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ORIGINAL ARTICLE

Adherence of NSAID Administration in Patients with Mild and Moderate Traumatic Brain Injury in Dr. Soetomo General Hospital, Surabaya

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A B S T R A C T

Introduction: Traumatic brain injury (TBI) has a concerning incidence rate. One of the therapies for patients with TBI is non-steroidal anti-inflammatory drugs (NSAID) administration as an analgesic with proper adherence to achieve optimal therapy results. This research aimed to evaluate physicians' NSAID administration adherence in patients with mild and moderate TBI in Dr. Soetomo General Hospital, Surabaya.

Methods: This was an observational descriptive study with a retrospective design. NSAID administration adherence was graded by evaluating the dose, route, frequency, and interval of NSAID administration. The variables were evaluated by observing the medical records of inpatients with mild and moderate TBI from 1 January to 31 December 2018.

Results: NSAIDs used for TBI management were metamizole, paracetamol, mefenamic acid, and ketorolac. Metamizole was administered in 10 patients (34.5%), paracetamol in 1 patient (3.4%), metamizole and paracetamol in 15 patients (51.7%), metamizole and mefenamic acid in 1 patient (3.4%), metamizole and paracetamol with mefenamic acid in 1 patient (3.4%), and metamizole and ketorolac in 1 patient (3.4%). Adherence of paracetamol, mefenamic acid, and ketorolac administration in patients with mild and moderate TBI were well-administered in every evaluated variable. Metamizole administration's adherence was already well-administered in drug dosage and drug administration route, but it was not well-administered in drug administration interval and frequency.

Conclusion: Physicians' adherence to NSAID administration in patients with mild and moderate TBI in Dr. Soetomo General Hospital, Surabaya was well-administered, except for metamizole.

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Introduction

Traumatic brain injury (TBI) is an injury on the brain with sudden onset caused by external forces resulting in significant damage in the brain.[1] Around 69 million individuals in the world are estimated to suffer from TBI each year.[2] WHO predicted that in 2020, road accidents that would potentially cause TBI will ascend from ninth place to third place in developed countries and from third place to second place in developing countries.[3] In 2013, 2,797,957 cases of TBI were recorded in the United States, with 2,460,420 patients visiting Emergency Rooms, 281,610 inpatients, and 55,927 deceased patients.[4] In Indonesia, a study showed that in 2018 TBI has a percentage of 11.9% among injuries in other body parts and 42.8% of these injuries happened in the streets.[5] It is noted that in 2016, there were 672,105 incidences of TBI in Indonesia, with a rate of 264 cases per 100,000.[6] The number of TBI cases in Dr. Soetomo General Hospital Surabaya recorded in 2013 was 1,411 cases with 6.171% to 11.22% mortality from 2002 to 2013.[7]

TBIs are associated with damages of brain tissues that induce the release of endogen factors that acts as damage-associated molecular patterns (DAMPs) and will later be bonded with toll-like receptors (TLRs) that will release proinflammation factors.[8]

Non-steroidal anti-inflammation drugs (NSAIDs) are given as analgesics and anti-inflammatory therapy in patients diagnosed with patients.[9] Prolonged administration of NSAID in patients with TBI may decrease functional capabilities of the patients.[10] Adherence to NSAID administration must be monitored and evaluated.

Patients' adherence to consuming the prescribed drugs must be monitored to obtain optimal therapy results. Research shows that among 1040 interviewed patients, 79.7% have good adherence to consuming prescribed NSAIDs.[11] Factors evaluated to measure patients' adherence were various, which can include patients' memory of the drugs' names, frequency of drug administration, distastefulness of the drugs, price of the drugs, clarity of drug administration information from the physician or pharmacists, patient's own business and forgetfulness.[12]

However, in hospitalized patients, consumption of prescribed drugs will be monitored by the nurses available. Hence, the one that needs to be evaluated is the adherence of physicians who prescribe NSAIDs and the nurses who administer NSAIDs during hospitalization. Non-adherence to drug prescription and administration may worsen symptoms and prolong the hospitalization period, increasing hospital bills.

The authors are interested in evaluating adherence to physicians' prescription and nurses' administration of NSAID in hospitalized patients with mild and moderate TBI who do not receive surgery treatment in Dr. Soetomo General Hospital, Surabaya.

