells in two French soldiers who experienced weakness.(Arifin, nd),(Pati, 2022). This disease occurs throughout the world in every season and can attack all ages. The overall annual incidence rate of GBS in the United States is 1.65-1.79 per 100,000 people with a male-to-female incidence ratio of 3:2. Several infections are involved in the development of GBS(Syakhsiyah, 2021),(Gunawan, Noviandi, & Samosir, 2023). Approximately two-thirds of patients with respiratory tract infections or gastrointestinal symptoms had been reported in the three weeks before the onset of GBS symptoms. The strongest evidence is in Campylobacter jejuni infection, but GBS has also been reported in the following infections, namely Mycoplasma pneumoniae, Haemophilus influenzae, cytomegalovirus, and Epstein-Barr(Reynaldo & Desiree, 2019),(Emril, Fajri, & Rahayu, 2020)

The incidence of GBS disease is approximately 0.6-1.6 per 10,000-40,000 population. The difference in incidence rates in developed and developing countries is not visible. This case tends to be more common in men than women(Hidayat, Sugiarto, Aditianingsih, & George, 2018). The cause of GBS was initially unknown, so this disease has another name: Acute idiopathic polyneuritis or acute idiopathic polyneuritis. Idiopathic comes from the word "idiot" or "don't know"(Rahayu, 2013). Over time it became known that GBS can be caused by damage to the immune system. Damage to the immune system causes swelling of the peripheral nerves, resulting in no messages from the brain to carry out movements that can be received by the affected muscles.(Rachmawati, Mardiyantoro, Silviana, Nugraeni, & Amran, 2022). If many nerves are attacked, one of which is the immune system nerves, our immune system will be in chaos, without being ordered it will release immune system fluids in unwanted places.(Do, 2022). Treatment will cause the body's immune system to stop attacking the nerves and work as it should and the symptoms will disappear and you can return to normal health(Majid, 2020). Everyone can get GBS but in general it occurs more often in older people(Nusantoro & M Kep, 2018). People aged 50 years and over are the group with the highest risk of experiencing GBS (CDC, 2012). However, according to the chairman of the Association of Indonesian Neurologists (PERDOSSI) dr. Darma Imran, Sp S(K) said that GBS can be experienced by all ages, from children to the elderly, but its peak is in patients of productive age.(Hanum & Kurniawan, 2023),(Budiyono, 2023). The above situation shows that although GBS cases are relatively rare, in recent years the number of cases has continued to increase. Private Hospital "X" recorded an increase in GBS cases in the last 3 years(GE'E, nd). The recommended treatment for GBS is intravenous administration of immunoglobulin and plasmapharesis or the removal of antibodies that damage the peripheral nervous system by replacing blood plasma.(Mexitalia, Soetadji, TS, Utari, & Sareharto, nd),(Kondra, nd). The treatment the patient receives is not a cheap treatment, even if treatment is carried out too late it will cause death. Based on the facts above, researchers need to know GBS disease in more detail regarding the patient profile and treatment of GBS patients(Januraga, Wirawan, Harjana, & Ulandari, 2021),(FAUZIAH, 2019).

RESEARCH METHOD

This research is observational with secondary sampling and a retrospective study on Guillain Barre Syndrome (GBS) patients in the period 1 January 2019 - 31 December 2022. The inclusion criteria for this study are Guillain Barre Syndrome (GBS) patients who have been diagnosed and are undergoing treatment at the hospital. ”X”, complete medical record data.

RESULTS AND DISCUSSIONS

The intended characteristics of GBS patients are based on demographic data determined in this study. Inclusion criteria: There are not many GBS sufferers treated at "X" Private Hospital. In 2019 there were no GBS patients and in 2021 there were 1 patient, whereas during 2020 "X" Private Hospital received many Covid-19 patients, and no GBS patients were found. In 2022 there will be 5 patients suffering from GBS.

