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Exclusive Breastfeeding And Acute Diarrhea In Children: A Cross-Sectional Study

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Abstract

Introduction : Breastmilk is known to contain molecules such as oligosaccharides, sIgA and lactoferrin which hold vital importance in immune system. These molecules specifically functioned to protect the body from pathogens including those causing diarrhea. The objective of this study is to define the relationship between exclusive breastfeeding and acute diarrhea incidence frequency in children as primary outcome and age of first acute diarrhea occurrence in children as secondary outcome.

Methods: This is an analytic observational cross-sectional study which included 35 children aged 6-24 months who were admitted to Kaswari Ward Wangaya General Hospital Denpasar between 01 June 2018 to 16 August 2018. Samples were obtained through consecutive sampling method and analyzed data were presented in both tables and narrative.

Results: From 35 samples included in this study, 13 were exclusively breastfed (37,1%) and 22 were non-exclusively breastfed (62,9%). Sample characteristics including gender, number of siblings, nutritional status, residence, source of water, age of mother, parent's occupation and education were comparable between two groups. Total samples who were exclusively breastfed and experience less diarrhea is 13 (p = 0,031; PR = 1,47 CI 95% 1,10-1,95). Total samples who were exclusively breastfed and first age of experiencing diarrhea over 12 months old is 11 (p = 0,002 ; PR = 3,10 CI 95% 1,47-6,27).

Conclusion: There is statistically significant relationship between exclusive breastfeeding and acute diarrhea incidence frequency and age of first acute diarrhea occurrence in children aged 6-24 months in Kaswari Ward Wangaya General Hospital.

Introduction

Diarrhea is still a major health burden as it is the leading cause of mortality and morbidity in children under 5. Diarrhea is responsible for approximately 6 million deaths of children every year mainly occurred in developing countries such as Indonesia. Of all number of deaths in children aged 29 days to 11 months in Indonesia, 34% caused by diarrhea.
According to data from Indonesian Ministry of Health, there is an increase in the incidence of diarrhea cases nationally from 2016, namely 6.897.463 cases to 7.077.299 cases in 2017. Toddlers are the most susceptible group due to immature immune system and life dependency to parents. An estimated 33,2% of diarrhea cases occur in children under age of 4 and half occur in infants under 12 months old.[1–6]

Breastmilk is long known as the most ideal source of nutrition for babies. It enhances immune system and optimize response to vaccination through the work of oligosaccharides, sIgA and lactoferrin. The World Health Organization recommend exclusive breastfeeding for the first 6

months of life. Based on the data from Indonesian Ministry of Health in 2017, exclusively breastfed babies in Indonesia only comprises 35,73% of the population and still far below the national target of 80%. This can have an impact on increasing rate of infections such as diarrhea, otitis media, neonatal sepsis, necrotizing colitis, urinary tract infection and lower respiratory tract infection. Considering the low number of exclusive breastfed children and increasing cases of acute diarrhea in Indonesia, this study aims to define the relationship between exclusive breastfeeding and acute diarrhea by analyzing the incidence frequency and age of first acute diarrhea occurrence.[4,7–10]

Methods

Study Population and Design

During the period from 01 June 2018 to 16 August 2018, this cross-sectional study was carried out at the Kaswari Ward, Wangaya
General Hospital, Bali, Indonesia. Samples were obtained with consecutive sampling method.

All 6-24 months children, male or female with parental consent were included in the study. Exclusion criteria consist of immunocompromised children, children whose mothers have HIV infection, children with congenital anomalies, children diagnosed with cow's milk allergy or lactose intolerance, children on iron supplementation, children consuming laxatives, children with overuse of antibiotics and children immunized with rotavirus vaccine. With regard of 5% α, minimum samples of 31 were calculated.

Statistical Methods

Data were analyzed using standard computer program SPSS Windows version 20. (SPSS Corporation, USA). Continuous data were expressed in the form of the mean ± SD. Categorical data were expressed as numbers and percentage. For comparison of categorical data, we used chi-square test and exact Fischer test. The risk of acute diarrhea incidence in exclusively breastfed children were expressed with prevalence ratio with confidence interval of 95%. P value of < 0,05 indicates significant results.

Results

Over the period of 01 June 2018 to 16 August 2018, there are 162 patients admitted to Kaswari Ward, Wangaya General Hospital. Only 51 patients were between the age of 6-24 months and 35 met inclusion and exclusion criteria. From 16 patients who were excluded, 10 with congenital anomalies, 5 diagnosed with cow's milk allergy and 1 was vaccinated with Rotavirus. The demographic data of the samples are shown in table (1).

Table 1. Demographic data of the samples

Characteristics	Exclusively breastfed (n=13)	Non-exclusively breastfed (n=22)
Age, month (SD)	15,2 (1,5)	12,5 (1,3)
Gender		
Male, n	7	12
Female, n	6	10
Siblings		
None, n	6	10
One or more, n	7	12
Nutritional status		
Normal, n	12	20
Abnormal, n	1	2
Place of living		
Urban, n	13	20
Suburb, n	0	2
Water resources		
Filtered water, n	3	6
Ground water, n	10	16
Maternal age		
Under 30 years old, n	9	17
Over 30 years old, n	4	5
Maternal occupation		
None, n	9	10

Working mother, n	4	12
Paternal occupation		
Working class, n	9	17
Entrepreneur, n	4	5
Maternal education		
Primary education, n	4	13
Secondary education, n	9	9
Paternal education		
Primary education, n	4	4
Secondary education, n	9	18

The primary outcome of this study is to define the relationship between exclusive breastfeeding and acute diarrhea incidence which shown in table (2).

Table 2

Variables	Acute Diarrhea Incidence Frequency		PR (CI 95%)	*p*
	Infrequent (<2x)	Frequent (≥2x)		
Exclusively breastfed, n	13	0	1,47 (1,10-1,95)	0,031*
Non-exclusively breastfed, n	15	7		

* Chi-square

The secondary outcome of this study is to define the relationship between exclusive breastfeeding and age of first acute diarrhea occurrence which shown in table (3).

Table 3

Variables	Age of first acute diarrhea occurrence		PR (CI 95%)	*p*
	Older than 12 months old	0-12 months old		
Exclusively breastfed, n	11	2	3,10 (1,51-6,38)	0,002*
Non-exclusively breastfed, n	6	16		

* Fischer exact test

Discussion

From all of the patients experiencing less than twice acute diarrhea episodes, 46,4% were exclusively breastfed and 53,6% were not. There was one cell with zero actual count and the expected numbers were more than 20%. Therefore, Fischer exact test were employed with p-value of 0,031 (two-way analysis). Null hypothesis was rejected which mean there is statistically significant relationship between exclusive breastfeeding with acute diarrhea incidence in children. From calculation of prevalence ratio, exclusively breastfed children were 1,47 times more likely to experience less than twice diarrhea episodes before the age of 2 when compared to non-exclusively breastfed children (CI95% 1,10 – 1,95). Nevertheless, there were 15 non-breastfed children who experienced less than twice diarrhea episodes which can be a result from good personal hygiene and correct knowledge on how to sterilize bottles.

The finding of this study supported prior study by Begum and Absar stating exclusive breastfeeding may prevent acute diarrhea incidence frequency in children under 2 years old. Bener, Ehlayel and Abdulrahman also found that exclusive breastfeeding has an important role in suppressing acute diarrhea in children. In Indonesia, studies by Sudiyanto dkk, Rohmah dkk and Rizky dkk in Mojokerto, Bandung and Pontianak Timur respectively were conducted in babies under 6 months old and found significant relationship between exclusive breastfeeding and diarrhea incidence.[11–15]

Interestingly, studies overseas reveal higher percentage of exclusively breastfed

children compared to non-exclusively breastfed children in the samples taken. However, studies conducted in Indonesia including this study involved majority of non-exclusively breastfed children (62,9% compared to 37,1%). This may reflect the gap between the low coverage of exclusively breastfed children in Indonesia compared to other countries.

Secondary outcome of this study revealed that from all of children experiencing first episode of diarrhea under 12 months old, 64,7% were exclusively breastfed and 35,3% were not.