Methods

This was an observational descriptive study with a retrospective model, conducted from 1 January to 31 December 2018 to evaluate NSAID administration by evaluating the secondary data obtained from mild and moderate TBI inpatient medical records in Dr. Soetomo General Hospital Surabaya. The data obtained were processed with SPSS version 23. Ethical clearance number 0754/KEPK/X/2018 was obtained from the Ethical Committee in Health Research of Dr. Soetomo General Hospital, Surabaya. Variables evaluated were NSAID dosage, route of administration, frequency of administration, and interval of administration. Patients requiring surgery were excluded. NSAIDs used for TBI management are metamizole, paracetamol, mefenamic acid, and ketorolac.

The samples were taken using total sampling method. Inclusion criteria of samples in this study were patients with mild or moderate TBI as the primary diagnosis from 1 January to 31 December 2018. Exclusion criteria for the samples were patients who underwent surgery as the therapy for TBI.

NSAIDs evaluated were metamizole, ketorolac, paracetamol, and mefenamic acid. The preferred dosage of metamizole is 500-1,000 mg per 6 hours and administered through per oral intravenous, or per rectum.[7] The preferred administration of ketorolac is single-dose intravenous 30 mg or intravenous 30 mg per 6 hours, with a maximum dose of 120 mg per day. Paracetamol and mefenamic acid are administered 500 mg per 8 hours per oral.

Results

Samples fulfilling the inclusion criteria were 40 in total, with only 29 medical records obtained. The remaining 11 medical records could not be found in the medical records storage room. Among 29 patients, 17 patients (58.6%) were diagnosed with mild TBI, and 12 patients (41.4%) were diagnosed with moderate TBI.

Table 1. Characteristics of patients with TBI in Dr. Soetomo General Hospital, Surabaya from 1 January to 31 December 2018

Characteristics	Frequency	Percentage (%)
Gender		
Male	20	69
Female	9	31
Age		
0-10 years old	2	6.9
11-20 years old	8	27.6
21-30 years old	9	31
31-40 years old	2	6.9
41-50 years old	3	10.3
51-60 years old	3	10.3
61-70 years old	2	6.9

The data shows that patients with TBI were mostly males (69%). The age group of 21-30 years old was the

one with the most TBI cases (31%), followed by the age group of 11-20 years old (27.6%). Meanwhile, the age groups of 0-10 years old, 31-40 years old, and 61-70 years old had the least cases of TBI.

Table 2. Prescribed NSAID in patients with mild and moderate TBI

NSAID	Frequency	Percentage (%)
Metamizole	10	34.5
Paracetamol	1	3.4
Metamizole + Paracetamol	15	51.7
Metamizole + Mefenamic Acid	1	3.4
Metamizole + Paracetamol + Mefenamic Acid	1	3.4
Metamizole + Ketorolac	1	3.4

NSAID prescribed to patients with mild and moderate TBI during the hospitalization period were mostly metamizole with paracetamol (51.7%) and metamizole only (34.5%). Patients with multiple drugs were primarily administered metamizole in the first few days of hospitalization and then given either paracetamol or mefenamic acid. It is important to note that children and adult management of TBI are not differentiated. The patient receiving paracetamol-only treatment is a referred patient from another hospital who has been given initial management at the said hospital.

Table 3. Adherence of NSAID administration

NSAID	Adherence Percentage (n)			
	Administration route	Dosage	Administration interval	Administration frequency
Metamizole	100% (10)	100% (10)	0% (0)	0% (0)
Paracetamol	100% (1)	100% (1)	100% (1)	100% (1)
Metamizole + Paracetamol				
Metamizole	100% (15)	100% (15)	0% (0)	0% (0)
Paracetamol	100%(15)	100%(15)	100% (15)	100% (15)
Metamizole + Mefenamic acid				
Metamizole	100% (1)	100% (1)	0 (0)	0 (0)
Mefenamic acid	100% (1)	100% (1)	100% (1)	100% (1)
Metamizole + Paracetamol + Mefenamic acid				
Metamizole	100% (1)	100% (1)	0% (0)	0% (0)
Paracetamol	100% (1)	100% (1)	100% (1)	100% (1)
Mefenamic acid	100% (1)	100% (1)	100% (1)	100% (1)
Metamizole + Ketorolac				
Metamizole	100% (1)	100% (1)	0% (0)	0% (0)
Ketorolac	100% (1)	100% (1)	100% (1)	100% (1)

It was found that paracetamol, mefenamic acid, and ketorolac administrations have 100% adherence in every variable evaluated. Meanwhile, metamizole administration has 0% adherence in administration frequency and administration interval. Metamizole and ketorolac were injected through the intravenous route. Meanwhile, paracetamol and mefenamic acid were given through oral administration. All of the NSAIDs administered were prescribed to be administered three times per day. The administered metamizole dosage was 1000 mg per 8 hours, 500 mg per 8 hours for paracetamol, 500 mg per 8 hours for mefenamic acid, and 30 mg per 8 hours for ketorolac.

