KEMENTERIAN PENDIDIKAN, KEBUDAYAAN, RISET DAN TEKNOLOGI
UNIVERSITAS HASANUDDIN FAKULTAS KEDOKTERAN
KOMITE ETIK PENELITIAN UNIVERSITAS HASANUDDIN
RSPTN UNIVERSITAS HASANUDDIN
RSUP Dr. WAHIDIN SUDIROHUSODO MAKASSAR
Sekretariat : Lantai 2 Gedung Laboratorium Terpadu
JL.PERINTIS KEMERDEKAAN KAMPUS TAMALANREA KM.10 MAKASSAR 90245.
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REKOMENDASI PERSETUJUAN ETIK

Nomor : 426/UN4.6.4.5.31/ PP36/ 2017

Tanggal: 19 Juni 2017

Dengan ini Menyatakan bahwa Protokol dan Dokumen yang Berhubungan Dengan Protokol berikut ini telah mendapatkan Persetujuan Etik :

No Protokol	UH17050301	No Sponsor Protokol	
Peneliti Utama	**dr. Fitriah Handayani**	Sponsor	**Pribadi**
Judul Peneliti	Hubungan Hipersomnia pada Pasien Non Hemoragik Stroke dengan Luaran Klinis berdasarkan The National Institutes of Health Stroke Scale(NIHSS)		
No Versi Protokol	**2**	Tanggal Versi	**9 Juni 2017**
No Versi PSP	**2**	Tanggal Versi	**9 Juni 2017**
Tempat Penelitian	RSUP dr. Wahidin Sudirohusodo dan RS Jejaring di Makassar		
Jenis Review	☐ Exempted ☒ Expedited ☐ Fullboard Tanggal	Masa Berlaku **19 Juni 2017** sampai **19 Juni 2018**	Frekuensi review lanjutan
Ketua KEP Universitas Hasanuddin	Nama **Prof.Dr.dr. Suryani As'ad, M.Sc.,Sp.GK (K)**	Tanda tangan	
Sekretaris KEP Universitas Hasanuddin	Nama **dr. Agussalim Bukhari, M.Med.,Ph.D.,Sp.GK (K)**	Tanda tangan	

Kewajiban Peneliti Utama:

- Menyerahkan Amandemen Protokol untuk persetujuan sebelum di implementasikan
- Menyerahkan Laporan SAE ke Komisi Etik dalam 24 Jam dan dilengkapi dalam 7 hari dan Lapor SUSAR dalam 72 Jam setelah Peneliti Utama menerima laporan
- Menyerahkan Laporan Kemajuan (progress report) setiap 6 bulan untuk penelitian resiko tinggi dan setiap setahun untuk penelitian resiko rendah
- Menyerahkan laporan akhir setelah Penelitian berakhir
- Melaporkan penyimpangan dari prokol yang disetujui (protocol deviation / violation)
- Mematuhi semua peraturan yang ditentukan

IJIRR

International Journal of Information Research and Review
Vol. 05, Issue, 05, pp.5511-5513, May, 2018

REVIEW ARTICLE

CLINICAL OUTCOMES OF THE ISCHEMIC STROKE PATIENTS WITH HYPERSOMNIA

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ARTICLE INFO

Article History:

Received 27th February, 2018
Received in revised form
20th March, 2018
Accepted 18th April, 2018
Published online 30th May, 2018

Keywords:

Ischemic stroke,
Hypersomnia,
NIHSS,
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Design: observational analytic study with longitudinal cohort approach
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Procedure:72 subjects diagnosed with ischemic stroke, divided into two groups by using Sleep Diary Test. One group with hypersomnia while other without hypersomnia.
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RESULTS AND DISCUSSION

Participants demographic: This study included 72 subjects (30 males/42 females), consisted of 28 subjects acute ischemic stroke patient with hypersomnia and 44 subject without hypersomnia. Mean age recorded 53.68 ± 7,089 years with the age range from 43 to 66 years. Median score of NIHSS 1st day assessed showed total of 19 sore equal between ischemic stroke patients with hypersomnia and without hypersomnia group. While median NIHSS score for last day (7th day hospitalization) showed hypersomnia group 16.5 and without hypersomnia 15.5. Ischemic stroke patients with hypersomnia group showed bigger median score of NIHSS, that indicated heavier strokes degrees and worse clinical outcomes. The research obtained mean rank of ΔNIHSS score (1st and 7th daycare) were 47.88 (hypersomnia) vs 29.26 (non hypersomnia) with p value= 0.000 (Mann-Whitney Test). It was also showed significant difference between those 2 groups. Table 1 showed the change of NIHSS score of ischemic stroke patient, mean rank were 45.93 (hypersomnia) vs 30.50 (non hypersomnia)p = 0.002 ((Mann-Whitney Test). It showed that ischemic stroke patients with hypersomnia group had worse clinical outcomes. Normally, a person sleeps through 4 to 6 sleep cycles, alternating between REM and non-REM (Mayo Clinics, 2016). Increased sleep duration on hypersomnia (over 10 hours per day) would improve both REM and non-REM sleep. Petit *et al.* (2015) found that REM sleep had metabolic consequences such as increasing metabolic rate and higher utilization of glucose during sleep. Using too much glucose accompanied with increasing metabolism rate induce lack of glucose that required for body / brain cells on healing process (Petit *et al.,* 2015).