Chi-square test was employed with p-value 0,002 so that null hypothesis was rejected. From calculation of prevalence ratio, exclusively breastfed children were 3,10 more likely to experience first episode of diarrhea after the age of 1 when compared to non-exclusively breastfed counterparts (CI95% 1,47 – 6,27). This finding also corresponds to study by Begum and Absar which revealed exclusive breastfeeding can postpone age of first acute diarrhea occurrence in children under 2 years old. We still found 2 exclusively breastfed children who experienced first diarrhea episode before 12-months-old but both between 6-12 months old probably caused by poor hygiene of the complementary food given. Our finding is consistent with Lamberti et al stating protective effect of breastmilk is the highest in first 6 months of life. From all of the children experiencing first diarrhea episode after age of 1, 6 patients (35,9%) were not exclusively breastfed which can be a result from good personal hygiene and correct knowledge on how to sterilize bottles.[16,17]

Study limitations

There are several limitations of this study including majority of samples was dominated with non-exclusively breastfed children, poor confounding factors control such as food recall and personal hygiene were not assessed and inevitable recall bias.

Conclusion

There is statistically significant relationship between exclusive breastfeeding and acute diarrhea incidence frequency which show that
exclusively breastfed children experience less acute diarrhea episode. Exclusive breastfeeding also proven statistically significant to protect children from experiencing acute diarrhea earlier in life (< 12 months old).

Conflict Of Interest

The authors declare none.

References

1. Yusuf S. Profil Diare di Ruang Rawat Inap Anak. Sari Pediatr [Internet]. 2011;13(4):265–70. Available from: https://saripediatri.org/index.php/sari-pediatri/article/download/424/356

2. Christy MY. Factors Associated with Diarrheal Dehydration in Toddlers at Kalijudan Health Center Work Area. J Berk Epidemiol. 2014;2(3):297–308.

3. Kementerian Kesehatan Republik Indonesia. Profil Kesehatan Indonesia. Profil Kesehatan Provinsi Bali. 2016. 1-220 p.

4. Kementerian Kesehatan RI. Profil Kesehatan Indonesia 2017. Profil Kesehat Indones 2017. 2018;100.

5. Dinas Kesehatan Provinsi Bali. Profil Kesehatan Provinsi Bali [Internet]. 2016. Available from: http://www.depkes.go.id/resources/download/profil/PROFIL_KES_PROVINSI_2012/17_Profil_Kes.Prov.Bali_2012.pdf

6. Kemenkes RI. Situasi diare di Indonesia. J Bul jendela data Inf Kesehat. 2011;2:1–44.

7. Black RE, Allen LH, Bhutta ZA, Caulfield LE, de Onis M, Ezzati M, et al. Maternal and child undernutrition: global and regional exposures and health consequences. Lancet. 2008;371(9608):243–60.

8. Suwandi RS. Air Susu Ibu Eksklusif: Kegunaan Bagi Bayi dan Ibu. Ebers Papyrus. 2009;15(1): 5 –7.
9. Fahriani R, Rohsiswatmo R, Hendarto A. Faktor yang Memengaruhi Pemberian ASI Eksklusif pada Bayi Cukup Bulan yang Dilakukan Inisiasi Menyusu Dini (IMD). Sari Pediatr. 2014;15(6):394–402.

10. PATH. Breastfeeding and Diarrhea. Seattle; 2013.

11. Bener A, Ehlayel MS, Abdulrahman HM. Exclusive breast feeding and prevention of diarrheal diseases: a study in Qatar. Rev Bras Saúde Matern Infant [Internet]. 2011;11(1):83–7. Available from: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S1519-38292011000100009&lng=en&tlng=en

12. Sudiyanto H, Ariyanto FW, Mujiadi, Nalinda R. Pengaruh Pemberian ASI Eksklusif Terhadap Kejadian Diare Akut pada Bayi Usia 0-6 Bulan di RSU Al-Islam H.M Mawardi Sidoarjo [Internet]. 2017. Available from: http://elib.pdii.lipi.go.id/katalog/detailkatalog/q4008o4110m4194t4134k4194/z3804d3798c3834y3792n3846r3846

13. Rizky GH, Budiharto I, Sukarni. Hubungan Pemberian Air Susu Ibu (ASI) dengan Kejadian Diare pada Bayi 0-6 Bulan di Puskesmas Kampung Dalam Pontianak Timur. Vol. 39. 2010.

14. Rahmadhani EP, Lubis G, Edison. Hubungan Pemberian ASI Eksklusif dengan Angka Kejadian Diare Akut pada Bayi Usia 0-1 Tahun di Puskesmas Kuranji Kota Padang. J Kesehat Andalas. 2013;2(2):62 – 6.

15. Rohmah H, Hafsah T, Rakhmilla LE. Role of Exclusive Breastfeeding in Preventing Diarrhea. Althea Med J [Internet]. 2015;2(1):78–81. Available from: http://journal.fk.unpad.ac.id/index.php/amj/article/view/436

16. Begum MUH, Absar MN. Diarrhea in Breastfed versus Formulafed Baby : A Hospital Based Study in 150 Children. 2016;34(1):1–5.

17. Lamberti LM, Fischer Walker CL, Noiman A, Victora C, Black RE. Breastfeeding and the risk for diarrhea morbidity and mortality. BMC Public Health [Internet]. 2011;11(SUPPL. 3):S15. Available from: http://www.biomedcentral.com/1471-2458/11/S3/S15

The Relationship Between Brain Tumor And Sleep Components (Psqi) In Siloam Hospitals Lippo Village 2015-2018

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Abstract

Introduction: Brain tumor can cause symptoms such as headache and seizure which might reduce sleep quality. Currently, sleep quality in brain tumor patients aren't getting much attention. This study's purpose is to determine the effect of brain tumor to sleep quality and its components in patients.

Methods: The design of this study is a retrospective cohort, and it is done in Siloam Hospitals Lippo Village and Paviliun Umum Rumah Sakit Siloam from January-April 2019 with sample population consisting of brain tumor patients from age 19 until 59 years old. The sample amount is 29 subjects. PSQI is used to assess sleep quality and components. Data analysis uses the SPSS version 24.0 software and statistical analysis using chi^2.

Result: Brain tumor patients have worse sleep quality compared to the control, with 26 patients (89.7 %) having bad sleep quality. For the control, there are only 18 people (62.1%) who have bad sleep quality. The relationship between brain tumor and sleep quality have a p value of 0.032 and relative risk (RR) of 3,7. Brain tumor has a significant relationship with sleep latency (p value 0,015) and daytime dysfunction (p value 0,02)

Conclusion: The relationship between brain tumor and sleep quality in brain tumor patients of Siloam Hospitals Lippo Village and Paviliun Umum Rumah Sakit Siloam, which was measured with the PSQI questionnaire is significant. Brain tumor also has a significant relation with sleep latency and daily dysfunction.

Introduction

Brain tumor is an uncontrolled growth of cells from within the brain (primary brain tumor) or arise from cells outside the brain (metastatic tumor). Primary tumors consist of glial which arise from glial cells and non-glial which can arise from nerves, blood vessels, or glands.[1] Brain tumor can cause symptoms such as headache and seizure which can decrease sleep quality.[2] Sleep quality in brain tumor patients is generally not noticed even though sleep disturbance is reported in 17-54 % of Brain tumor patients.[3] According to the *Central Brain Tumor Registry of The United States* (CBTRUS), Brain tumor in The United States has an incidence rate of 57.3 in every 100000 people per year.[4] A Systematic review and meta analysis found that Brain tumor worldwide has an incidence rate of 10.82 in every 100000 people per year.[5]

There are only a few studies that have researched about the relationship between brain tumor and sleep. One study found that glioma has a relationship with insomnia, which is affected by many factors.[6]

Another study found that sleep disturbance is a common occurrence in primary brain tumor patients, especially those undergoing radiotherapy.[7]
The guideline for Brain tumor Care which is published by the Health Ministry in Indonesia doesn't have a part that discusses about sleep in Brain tumor patients, so it can be inferred that it is also not noticed much in Indonesia.[8]

Information about sleep quality in Brain tumor patients in Indonesia is needed because Indonesia have factors such as race and culture that separates it from other countries. There are also some studies which determined that Indonesian people have less sleep disturbance compared to another Asian country such as Bangladesh[9] and that there are fewer people with longer sleep duration and bad sleep quality in southeast Asia compared to other regions such as the middle east, central Asia and Latin America.[10] The amount of attention to sleep in brain tumor patients is concerning, because sleep quality is very important for a good prognosis which is why research about this topic is needed.