Discussion

Patients with mild and moderate TBI were mostly males (69%). In contrast, female patients have a fewer percentage (31%). The percentage difference is not significant with a study that stated that male patients with mild or moderate TBI have a percentage of 72.5%, while female patients have a percentage of 27.5%.[13]

The age group of 21-30 years old has the most number of cases of TBI (31%). People in this age group might be more productive in job seeking and actively mobilizing from one place to another, increasing the risk of trauma than those whose mobilization is not as active as the others. The age groups of 0-10 years old, 31-40 years old, and 61-70 years old have the lowest number of cases of TBI. This might be caused by activities of people in this age group that are not as active as people in the age group of 21-30 years old.

Metamizole-only therapy was administered in 10 patients (34.5%). This percentage is different from research conducted in Prof. Dr. R. D. Kandou General Hospital Manado, which stated that metamizole-only was used in 28.85% of TBI patients.[14] Metamizole may cause agranulocytosis as its side effect.[15] In 41 patients diagnosed with agranulocytosis, 14 patients (34%) consumed metamizole for 1-2 days, 10 patients (24%) for 3-7 days, 12 patients (29%) for 8-21 days, and 5 patients (12%) for more than 21 days.[15] However, among patients who consumed metamizole, the incidence of agranulocytosis was low with a rate of 1.35 cases per 1,000,000 cases per year for females and 0.54 cases per 1,000,000 cases per year.[16] This study did not observe the incidence of agranulocytosis, thus it cannot be evaluated.

Paracetamol-only therapy was given to one patient referred from another hospital and had been given initial treatment in the said hospital. Metamizole combined with paracetamol was the most administered NSAIDs in TBI management (51.7%). Metamizole was only used in the first few days of hospitalization, and then the therapy will be continued with paracetamol instead of metamizole. Paracetamol has weaker analgesic effect than

metamizole.[17] The change of NSAID therapy might be caused by the decrease of patients' pain after a few days of metamizole administration, thus paracetamol was given because the route of administration was more comfortable and less invasive than matamizole. However, there were a few cases where metamizole and paracetamol were given in between each other, and patients' irregular sense of pain might cause it.

The few administration of mefenamic acid might be caused by the use of the drug as a substitute for paracetamol that might cause allergic reactions in patients. Ketorolac administration as initial therapy continued with metamizole only has a percentage of 3.4%. This percentage is significantly different from research conducted in Prof. Dr. R. D. Kandou General Hospital, Manado, which stated that ketorolac administration has a percentage of 59.61%.[14]

NSAID administration adherence evaluated from administration interval, administration frequency, dosage, and administration route shows that administration of paracetamol, ketorolac, and mefenamic acid had good administration adherence. Metamizole administration was well-administered in route of administration and dosage. However, the frequency and interval of administration were not adherents to the guideline. Metamizole as an analgesic will take effect 30 minutes after administration, and its analgesic effect will last for 6 hours.[17] The observed metamizole administration frequency was three times a day with an 8-hour interval. This may be caused by a higher dose of metamizole administration than stated in the previous statement.[17] Metamizole administration in Dr. Soetomo General Hospital, Surabaya has a dosage of 1000 mg per 8 hours. A higher dosage of metamizole may be expected to give a longer analgesic effect. Hence, the administration interval will be prolonged, and administration frequency will be reduced. Other than that, prolonged administration interval and reducted administration frequency of metamizole administration might be caused by the regulations from BPJS (healthcare and social security agent).

Conclusion

NSAIDs administered in patients with mild and moderate TBI are well-administered, except for metamizole which administration did not follow the guideline. Further research needs to be conducted regarding the effect of non-adherence of drug administration.

CONFLICT OF INTEREST

The author stated there is no conflict of interest in this study.

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