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Non Hypersomnia	44	30.50	0.002

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Based on table 2 below, it showed group of ischemic stroke patients with hypersomnia where infarct located in basal ganglia, based statistic measure significantly had worse clinical outcomes (p=0.026, Mann-Whitney Test). The mean rank were 21.95 (hypersomnia) vs 8.00 (non hypersomnia).Such conditions may be explained by Geraschenko D *et al.* (2006), Qiu *et al.* (2010), and Vetrivelan R *et al.* (2010). Lesions in Caudate Putamen (CPu), Nucleus accumbens (NAc), and external ganglia basalis (GPe) in mice showed increasing of NREM and NREM stage sleep waves in the cortex electroencephalogram (EEG). This mechanism is related to GABA affecting the inferior GPe which inhibits the pramidal cells, which in turn promotes sleep and increasing number of

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Table 2. Relationship between infarct lesion and NIHSS score changes in ischemic stroke patients

Lesion	n	Mean rank NIHSS change	p value
Thalamus			
Hypersomnia	8	7.50	1.00
Non Hypersomnia	6	7.50	
Internal capsule			
Hypersomnia	6	19.08	0.45
Non Hypersomnia	26	15.90	
Basal ganglia			
Hypersomnia	5	15.60	0.009
NonHypersomnia	9	8.00	
Broad lesions (≥ 2lobes)			
Hypersomnia	9	6.89	0.51
Non Hypersomnia	3	5.33	

Table 3. Relationship between hemisphere location of infarctand NIHSS score changes in ischemic stroke patients

Lesion	n	Mean rank NIHSS change	p value
Left hemisphere			
Hypersomnia	10	21.95	0.026
NonHypersomnia	22	14.02	
Right hemisphere			
Hypersomnia	18	24.42	0.055
NonHypersomnia	22	17.30	

The occurrence of insomnia under these conditions is due to the influence of the thalamus, and the brainstem, especially the thalamoencephalic region of the pontomesencephalic region, and / or the pontine tegmentum which causes reversal of the sleep and waking cycle of the night (Fere *et al.,* 2013). The insomnia incidence is approximately 18.1% of ischemic stroke patients (Leppavuori *et al.,* 2012).In line with Penazola *et al.* (1964), Stermandan Clemente (1962) found experimentally that the rat cortex area is very influential on sleep stimulation. Villablanca and Marcus (1972) found neocortical lesions and striatum associated with insomnia. Different theory suggested by Vock *et al.* (2002), they subscribe mild hemispheric stroke lesions are consistent with the onset of insomnia, not based on differences in left or right hemisphere lesions (Vock *et al.* 2012).But in our study, we did not observed the lesion size.

Conclusion

This study implies that short-term clinical outcome of ischemic stroke patients with hypersomnia is worse than ischemic stroke patients without hypersomnia based on NIHSS score changes. Also patient with left hemisphere lession or with basal ganglia lession implies worse outcome.

Recommendation: Active screening and particular attention for hypersomnia condition after ischemic stroke are important, especially patients with left hemisphere lesions and / or with basal ganglia lesions. As hypersomnia (over 10 hours per day) associated with worse short-term clinical outcomes in ischemic stroke patients.

Acknowledgement: The author wish to thank the Head of Dr. Wahidhin Sudirohusodo General Hospital and Principal for providing the infrastructure facilities in Neurology Department Medical Faculty of Hasanuddin University, Indonesia.

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Andi_Kurnia_Bintang_Hypersomnia.pdf

by Andi Kurnia Bintang

FILE	ANDI_KURNIA_BINTANG_HYPERSOMNIA.PDF (220.17K)		
TIME SUBMITTED	27-JUL-2019 10:46PM (UTC+0700)	WORD COUNT	2725
SUBMISSION ID	1155393884	CHARACTER COUNT	15456

IJIRR
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ARTICLE INFO

Article History:

Received 27th February, 2018
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Internal capsule			
Hypersomnia	6	19.08	0.45
Non Hypersomnia	26	15.90	
Basal ganglia			
Hypersomnia	5	15.60	0.009
NonHypersomnia	9	8.00	
Broad lesions (≥ 2lobes)			
Hypersomnia	9	6.89	0.51
Non Hypersomnia	3	5.33	

Table 3. Relationship between hemisphere location of infarctand NIHSS score changes in ischemic stroke patients

Lesion	n	Mean rank NIHSS change	p value
Left hemisphere			
Hypersomnia	10	21.95	0.026
NonHypersomnia	22	14.02	
Right hemisphere			
Hypersomnia	18	24.42	0.055
NonHypersomnia	22	17.30	

The occurrence of insomnia under these conditions is due to the influence of the thalamus, and the brainstem, especially the thalamoencephalic region of the pontomesencephalic region, and / or the pontine tegmentum which causes reversal of the sleep and waking cycle of the night (Fere *et al.,* 2013). The insomnia incidence is approximately 18.1% of ischemic stroke patients (Leppavuori *et al.,* 2012).In line with Penazola *et al.* (1964), Stermandan Clemente (1962) found experimentally that the rat cortex area is very influential on sleep stimulation. Villablanca and Marcus (1972) found neocortical lesions and striatum associated with insomnia. Different theory suggested by Vock *et al.* (2002), they subscribe mild hemispheric stroke lesions are consistent with the onset of insomnia, not based on differences in left or right hemisphere lesions (Vock *et al.* 2012).But in our study, we did not observed the lesion size.

Conclusion

This study implies that short-term clinical outcome of ischemic stroke patients with hypersomnia is worse than ischemic stroke patients without hypersomnia based on NIHSS score changes. Also patient with left hemisphere lession or with basal ganglia lession implies worse outcome.

Recommendation: Active screening and particular attention for hypersomnia condition after ischemic stroke are important, especially patients with left hemisphere lesions and / or with basal ganglia lesions. As hypersomnia (over 10 hours per day) associated with worse short-term clinical outcomes in ischemic stroke patients.

Acknowledgement: The author wish to thank the Head of Dr. Wahidhin Sudirohusodo General Hospital and Principal for providing the infrastructure facilities in Neurology Department Medical Faculty of Hasanuddin University, Indonesia.

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