Methods

This study was a retrospectional cohort.The subjects are brain tumor patients aged 19-59 years old from Siloam Hospitals Lippo Village and Paviliun Umum Rumah Sakit Siloam in January-April 2019. The control group were subjects aged 19-59 years old without a brain tumor. Sleep quality and sleep components are determined using the Pittsburgh Sleep Quality Index (PSQI) questionnaire. The PSQI consists of 19 self-rated questions and five questions rated by the bedpartner or roommate. These I9 items are grouped into seven component scores, each weighted equally on a 0-3 scale. The seven component scores are then summed to yield a global PSQI score.

The PSQI global score below 5 is defined as good sleep quality while PSQI global score of 5 and above are defined as poor sleep quality. Subjective Sleep quality habitual sleep efficiency is defined by a score of 0-1 (good) and 2-3 (poor). Habitual sleep efficiency is defined by a score of 0-1 (≥ 85%) and 2-3 (< 85%). Sleep disturbance and daytime dysfunction is defined by a score of 0 (none), 1 (mild), 2 (intermediate), and 3 (severe). Sleep latency is defined by a score of 0 (none), 1 (seldom), 2 (sometimes), and 3 (often). Sleep duration is defined by a score of 0 (>7 hours) and 1-3 (≤7 hours). Use of sleep medication is not included in this study.

Inclusion criteria is patients aged 19-59 years old and diagnosed with brain tumor. Subjects with obesity, caffeine consumption 6 hours before sleep, pregnancy, use of sleep medication and alcohol consumption were excluded. There were 58 subjects in this study with 29 brain tumor patients and 29 subjects in the control group. Chi^2 was used to determine p value and relative risk between the variables.

Result

Table 1. Analysis of Relationship between Brain tumor and Sleep Component

Sleep Components		Brain Tumor (n)	Control Group (n)	P Value	Relative Risk (RR)	CI (95%)
Sleep Quality	Good	3	11	0.032	3.7	1.14-11.793
	Poor	26	18			
Subjective Sleep Quality	Good	17	21	0.4	1.5	0,72-3,12
	Poor	12	8			
Sleep Duration	>7 hours	10	10	1	1	0,68-1,45
	≤7 hours	19	19			
Sleep Latency	Sometimes/often	12	3	0.015	4	1.25-12.7
	None/seldom	17	26			
Habitual Sleep Efficiency	≥ 85%	27	29	0.97	2.07	0,2-21,6
	< 85%	2	0			
Sleep Disturbance	Intermediate-severe	4	0	0.32	4.1	0.5-34.9
	None-mild	25	29			
Daytime dysfunction	Severe	12	3	0.02	4	1.67-9.63
	Intermediate	10	15			
	Mild	6	6			
	None	1	5			

Analysis using SPSS version 24.0 found that the relationship between brain tumor and sleep quality has a p value of 0,032 which is significant, with a relative risk of 3.7 which means that a brain tumor patient is 3.7 times more likely to have poor sleep quality. The relationship between brain tumor and sleep latency has a p value of 0.015 which is significant, with a relative risk of 4 so a brain tumor patient is 4 times more likely to have sleep latency. Relationship of brain tumor and daytime dysfunction has a p value of 0.02 which is significant, with a relative risk of 4 so a brain tumor patient is 4 times more likely to have daytime dysfunction. Analysis of the relationship between brain tumor and sleep components subjective sleep quality, sleep duration, habitual sleep efficiency, and sleep disturbance has a p value above 0.05 so they are not significant.

Discussion

Analysis of the relationship between brain tumor and sleep quality has a p value 0.032 which is significant. With a relative risk of 3.7, this means that a brain tumor patient is 3.7 times more likely to have poor sleep quality. This finding is also found in studies done by Leistner *et al* (2015) and Pickering *et al* (2014) where they also found that brain tumor patients have worse sleep quality compared to the control group using PSQI.[11-12] Sleep latency is another component that has a significant relationship with brain tumor, having a p value of 0.015 and relative risk of 4. Sleep latency is defined as the amount of time it takes from when the lights are turned off and someone falling asleep.[13] Having more sleep latency might explain why brain tumor patients have worse sleep quality compared to normal people.

The result of having can be seen in brain tumor patients having more daytime dysfunction. Analysis of the relationship is significant with a p value of 0.02 and relative risk of 4 so brain tumor patients are more likely to be sleepy during the day which affects their daily activities and performance at work. Even though sleep quality is significant in relation to brain tumor, subjective sleep quality assessed by PSQI is not significant, which might be affected by this study being a retrospective cohort so the subjects may not have good memory of it.

Sleep quality, sleep latency and daytime dysfunction having a significant relationship with brain tumor is an indication that this is a problem that brain tumor patients experience, and should be an aspect that is noticed more in caring for them.

Other studies have already concluded the relationship between poor sleep and chronic illnesses such as a study done by Kristen *et al* (2006) that poor sleep quality increases the risk of having Diabetes Mellitus type 2,[14] while Nagai *et al* (2010) found that shorter sleep duration is a risk factor for hypertension and coronary heart disease.[15] So having a good sleep quality is important for preventing those diseases. For brain tumor patients having good sleep quality might be important to prevent the disease from getting worse and having a better sleep quality, as good sleep quality has an impact in creating better quality of life.[16]

In a study done by Mark *et al* (2015), it is stated that sleep has a bidirectional relation with the immune system where sleep deficiency can cause inflammation, while an immune response itself can also affect someone's sleep. This is important because it explains why sleep can increase the risk of having cancer, where it is found that sleeping in the afternoon can reduce the risk of having cancer.[17] This also applies in brain tumor where Terri *et al* (2016) found that sleep disturbance is directly connected with worse symptoms for the patient.[3]

In treatment it is important to consider the patient's sleep quality in order to pursue a better response to the treatment. But, in brain tumor it isn't so simple as some treatments for brain tumor can negatively impact their sleep quality. Hong *et al* (2014) found that chemotherapy can cause peripheral nerve damage which causes symptoms that can affect sleep. When someone already has damage to their peripheral nerves a doctor can consider reducing the dose, changing the drug or even stopping the chemotherapy.[18] But, this can't always be done as chemotherapy is an important part of treatment for the patient. Terri *et al* (2016) found that radiotherapy can cause sleep disturbance[3], and Sejal *et al* (2013) also found that antiepileptic drugs could also affect someone's sleep.[19] So, preserving someone's sleep quality in brain tumor treatment is not easy but it is something important to consider.

Conclusion

Brain tumor has a significant relation with poor sleep quality, sleep latency and daytime dysfunction. Sleep quality is still seldom considered in the treatment of brain tumor, which is a problem. This study can hopefully raise more awareness to the subject in treating brain tumor.

Acknowledgement

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Conflict Of Interest

None

References

1. Butowski NA. Epidemiology and Diagnosis of Brain Tumors. Contin Lifelong Learn Neurol [Internet]. 2015 Apr [cited 2018 Sep 6];21(2 Neuro-oncology):301–13. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25837897

2. Comelli I, Lippi G, Campana V, Servadei F, Cervellin G. Clinical presentation and epidemiology of brain tumors firstly diagnosed in adults in the Emergency Department: a 10-year, single center retrospective study. Ann Transl Med [Internet]. 2017 Jul [cited 2018 Sep 16];5(13):269. Available from: http://www.ncbi.nlm.nih.gov/pubmed/28758095

3. Armstrong TS, Shade MY, Breton G, Gilbert MR, Mahajan A, Scheurer ME, et al. Sleep-wake disturbance in patients with brain tumors. Neuro Oncol. 2017;19(3):323–35.

4. Ostrom QT, Gittleman H, Liao P, Vecchione-Koval T, Wolinsky Y, Kruchko C, et al. CBTRUS Statistical Report: Primary brain and other central nervous system tumors diagnosed in the United States in 2010–2014. Neuro Oncol [Internet]. 2017;19(suppl_5):v1–88. Available from: http://academic.oup.com/neuro-oncology/article/19/suppl_5/v1/4596648

5. de Robles P, Fiest KM, Frolkis AD, Pringsheim T, Atta C, St Germaine-Smith C, et al. The worldwide incidence and prevalence of primary brain tumors: a systematic review and meta-analysis. Neuro Oncol [Internet]. 2015 Jun [cited 2018 Sep 6];17(6):776–83. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25313193

6. Robertson ME, McSherry F, Herndon JE, Peters KB. Insomnia and its associations in patients with recurrent glial neoplasms. Springerplus. 2016;5(1):1–5.