Table 1. Patient characteristics based on gender

No	Gender	Amount	Percentage
1	Man	4	67 %
2	Woman	2	33 %
	TOTAL	6	100%

Table 2. Patient characteristics based on nationality

No	Types of Citizens	Amount	Age	Percentage
1	Indonesian citizen	1	14 yrs	17 %
2	foreigner	5	(22-23-38-41-77) yrs	83 %
	TOTAL	6		100%

Table 3. Use of GBS drugs

Medicine name	Group	Amount of Use	Percentage
pantoprazole	PPI	6 patients	100%
Primperan	Antiemetic	3 patients	50%
Paracetamol	Antianalgesics (NSAIDs)	6 patients	100%
Methycobalamin	Vitamin B12	6 patients	100%
Indexone 5 mg	Corticosteroids	3 patients	50%
Privigen	Immunotherapy (IVIG)	4 patients	67%
Medixone 125 mg	Corticosteroids	3 patients	50%
Provelyn	GABA analogues	2 patients	67%
Myonal	Muscle relaxant	1 patient	17%
ondansetron	Antiemetic	3 patients	50%
Gammaras	Immunotherapy (IVIG)	2 patients	67%
ceftriaxone	Antibiotics	1 patient	17%

Discussion

Patient Profile

Based on this research, the incidence of GBS is mostly experienced by male patients. These gender differences will appear in sufferers after pubertal changes which are influenced by gonadal hormones (Nunn CL et al, 2009). This gender predominance is explained by the fact that women have a stronger immune system compared to men. The immune system referred to is the CD4+: CD8+, Tcell, Nutrophil ratio component, so that women will be stronger if they are attacked by an infection and have higher immune tolerance compared to men (McCombe PAG JM, 2020; Nunn CL et al, 2009). The immune system CD8+ cells and NK cells in men tend to be higher than in women. This causes an increase in the level of immune components that play a role in developing GBS disease in male patients (McCombe PAG JM, 2020; Yang M, 2015; Cerutti A, 2012). There are some suggestions that sex differences influence the activation of plasmablasts and plasma cells (Yin PQ et al, 2016). Further exploration of the role of plasmablast activation could be useful in understanding GBS and exploring the influence of sex differences (Pioli PC,M, 2021; Yin PQ et al, 2016).

Genome-wide gene expression analysis of peripheral leukocytes has shown differences between male and female patients with GBS. In one study, male GBS patients had 20 genes involved in various immunological processes, including macrophage and leukocyte migration, and

female GBS patients were enriched for 62 genes including those for viral infection and defense (Sejvar JJ, 2011). The large number of genes involved in immunological processes in the female sex means that the prevalence of GBS in women is smaller than in men. The gene involved in the production of matrix metalloproteinase-9 (MMP9), which has previously been shown to be associated with disease severity in GBS, is highly expressed in males implicating MMP9 as potentially relevant to the higher prevalence of GBS in males (Yin PQ et al, 2016; Overell JR et al, 2007)

Based on research data at "X" Hospital (table 2), more sufferers come from foreigners. Cases of GBS type MFS (Miller Fisher Syndrome) occur in 5-10% of GBS cases in Western countries, more frequently occurring in East Asia, accounting for up to 25% of Japanese cases (Alter M. 1990). This is not in line with epidemiological research that has been carried out previously. Symptoms experienced by patients treated at "X" Hospital usually include paresthesia and dysesthesia in the distal extremities. These sensory symptoms are generally mild, except in patients with GBS subtype AMSAN (Acute motor-sensory axonal neuropathy) (Newswanger DL, 2004; Miller A, 2009).

GBS patients treated at "X" Hospital generally suffer from sensory nerve damage in the form of muscle weakness. The pain is described as severe, deep pain, like aching or cramping/stiffness in the affected muscles, often worse at night. Pain is nociceptive and/or neuropathic. This pain is usually the initial manifestation in more than 50% of patients which can lead to a diagnosis of GBS (Newswanger DL, 2004; Miller A, 2009).

Based on research data at "X" Hospital, there were no patients with a history of degenerative diseases that worsened the patient's condition. Several cases show that patients who experience GBS are exacerbated by risk factors such as; respiratory or digestive infections, SLE (Mishra A, G, 2017.