7. Jeon MS, Dhillon HM, Agar MR. Sleep disturbance of adults with a brain tumor and their family caregivers: A systematic review. Neuro Oncol. 2017;19(8):1035–46.

8. Aman RA, Soenarya MF, Andriani R, Aninditha T, Munandar A, Tadjoedin H, et al. Pedoman Nasional Pelayanan Kedokteran Tumor Otak [Internet]. Kementerian Kesehatan Republik Indonesia; Available from: http://kanker.kemkes.go.id/guidelines/PNPKOtak.pdf

9. Endeshaw Y. Aging, subjective sleep quality, and health status: the global picture. Sleep [Internet]. 2012 Aug 1 [cited 2019 Jul 4];35(8):1035–6. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22851799

10. Peltzer K, Pengpid S. Sleep duration, sleep quality, body mass index, and waist circumference among young adults from 24 low- and middle-income and two high-income countries. Int J Environ Res Public Health. 2017;14(6).

11. Leistner SM, Klotsche J, Dimopoulou C, Athanasoulia P, Roemmler-zehrer J, Pieper L, et al. Reduced sleep quality and depression associate with decreased quality of life in patients with pituitary adenomas. 2015;

12. Pickering L, Jennum P, Gammeltoft S, Poulsgaard L, Feldt-rasmussen U, Klose M. Sleep – wake and melatonin pattern in craniopharyngioma patients. 2014;(2).

13. Shrivastava D, Jung S, Saadat M, Sirohi R, Crewson K. How to interpret the results of a sleep study. 2014;1:1–4.

14. Kristen L. Knutson P, Armand M. Ryden M, Bryce A. Mander B. Role of Sleep Duration

and Quality in the Risk and Severity of Type 2 Diabetes Mellitus. Arch Intern Med [Internet]. 2006; Available from: https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/410883

15. Nagai M, Hoshide S, Kario K. Sleep Duration as a Risk Factor for Cardiovascular Disease- a Review of the Recent Literature. 2010;54–61.

16. Roeser K, Eichholz R, Schwerdtle B, Schlarb AA, Kübler A. Relationship of sleep quality and health-related quality of life in adolescents according to self- and proxy ratings: a questionnaire survey. Front psychiatry [Internet]. 2012 [cited 2018 Oct 31];3:76. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22969731

17. Opp MR, Krueger JM. Sleep and Immunity: A Growing Field with Clinical Impact. [cited 2018 Sep 16]; Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4685944/pdf/nihms-694135.pdf

18. Hong JS, Tian J, Wu LH. The influence of chemotherapy-induced neurotoxicity on psychological distress and sleep disturbance in cancer patients. Curr Oncol [Internet]. 2014 Aug [cited 2018 Sep 21];21(4):174–80. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25089099

19. Jain S V., Glauser TA. Effects of epilepsy treatments on sleep architecture and daytime sleepiness: An evidence-based review of objective sleep metrics. Epilepsia [Internet]. 2014 Jan [cited 2018 Sep 21];55(1):26–37. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24299283

Short-Term Memory Comparison Of Students Of Faculty Of Medicine Pelita Harapan University Batch 2015 Between The Handwriting And Typing Method

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Abstract

Introduction : A lot of research has been done to determine if handwriting or typing note influenced short-term memory, however, the results obtained are still controversial. Therefore this study is structured to see the effect of note taking methods by handwriting and typing on short-term memory.
Aim : The aims of this study were to increase the performance of students in Faculty of Medicine Pelita Harapan University as well as providing the right and effective method of taking notes.
Method : Experimental study design was chosen in this study. Study population is students of faculty of medicine Pelita Harapan University batch 2015. 40 samples will be divide randomly into two, one group will take a note by handwriting and another by typing. Each group is required to watch a video about 15 minutes long. The results were analyzed statistically using T-test.
Result : The average of new information that can be remembered by group that take a note by handwriting significantly ($p<0,05$) higher than group than take a note by typing with a p-value of 0,009.
Conclusion : Take a note by handwriting allows people to remember more new information than typing.

Introduction

There are different stages of memory formation called, sensory memory, short-term memory, and long-term memory. Perception of stimuli (new information) is encoded to sensory memory, and then stored as short-term memory in prefrontal cortex.[1] Short-term memory is a process of temporarily storing new information, and only remembered as long as we focus on it.[2]

As the technology develops, many students take notes using electronic devices.[3] Whilst handwriting consists of more complex motor skills, typing consists of repetitive movements, but does't have specific motor movements. There for, short-term memories formation might be worse than handwriting, but the results obtained from previos studies are still controversial.[4,5,6]

The aims of this study were to increase the performance of students in Faculty of Medicine Pelita Harapan University as well as providing the right and effective method of taking notes.

Material And Method

This experimental study had been conducted in students of faculty of medicine Pelita Harapan University batch 2015 between January 2018 and march 2018. Informed consent had been conducted from all of the students.

Inclusion Criteria

Students of faculty of medicine Pelita Harapan University batch 2015 who are cooperative, right-handed, and don't have knowledge about the videos used in this research.

Exclusion Criteria

Students of faculty of medicine Pelita Harapan University batch 2015 who are not cooperative, left-handed, and taking drugs with side effects that affect concentration.

Randomisation

40 students of faculty of medicine Pelita Harapan University batch 2015 were devided into two groups by computer generated randomization.

Design Of The Study

In this experimental study, samples had been devided into two groups (handwtiring and typing group). Both group had done pre-test and post-test. The results were compared against their short term memory.

Statistical Analysis

Statistical analysis was performed by using SPSS 22 version and Microsoft Office Excel 2011 version. Shapiro-Wilk test were used to compare the data. Independent T-test were used for bivariate statistical analysis of data : mean±standart deviation was used for numeric variables. When $p < 0.05$ accepted as statistically significant.

Result And Discussion

40 students out of 199 were randomly chosen to participate in this study. The 40 students then randomly assigned to the handwriting (n = 20) and typing (n = 20) group. Each group were divided into 3 small groups with different video. Handwriting group : video1 (n = 6), video2 (n = 7), video 3 (n = 7). Typing group : video1 (n = 7), video2 (n = 7), video 3 (n = 6).

Samples characteristics : male (17.5%) vs female (82.5%), age 20 - <21 (72,5%), 21 - <22 (17,5%), 22 - <23 (5%), 18 - <19 (2,5%), and 19 - <20 (2,5%). Average amount of new information remembered in handwriting group : video1 6,83 (56,49%), video2 5,43 (45,22%) and video3 6,86 (57,29%) (mean 6.53 (53.08%)). Typing group : video1 5,1 (42,86%), video2 5 (41,67%) and video3 5,5 (45,83%) (mean 5.20 (43.42%)).

Table 1. Sample characteristics based on new information that can be remembered

Variable	n	Persent	New Information Obtained		
Note Taking Method			Mean ± SD	Minimal (%)	Maximal (%)
Handwriting	20	50%	6,35 ± 1,348	33,33	75
Typing	20	50%	5,20 ± 1,281	16,67	58,33

Table 2. Comparison of the Average Amount of New Information that Can be Remember Between Method of Taking Notes by Handwriting and Typing

	Note Taking Method	Mean	SD	P value
1	Writing	6,35	1,348	0,009
2	Typing	5,20	1,281	

Table 3. Table 2x2 Method of Taking Notes by Handwriting and Typing

Method	The amount of new information that can be remembered		
	≤ 5	> 5	Total
Typing	11	9	20
Handwriting	5	15	20
Total	16	24	40

The handwriting group remembered more new information compared to typing group with $p = 0,009$ or $p < 0,05$, with Odd ratio 3,68 and Relative risk 2.2

Discussion

Reaserch Subjects Overview

The reaserch subjects were 40 students from batch 2015, which the age range is not too wide (18-22 years old) and the activities carried out daily are not too different. 18 to early 20 is the peak age where someone is best at remembering various information in a short time.[7] This condition affects the amount of new information that can be remembered between handwriting and typing. If the age difference is too far, then the results may not be representative, because there is a decline in cognitive function and memory in adulthood (over 25 years).[7]

Researchers use videos of approximately 15 minutes, on the grounds that glucocorticoids are produced approximately 10 minutes after someone learns something new. Glucocorticoids are secreted by the adrenal cortex when a person faces a stressful situation. This hormone will enter the brain and bind to the adrenal steroid receptors (glucocortokiod receptors), then, transcription of many genes occurs resulting in protein synthesis. This protein helps memory formation.[8]

Comparison of Short-Term Memory Between the Handwriting and Typing Method independent T-test (table 2.) shows that the handwriting group M = 6,35 (SD = 1,348) statistically significant to remembered more new information compared to typing group M = 5,2 (SD = 1,281) with p = 0,009 or p < 0,05.