Drug Use Profile

GBS treatment is aimed at treating abnormal activity of antibodies that attack peripheral nerves to relieve GBS symptoms and speed up recovery. GBS patients receive two types of therapy; symptomatic therapy and causative therapy. Symptomatic therapy is used to treat clinical manifestations of GBS such as motor paralysis, dysautonomia, neuromuscular respiratory failure, pain, deep vein thrombosis and nosocomial infections (Doets AY, 2018).

The first causative GBS treatment method is administration of intravenous immunoglobulin (IVIg). Using this method, the doctor will take healthy immunoglobulin from a donor and inject it into the GBS sufferer to fight the immunoglobulin that attacks the sufferer's nerves. Treatment for GBS patients is divided into IVIG and plasma exchange. Apart from IVIg and plasma exchange, no other procedures or treatments have been shown to be effective in the treatment of GBS. In this study, the use of IVIG in hospitals was divided into 2 brands, namely gammaras and privigen. IVIG use is based on guidelines, namely 0.4 g/kg body weight per day for 5 days. IVIg is also easier to administer and generally more widely available than plasma exchange, so IVIg is the treatment of choice (Doets AY, 2018).

In this research data, it was found that the use of IVIg together with corticosteroids. Several studies regarding the efficacy of corticosteroids in GBS did not find significant benefits, and oral corticosteroid therapy even had a negative effect on GBS (van Koningsveld R et al, 2004). This is in contrast to other studies showing that the combination of IVIG and intravenous methylprednisolone is not more effective than IVIG alone (van Koningsveld R et al, 2004), even when known prognostic factors are changed, combination treatment shows short-term efficacy (Mishra A, G. 2017; Michon B, et al. Although these studies do not show a positive impact of immunotherapy and corticosteroids on the course of GBS disease, there is still a need for new research with this combination treatment and other therapies aimed at improving the prognosis and outcome of GBS. Based on observations from this study, patients who used a combination of

IVIg and corticosteroids showed significant clinical improvement in an average of 5 days during the treatment period.

IVIg at hospital "X" in this study was also used in pediatric patients. When compared with administering IVIg with plasma exchange, plasmapheresis or plasma exchange which is the first line therapy for children with GBS (Benstead T, et al. 2007). Plasmapheresis is only available in health centers experienced in its use and is considered more uncomfortable and has a higher complication rate than IVIg in children, so the use of IVIg is the only choice as therapy in pediatric patients with GBS. The dosage for giving IVIg to children is different, there are 2 dosage options that affect the length of time IVIg is given to children. Studies have shown that IVIg occurs more frequently at a dose of 2 g/kg (body weight) (El-Bayoumi MA et al, 2011; Korinthenberg R, 2005). Another dose that may be given is 400 mg/kgbb once a day for 5 days (El-Bayoumi MA et al, 2011; Brannagan TH, 1996).

The use of IVIg in several studies has had side effects in patients. In research at "X" Hospital, there was 1 patient who experienced a side effect reaction in the form of headache. Headache also occurs 6 to 12 hours after the infusion and may last 24 to 72 hours. High-dose immunoglobulin infusion is a major risk factor for headaches. Several studies have found that patients with a history of migraine are susceptible to headaches after IVIG infusion (Feldmeyer L et al, 2010; Lemm G, 2002), however, in this study, patients had a history of migraine, so they cannot be used as a basis for the occurrence. adverse drug reactions in patients using IVIg. Patients who experienced side effects using Privigen at "X" Hospital experienced persistent dizziness even though the infusion rate was slowed down. An alternative therapy for these patients is to change the type of IVIg from privigen to gammaras (Lexicomp, 2021). With the change in brand, the patient did not experience side effects in the form of dizziness 6-12 hours after the infusion took place.