In addition, the results are also supported by the value of odd ratio and relative risk. The handwriting group remembered more new information compared to typing group with p = 0,009 or p < 0,05 means there were statistically significant difference.Odd ratio 3,68 (odd ratio >1) can be interpreted as there is an association between the method of note taking with the amount of new information that can be remembered. Based on these results, typing has a greater chance to make someone remember less new information than handwriting. Relative risk 2.2 means taking notes by typing have 2.2 times grater risk to remember less than 5 information compared to handwriting.

Like our study, Timothy J. Smoker, Carrie E. Murphy & Alison K. Rockwell (2009) stated that people who take notes by handwriting are better at remembering short-term information compared to people who take notes by typing.[6]

Short-term memory formation involves several components. New information (stimuli) detected by sensory neuron. Whilst information deemed as important is passed through the connecting neuron to be forwarded to short-term memory in the prefrontal cortex, information that considered insignificant will be lost. Short-term memory will be sent to the hippocampus and stored as long-term memory. Besides being stored in the cerebral cortex, long-term memory is also stored in various locations throughout the nervous system and even throughout the body because receptors in the brain are also found in all cells of the body.[9]

Handwriting movements when taking notes helps to form memory in the sensormotor parts of the brain and the memory is also stored along the nervous system in the muscles of the fingers to become motor memory.[9] Using motor skills to remember information makes the information more memorable than just listening.[1]

Handwriting allows a person to remember more new information, possibly due to making someone more familiar with words that are important to remember and induced formation of more complex memories. Whereas typing consist of repetitive movements but don't have specific movements and more using visual abilities than motor skills.[5]

Comparison of Short-Term Memory Between the Handwriting and Typing Method on Magnetic Resonance Imaging (MRI)

According to previous research using MRI, handwriting activated many parts of the brain. Such as involvement of the inferior frontal gyrus (IFG), anterior cingulate cortex (ACC), and fusiform gyrus (FG). Whereas, typing involves fewer parts of the brain, sprecifically the posterior parietal cortex (PPC) and FG.[10]

IFG plays a role in language processing. At the posterior part there is a dominant broca area for understanding language and the ability to speak. The ACC part is connected to the prefrontal cortex, parietal cortex, and also related to the motor and visual system. ACC is activated when someone does something that requires concentration and high attention. In addition, ACC also plays an important role in decision-making, emotions, and empathy. FG is significantly active to recognize and distinguish faces (visual), colors and words. PPC is known to

be involved in the ability to receive various inputs (information) from the sensory area and unite the information to be understood.[10]

These data indicate that handwriting, activated parts of the brain that process motor, visual, language, and parts of the brain that help to recognize words. Meanwhile, by typing the dominant part of the brain that is activated is the part that processes the sensory stimulus and visual area.

Therefore, the short-term memory produced by handwriting is more complex than typing.

Conclusion

Take a note by handwriting allows people to remember more new information than typing and the difference is statistically significant.

Recomendation

Glucocorticoid levels in the blood need to be measure before and after watching the video to get more accurate results. Also, long-term memory test need to be done one week after watching the video.

References

1. Jonides J, Lewis RL, Nee DE, Lustig CA, Berman MG. The mind and brain of short-term memory John. 2014;193–224.
2. Kumaran D. Short-term memory and the human hippocampus. J Neurosci. 2008;28(15):3837–8.
3. Aragón-Mendizábal E, Delgado-Casas C, Navarro-Guzmán J-I, Menacho-Jiménez I, Romero-Oliva M-F. A comparative study of handwriting and computer typing in note-taking by university students. 2016;24(48):101–7.
4. Julius MS, Meir R, Shechter-Nissim Z, Adi-Japha E. Children's ability to learn a motor skill is related to handwriting and reading proficiency. Learn Individ Differ. 2016;51:265–72.
5. Smoker TJ, Murphy CE, Rockwell AK. Comparing memory for handwriting versus typing. Proc Hum Factors Ergon Soc Annu Meet. 2009;53(22):1744–7.
6. Schoen I. Effects of method and context of note-taking on memory: handwriting versus typing in lecture and textbook-reading contexts. Pitzer Sr Theses. 2012;20(8):16-24
7. Howieson DB. Cognitive skills and the aging brain: What to expect. 2016; 121–130.
8. Roozendaal B. Glucocorticoids and the regulation of memory consolidation. Psychoneuroendocrinology. 2000;25(3):213–38.
9. May, Cynthia; Einstein G. Learning: a five-day unit lesson plan for high school psychology Teachers. 2013;(August):43.
10. James KH, Engelhardt L. The effects of handwriting experience on functional brain development in pre-literate children. Trends Neurosci Educ. 2012;1(1):32–42.

Magnesium Sulphate For Tetanus, review of two cases

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Abstract

Introduction: Tetanus is critically ill disease with long term hospitalization period. It need to be carefully monitored, usually in intensive care unit and involves critical care physicians. Benzodiazepine is preferred by World Health Organization (WHO) for muscle spasm control in tetanus, but it will be less costly if magnesium sulphate can be used alone to control spasm and autonomic dysfunction in tetanus. We report a series of 2 tetanus cases that were treated using magnesium sulphate to provide a brief clinical description about the use of magnesium sulphate in tetanus. We also give a brief review on epidemiology, pathophysiology, clinical findings, diagnosis, and treatment of tetanus to provide implications for intensive care physicians. Methods : Case series report

Results : Two patients with tetanus was given magnesium sulphate infusion to control muscle spasm and autonomic dysfunction with good results as expected. Both of them were survive and discharged home in healthy condition.

Conclusions :
Magnesium sulphate can also be used to control muscle spasm and autonomic dysfunction although WHO recommend benzodiazepines for controlling muscle spasm. Intensive care physicians should have enough knowledge about tetanus and how it should be managed adequately to ensure survival from tetanus.

Introduction

Tetanus is an infectious disease caused by exotoxin from *Clostridium tetani*. It causes generalized muscle spasm and autonomic dysfunction.[1, 2, 3] Onset of tetanus is acute and often fatal. Incubation period of tetanus varies between several days to several months.[3] The most common treatment for muscle spasm caused by tetanus are sedation, neuromuscular blockade, and controlled ventilation.[2] Benzodiazepines often used to control muscle spasm. Magnesium sulphate also has therapeutic properties to control spasms and autonomic dysfunction in tetanus.[1]

There are about 1 million cases of tetanus every year are hospitalized worldwide, and tetanus causes about 400 thousand death every year.[1] It is uncommon in developed country, mostly because of the good immunization system and coverage.[4] In Indonesia, tetanus reported as an outbreak after tsunami in Aceh province and earthquake in Yogyakarta province.[5,6] Approximately 1 month after tsunami in Aceh on December, 26th, 2004, 106 tetanus cases reported and most cases were in adults. Case fatality ratio was reported 18,9 %, and higher among older patients and among those with quite short incubation periods.[5] After earthquakes in Yogyakarta on May, 27th, 2006, 26 tetanus patients were reported.[6] In Siloam General Hospital, Lippo Karawaci, Tangerang, Indonesia, 30 cases of tetanus were recorded from 2012 – 2016.

Since majority of tetanus cases needed to be admitted to intensive care unit because of its effect to respiratory system and autonomic dysfunction,[2] it will spent so much money to take care of tetanus patients, especially in an outbreaks. In this case series report we review magnesium sulphate as an alternative drug to control muscle spasm and autonomic dysfunction with cheaper cost. We also give brief review about epidemiology, pathophysiology, clinical findings, diagnosis, and treatment of tetanus.

Case series :

Case 1

A 40 years old man with 60kg of body weight was brought to Siloam General Hospital Lippo Karawaci, Tangerang, Indonesia, with chief complain muscles spasm in entire body and had 1 episode of seizure at home. His left foot stepped on the rusty nail and was injured since 1 week ago. In admission the patient was conscious with Glasgow Coma Scale (GCS) was Eye (E) 4, Movement (M) 6, Verbal (V) 5, his mouth had 1 finger trismus (lockjaw), truncal rigidity (opisthotonus) was found. This patient was diagnosed as tetanus. In Emergency department, cross incision of the wound in his left foot was done and anti tetanus serum was given. This patient was admitted to intensive care unit and was given MgSO4 intravenous 2gram/hour to control spasm and autonomic dysfunction in this patient. Vital signs in admission were normal and no fever. Nasogastric tube and urine catheter were used. The empirical intravenous antibiotics given were Meropenem 1 gram 3 times daily and Levofloxacin 750mg 1 time daily. Calcium carbonate tablet 500mg was given 3 times daily through nasogastric tube to reduce the side effect of magnesium sulphate.
On day 4, we did debridement of the wound and also did tracheostomy and gave mechanical ventilation with Pressure Synchronized Intermittent Mechanical Ventilation mode to secure airway and ventilation to ensure adequate oxygenation because there was still generalized muscle spasm with pain, especially provoked by touch stimulus. We added morphine 1mg/hour and increase magnesium sulphate to 3 gram/hour. On day 5 we started to wean the mechanical ventilation and on day 7 the patient was able to breath adequately with tracheostomy mask only. On day 9, trismus reduced to 2 fingers, generalized muscle rigidity provoked by touch stimulus was greatly reduced, and opisthotonus disappeared. On day 14, trismus disappeared, but generalized muscle rigidity provoked by touch stimulus was still rarely happened. We decrease magnesium sulphate infusion to 1gram/hour. Antibiotics given were changed to cefoperazone sulbactam and amikacin from the result of sputum culture. On day 16, no muscle rigidity observed and the magnesium sulphate was stopped. Vital signs were stable when this patient minute. On day 13, muscle spasm was reduced significantly and Magnesium got magnesium sulphate infusion. We took blood Magnesium routinely and the blood magnesium ranged between 6.1 – 8.6 (N : 1.6 – 2.6). The patient moved to general ward on day 18. Tracheostomy was removed on day 22 and the patient discharged home on day 23.

Case 2

A 35 years old male with 66 kg of body weight was brought to Siloam General Hospital Lippo Karawaci, Tangerang, Indonesia, from other local private hospital with chief complain mouth, neck and waist stiffness since 2 days before admission. The patient was unable to eat and drink because he cannot open his mouth and also cannot swallow. He complained no fever, no headache, and no seizure. In previous local private hospital, the patient had been diagnosed as tetanus and had been given tetanus gammaglobulin intramuscularly and diazepam 5mg intravenously. The patient had a wound in his right foot because of a nail since 20 days ago. In admission, the patient's Glasgow Coma Scale (GCS) was E4 M6 V5 with 1 finger trismus, opisthotonus, and muscular spasm triggered by touch. Wound cross incision was done in Siloam General Hospital emergency room. This patient was admitted to intensive care unit. Magnesium sulphate infusion was given at 1 gram/hour combined with morphine 0.5 mg/hour and midazolam 0.25mg/hour. Vital signs was stable since admission with blood pressure 120 / 80, heart rate 90-100x / minute, temperature 36 – 37 ^{o} Celsius, respiratory rate 22x / minute and oxygen saturation 100% on oxygen 3 litters per minute. Meropenem 1 gram 3 times daily was given intravenously. Magnesium sulphate infusion was increased to 2gram/hour and then 4gram/hour on day 2 because of frequent periodic muscular spasm with pain. On day 3, there was respiratory depression. The patient was intubated and was given mechanical ventilation with Pressure Synchronized Intermittent Mechanical Ventilation mode. Magnesium Sulphate was continued at 4 gram/hour. On day 4, the patient got fever, increased heart rate, and blood pressure. Intravenous Levofloxacin 750mg once daily was added. Vital signs were stabilized on day 5. On day 7, tracheostomy and bad teeth extraction were done. The mechanical ventilation was weaned and was stopped at day 10 replaced by oxygen given through tracheostomy mask 6 litters / sulphate was given 3 gram / hour. On day 16, the patient was moved to high care unit

because no mechanical ventilation needed. On day 27, magnesium sulphate infusion was stopped. We took blood Magnesium routinely and the blood magnesium ranged between 1.5 – 11.2 (N : 1.6 – 2.6). The patient was moved to ward on day 32. Tracheostomy was removed on day 36, and the patient was discharged home on day 37.

Discussion

Epidemiology

Tetanus is still a major problem, especially in developing country. In developed country it is uncommon because of the good immunization coverage for tetanus.[4] Tetanus have caused approximately 1 million cases need to be hospitalized, and cause 400,000 deaths every year.[1] Another record inform that from 2002 there are 213,000 – 293,000 deaths caused by tetanus worldwide each year.[7]

In Indonesia, immunization programme for tetanus have been done since 1974 for pregnant women, infants and children. Surveillance data on tetanus in Indonesia showed that the incidence for tetanus of 0.2 per100,000 population annualy. In Hasan Sadikin Hopital, Bandung, from 1991 – 1995, there were 85 cases of tetanus in adults.[8] One month after tsunami in Aceh on December, 26th, 2004, there was an outbreak of tetanus. There were106 tetanus cases reported and most cases were in adults. Case fatality ratio was reported 18,9 %, and higher among older patients and among those with quite short incubation periods.[5] Other 26 cases of tetanus were reported in Yogyakarta after earthquakes on May, 27th, 2006.[6] In Siloam General Hospital, Lippo Karawaci, Tangerang, Indonesia, we have 30 cases of tetanus from 2012 – 2016.
Pathophysiology.

Clostridium tetani form spores that are able to live in soil and stools.[7, 9] *Clostridium tetani* spores enter the tissue through contaminated wound. In anaerobic condition they become bacilli.[7] tetanus bacilli produce two toxins : tetanospasmin and tetanolysin.[9] Tetanus is not transmitted from person to person.[10]

Tetanolysin damage the tissues surrounding the infection site.

Tetanospasmin cause the clinical syndrome of tetanus.[9] Tetanospasmin has 2 chain, heavy chain and light chain. Light chain acts at presynaptic site to prevent neurotransmitter release. Tetanospasmin binds to gangliosides on the membranes of local nerve terminals. Some toxin may enter the bloodstream and diffuses to nerve terminals in all of body parts. The tetanospasmin will be internalized and transported intra-axonally and retrogradely. Transport occurs in motor and autonomic nerves. Toxin can diffuse out and enter nearby neurons, spread to brainstem and midbrain. Tetanospasmin light chain will prevent neurotransmitter release, predominantly in inhibitory neurons, inhibiting release of glycine and gamma-aminobutyric acid (GABA). Interneuron inhibiting alpha motor neurons are first affected causes motor neurons lose inhibitory control. Effect on prejunctional of neuromuscular junction causes weakness between spasm.[9] Treatment with immune globulin is needed to binds free toxin, but it does not treat toxin that has entered within neurons.[7]

Uncontrolled efferent discharge with no inhibitory activities from motor neurons in spinal cord and brainstem cause muscular rigidity and spasm and mimic convulsion. Agonist and antagonist muscle groups contract simultaneously without inhibition reflex. Muscle spasm are very painfull. Autonomic discharge also have no inhibitory activity causes uncontrolled autonomic activities and sympathetic over activity. [9]

This neuronal binding is irreversible. It causes recovery need prolonged time duration. Recovery will be completed if the new nerve terminals grow.[9] It need approximately 4 – 6 weeks to be recovered from tetanus.[7]

Clinical findings.

Clinical findings can be presented as a triad of rigidity, muscle spasm, and autonomic dysfunction. Early symptoms are neck stiffness, sore throat, and trismus because of masseter spasm. Spasm of facial muscles causes typical facial expression called “risus sardonicus”.