Each formulation from the IVIg manufacturer has differences in terms of excipient components, which may increase the frequency of certain side effects. Lemm G, 2002 stated several causes of the risk of drug side effects including the sorbitol component (for patients who have congenital fructose intolerance), sucrose (risky in patients with kidney failure), glucose (risky in patients with diabetes mellitus), and high IgA component. at risk are patients who have a history of anaphylactic reactions (Gabriella K. 2013). Patients who experienced side effects from drugs in this study did not have a history of DM, kidney failure or a history of intolerance to sucrose, fructose or even glucose. In this study, patients at Hospital "X" did not use fluids containing fructose, sucrose or even glucose, therefore there were no anaphylactic reactions that occurred in this study.

In general, other therapies used by GBS patients, namely symptomatic therapy, include analgesics, anticoagulants, antibiotics, corticosteroids and vitamin B1, B6 and B12 therapy (Jain, Kewal K. 2011). In this study, all GBS patients were given vitamin B12 therapy. This therapy is not listed in the therapy guidelines for GBS but is almost always used in GBS patients (Jain, Kewal K. 2011). Vitamin B12 is known to be a neuroprotective agent that is used as a therapy for GBS to protect the nervous system from experiencing more severe damage or slows the progression of the disease (Zhang, Gang, 2011; Miller et al, 2005). Vitamin B12 functions to improve motor and sensory nerve recovery and terminal latency of the sciatic nerve. Other research shows that vitamin B12 plays a role as a cofactor in myelin formation, is an immunomodulator and has neurotrophic effects. Methylcobalamin as a co-enzyme of vitamin B12 can accelerate lecithin synthesis; a main component of the myelin sheath on nerve cells thereby reducing symptoms of muscle weakness. The dose of vitamin B12 for peripheral neuropathy is 500 g/day IM or IV route 3 times/week (Miller, 2005; Okada K, 2010). The dosage of vitamin B12 used in GBS patients at "X" Hospital varies from 500 g/day to 500 g a day 3 times. All patients at Hospital "X" receive neuroprotective therapy IV or IM. This takes into account the factor that drug absorption is faster compared to oral administration. The administration of mecobalamin or vitamin B12 in this study

was to prevent further irreversible neurological damage. This is also a consideration for administering mecobalamin IV or IM because it has a faster onset than orally (tablets). All GBS patients in this study received analgesic treatment in the form of paracetamol. Paracetamol is the first choice for mild to moderate pain. The use of paracetamol is considered less effective in treating neuropathic pain in GBS patients. Therefore, the use of other analgesics in GBS patients is supplemented with adjuvant analgesics, but not all patients in this study received adjuvant therapy. Fifty percent (50%) of patients received combination treatment with additional analgesics. Additional analgesics used are gabapentin and eperizone. Gabapentin works by blocking calcium channels that block the 2□-□ subunit, besides that gabapentin affects the metabolism and release of glutamate and reduces the synthesis of neurotransmitters and glutamate excitocin. Eperisone reduces the sensitivity of muscle cells by preventing the spontaneous discharge of gamma motor neurons, which expands calcium channels and blocks them. Patients treated with gabapentin did not receive eperisone therapy. Both adjuvant analgesics have side effects in the form of gastrointestinal disorders such as nausea, so the patient also received anti-nausea therapy and PPI (proton pump inhibitor) therapy.

In this study, there was 1 patient who used antibiotics in the form of ceftriaxone, due to a nosocomial infection in the form of pneumonia. Evaluation of the use of the antibiotic ceftriaxone in 1 patient for 48 to 72 hours. After the patient's clinical improvement, the IV antibiotic was changed to an oral antibiotic and continued for a total of 7 days from the first administration. One of the limitations of this study is the small number of cases of GBS at Hospital "X" over a period of 3 consecutive years.

CONCLUSION

The most common drug use profile in GBS patients is specific/etiological therapy in the form of immunotherapy in 6 patients (100%). There were 5 foreign patients and 1 Indonesian patient. The treatment profile for GBS (Guillain Barre Syndrome) patients at the "X" Bali Private Hospital during 2019 - 2022 follows the Guideline for Guillain Barre Syndrome (GBS) therapy.

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