Episodic muscles spasm cause convulsion – like appearance that can be spontaneous

or triggered by touch, visual, auditory, or emotional stimuli.[7,9] Continual spasm may lead to respiratory failure, strong spasm may cause fractures and tendon avulsions, pharyngeal and laryngeal spasms associated with aspiration and life threatening airway obstruction,[9] and truncal spasm made classical feature called opisthotonus.[7, 9] Muscle rigidity can cause rhabdomyolysis and resulted in renal failure.[7]

Sympathetic nervous system is badly affected. Increased sympathetic activity causes persistent tachycardia and hypertension, vasoconstriction and pyrexia. Basal catecholamine levels of plasma are raised. Severe hypertension and tachycardia, alternate with hypotension, bradycardia, or recurrent cardiac arrest are called “autonomic storms”. Profuse salivation, increased bronchial secretion, gastric stasis, ileus, diarrhoea and high output renal failure may be related to autonomic disturbances.[9]
Diagnosis.

Diagnosis of tetanus is clinical, based on history taking and typical physical findings of rigidity, spasms and trismus. Tetanus is lack of specific confirmatory laboratory tests. Differential diagnosis for tetanus are temporomandibular joint disease, alveolar abscess, cerebral malaria, encephalitis, subarachnoid haemorrhage, epilepsy, hypocalcaemia, drug induced movement disorder, stiff man syndrome, drug withdrawal, rabies, and strychnine poisoning.[7]

Philips, Dakar, and Udwadia are several grading systems for tetanus severity. The most widely used severity grading for tetanus is the system reported by Ablett. Ablett divide the grades of tetanus severity into 4 grades. The grades are : grade I (mild), grade II (moderate), grade III (severe), grade IV (very severe).[9]

Treatment

General measures, immunotherapy, antibiotic treatment, muscle spasm control, autonomic dysfunction control, airway/respiratory control, and adequate fluids and nutrition are treatment of tetanus recommended by WHO. General measures includes separated, shaded, and protected from stimulation ward/location designated for tetanus patients and debridement or clean up of the wounds.[10]

Immunotherapy includes administration of human Tetanus ImmunoGlobulin (TIG) 500 units intramuscularly or intravenously (depending on the preparation) and Tetanus Toxoid (TT) vaccine 0,5cc intramuscularly at separate site.

Tetanus disease does not induce immunity, so that patients without a history of primary TT vaccination should receive a second dose 1 – 2 months after first dose and also third dose 6 – 12 months later.[10]

Antibiotics recommended is metronidazole intravenously or orally 500mg every six hours and Penicillin G 100,000 – 200,000 IU /kg/day divided into 2 – 4 doses. Others antibiotics can be given are tetracyclines, macrolides, clindamycin, cephalosporins, and chloramphenicol.[10]

Benzodiazepines are preferred for controlling muscle spasm. Intravenous diazepam in increments of 5mg or lorazepam in increments of 2mg can be titrated until spasm control achieved in adults. In children, the doses are 0,1 – 0,2 mg/kg every 2 – 6 hours and can be titrated upward as needed. They can be given up to 600mg per day.[10]

Magnesium sulphate is an anticonvulsant and a vasodilator. Magnesium sulphate blocks pre-synaptic catecholamine release from nerves and adrenal medulla. It also reduces receptor responsiveness to released catecholamine. It antagonises calcium in the myocardium and neuromuscular junction and inhibits parathyroid hormone release. Hypotension and bradyarrhytmia may occur. Regular monitoring of serum magnesium and calcium levels were required.[9] Magnesium sulphate can be used alone or in combination with benzodiazepines to control muscle spasm and autonomic dysfunction. Loading dose can be given 5 gram or 75mg/kg intravenously and followed by maintenance dose 2 – 3 grams per hour until muscle spasm can be controlled adequately. Patellar reflex should be monitored and areflexia occur at the upper end of therapeutic range (4mmol/L). Other agents that can be used for controlling muscle spasm are baclofen, dantrolene, barbiturate (especially short acting), and chlorpromazine. [10]

Autonomic dysfunction can be controlled by magnesium sulphate or morphine. Beta blockers only esmalol is recommended, because the others can cause hypotension and sudden death.[10]

Airway or respiratory protections are needed if there is respiratory problem. Respiratory problem can be caused by the spasm or the drugs to control muscular spasm.[9, 10] Mechanical ventilation needed or if there is no mechanical ventilation available the patients must be monitored carefully and the medication doses adjusted in balance between spasm and autonomic dysfunction control and avoid respiratory failure. Early tracheostomy is preferred because endotracheal tube can provoke spasm.[10]

Fluid and nutrition should be given adequately, because spasm in tetanus produce high metabolic demands and a catabolic state. Nutritional support will enhance survival.[10]

Conclusions

According to WHO recommendation, treatment of tetanus consist of general measures, immunotherapy, antibiotic treatment, muscle spasm control, autonomic dysfunction control, airway/respiratory control, and adequate fluids and nutrition. Many drugs are available to control muscle spasm and autonomic dysfunction. WHO prefer benzodiazepine to control muscle spasm. Magnesium sulphate can also be used to control muscle spasm and autonomic dysfunction.

In developing countries, limited health budget makes healthcare practitioner should choose the cheapest medicine to achieve maximal results. The price of magnesium sulphate is lower than other drugs and optimal control of muscular spasm and autonomic dysfunction can be achieved safely.

Most of tetanus cases will need respiratory protection and control that can be given only in intensive care unit. For that reason, most of tetanus cases will be admitted to intensive care unit. Intensive care physicians should have enough knowledge about tetanus and how it should be managed adequately to ensure survival from tetanus.

References

1. Thwaites CL, Yen LM, Loan HT, Thuy TTD, Thwaites GE, Stepniewska K, et al. Magnesium sulphate for treatment of severe tetanus: a randomised controlled trial. The Lancet. 2006;368(9545):1436–1443.

2. Sutton DN, Tremlett MR, Woodcock TE, Nielsen MS. Management of autonomic dysfunction in severe tetanus: the use of magnesium sulphate and clonidine. Intensive Care Med. 1990;16(2):75–80.
3. Ahaduzzaman M. Updates on tetanus toxin: A fundamental approach. J Adv Vet Anim Res. 2015;2(1):23.

4. Amare A, Melkamu Y, Mekonnen D. Tetanus in adults: Clinical presentation, treatment and predictors of mortality in a tertiary hospital in Ethiopia. J Neurol Sci. 2012 Jun;317(1–2):62–5.

5. Aceh Epidemiology Group. Outbreak of tetanus cases following the tsunami in Aceh province, Indonesia. Glob Public Health. 2006 Jun;1(2):173–7.

6. Sutiono A, Qiantori A, Suwa H, Ohta T. Characteristic tetanus infection in disaster-affected areas: case study of the Yogyakarta earthquakes in Indonesia. BMC Res Notes. 2009;2(1):34.

7. Gibson K, Bonaventure Uwineza J, Kiviri W, Parlow J. Tetanus in developing countries: a case series and review. Can J Anesth Can Anesth. 2009 Apr;56(4):307–15.

8. Gunawan D. Tetanus in adults in Bandung, Indonesia. Neurol J Southeast Asia. 1996 ; 1 : 43 - 46.

9. Cook T.M., Protheroe R.T., Handel J.M. Tetanus : a review of the literature. British Journal of Anaesthesia. 2001; 87(3) : 477-87.

10. Organization WH, others. Current recommendations for treatment of tetanus during humanitarian emergencies: WHO technical note. 2010 [cited 2017 Jan 21]; Available from: http://apps.who.int/iris/handle/10665/70219

Treatment with High Dose Rifampicin in Tuberculous Meningitis: A Case Report

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Abstract

Introduction : Tuberculous meningitis continues to be associated with considerable mortality and morbidity. A randomized comparison of higher-dose intravenous rifampicin (approximately 13 mg/kg per day) versus a standard oral dose in adults with tuberculous meningitis showed that mortality among patients who received higher intravenous dose was 50% lower than those who received the standard dose.[1] While there are other contradictory results regarding the use of high-dose rifampicin in patients with tuberculous meningitis.

Method : We hereby report a case of a 20-year-old female patient presented with a history of fever, palpable neck lymph nodes and headache since 1 month before admission. Neurological examination revealed nuchal rigidity without other neurological deficits. Head MRI with contrast showed meningitis with tuberculoma in the right parietal lobe +/- 0.4 cm and neck ultrasonography showed multiple lymphadenopathy with 1 cm in diameter. Cerebrospinal fluid examination revealed tuberculous meningitis. The patient had been treated with rifampicin 450 mg, other tuberculosis regiments, levofloxacin, and dexamethasone. After one week of treatment, the patient developed generalized seizure and deterioration of consciousness. Imaging re-evaluation showed multiple acute infarction in the cortical and subcortical left frontal lobe, bilateral insula, bilateral temporal lobe, right parietal lobe to the corpus callosum, more prominent leptomeningeal contrast, and communicating hydrocephalus. Ventriculoperitoneal shunt was done. The patient was then treated with a higher dose of Rifampicin (15 mg/kg ~ 900 mg) and showed improvement after 2 weeks of treatment without any abnormal laboratory findings.

Conclusion : The usage of high dose rifampicin is still controversial. From this case we can conclude that by giving high dose rifampicin, the patient has a better outcome without any significant side effects. Thus, we support the hypothesis of using high-dose rifampicin in patients with tuberculous meningitis that does not respond to the standard treatment.

Introduction

Tuberculous meningitis (TBM) is one of the most common form of central nervous system infection with with a high frequency of neurologic sequelae and mortality if not treated promptly. TBM is typically a subacute disease with symptoms that may persist for weeks before diagnosis. One-third of the world's population is infected with latent TB.[1] These individuals are not clinically affected but carry a lifetime risk of 10% for developing active disease. There were an estimated 8.6 million incident cases of TB globally in 2012, with 1.3 million deaths. A total of 22 high-burden countries accounted for 81% of all estimated incident cases. TB is the leading cause of death in people living with HIV, accounting for approximately 1 in 5 deaths. The largest share of the global burden of TB is in the Southeast Asia, Western Pacific, and African regions.[2]

This report describes a case of a 20-year-old female with a diagnosis of tuberculous meningitis. Owing to the complexity of the case, the patient was treated with a higher dose of Rifampicin to reach a therapeutic amount without any known complications.

Case Report

A 20-year-old female presented with intermittent headache since 1 month before admission. Fever , frequent vomiting, and palpable lymph node were noticed 3 weeks ago. No other systemic features were present. Her past medical history was unremarkable. On neurological examination, the patient was conscious and alert with a GCS of 15. Nuchal rigidity was positive with cranial nerve functions were intact without any motor deficits. General examination found multiple immobile cervical nodules with +/- 1 cm in size. No other neurological deficits was found. Brain MRI with contrast showed meningitis and tuberculoma with a diameter of +/- 0.4 cm and neck ultrasonography revealed multiple lymphadenopathy of the neck with a diameter of +/- 1 cm, and colloid cyst of the right thyroid lobe. Laboratory investigations including full blood count, liver function, renal function, electrolytes, HIV and autoimmune were unremarkable except for positive IGRA spot TB, high CRP levels and ESR count of 65 mm/hours. Cerebrospinal fluid (CSF) examination revealed tuberculous meningitis (Figure 1). After diagnosis, the patient was then treated with Rifampicin 450 mg PO , Isoniazide 300 mg PO, Ethambutol 1000 mg PO, Pyrazinamide 1500 mg PO, Dexamethasone 5 mg IV, and Levofloxacin 750 mg IV.

Test	Result	Reference Range
Macroscopic		
Color	Colorless	Colorless
Clarity	Clear	Clear
Clot	Negative	Negative
Sediment	Negative	Negative
Microscopic		
Cell Count	509	< 10
PMN	3 %	
MN	97 %	
Random Blood Glucose	85 mg/dL	< 200 mg/dL
Chemicals		
Nonne	Positive	Negative
Pandy	Positive	Negative
Glucose	14 mg/dL	40 – 76 mg/dL
Protein (Quantitative)	1.92 g/dL	0.15 – 0.45 g/dL
Microbiology		
India ink direct smear	Cryptococcus (-)	
Bacteria gram stain	Negative	
Acid Fast Bacilli direct smear (ZN Stain)	Negative	

Figure 1. Cerebrospinal fluid results showing tuberculous meningitis

After one week of treatment, the patient developed generalized seizure with deterioration of consciousness. Upon physical examination, we found GCS score E3M5V2 with anisocoric pupil 3 mm/5mm and nuchal rigidity. Imaging re-evaluation with MRI contrast was done and showed more prominent leptomeningeal contrast and hydrocephalus. Chest X-Ray was performed and revealed no abnormalities. Ventriculoperitoneal shunt was performed for the hydrocephalus and the dose of Rifampicin was increased to 900 mg (15 mg/kg) per oral. After 2 weeks of treatment, the patient showed improvement with full consciousness and no headache. Laboratory evaluation after the higher dose was given showed no abnormalities.

Discussion

Patients with TBM develop typical symptoms and signs of meningitis including headache, fever, stiff neck, although meningeal signs may be absent in the early stages. The duration of symptoms before presentation ranges from several days to several months. Cranial nerve (CN) palsies, hemiparesis, paraparesis, and seizures are common and should raise the possibility of MTB as the etiology of meningitis.

Patients often present with multiple CN palsies, most commonly involving CN III, VI, and VII. Chest X-ray is suggestive of active or previous pulmonary TB in approximately 50% of cases.

Contrast-enhanced brain CT or MRI can help support a diagnosis of TBM because of the high frequency of abnormalities on initial presentation. The most common findings in descending order are meningeal enhancement, hydrocephalus, basal exudates, infarcts, and tuberculomas. Infarcts occur as a result of vasculitis affecting the vessels of the Circle of Willis, the perforating branches of the middle cerebral artery, and the vertebrobasilar circulation.[4] In the discussed study, the disease progressed from stage 2 to stage 3 TBM. The condition of the patient deteriorated significantly proving the progressiion of the disease. CSF examination is the mainstay in the diagnosis of tuberculous meningitis. CSF lymphocytosis, elevated proteins and reduction of CSF glucose by 40% than the concentration in blood serum suggest the diagnosis. CSF sample is still the best standard diagnostic tool in tuberculous meningitis. Treatment of MTB begins with a four drug regimen including isoniazid, rifampicin, pyrazinamide, and ethambutol which will be given for 2 months followed by rifampicin and isoniazid alone for about 6-9 months.

An Indonesian randomized controlled trial showed that oral administration of 750 mg and 900 mg rifampicin (17 and 20 mg/kg) daily resulted in geometric mean AUC $_{0\text{-}24}$ values in plasma that are approximately comparable with geometric mean exposure achieved after 600 mg (13 mg/kg) rifampicin IV during the first days of TBM treatment. Reversible liver function disturbance as reflected by increased plasma ALT values was common but was transient with continuation of treatment.[5] After given the standard regimen of TBM, the patient showed a progression of the disease with deterioration of consciousness which leads us to the increase dose of rifampicin with caution and repeated liver function test to evaluate the common side effects of rifampicin to the liver. Early diagnosis and commencement of specific therapy determines survival of the patient. Although the usage of high dose rifampicin is still controversial, this case showed that giving increase dose of rifampicin might decrease mortality rate and increase survival rate in patients with MTB without significant side effects.

References

1. Zumla A, Raviglione M, Hafner R, von Reyn CF. Current concepts: tuberculosis. N Engl J Med 2013;368:745–755

2. World Health Organization. Global tuberculosis report 2013. Available at: http://www.who.int/tb/publications/global_report/en/index.html. Accessed April 8,2018.

3. Ruslami R, Ganiem AR, Dian S, et al. Intensified regimen containing rifampicin and moxifloxacin for tuberculous meningitis: an open-label, randomised controlled phase 2 trial. Lancet Infect Dis 2013;13:27-35.

4. Chin JH. Tuberculous meningitis: Diagnostic and Therapeutic Challenges. Neurol Clin Pract. 2014 Jun; 4(3): 199-205.

5. Yunivita V, Dian S, Ganiem AR, Hayati E, Hanggono Achmad T, Purnama Dewi A, et al. Pharmacokinetics and safety/tolerability of higher oral and intravenous doses of rifampicin in adult tuberculous meningitis patients. Int J Antimicrob Agents. 2016 Oct; 48(4): 415-421.