

Hypnotherapy Increasing Standard Therapy Responses in Psychogenic Asthma Patient

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ABSTRACT

Asthma has negative effects in patient's Quality of Life. Usually, asthma treatment is only depending on pharmacotherapy, but it is not easy to achieve controlled asthma stage. This study aims to evaluate the effectivity of hypnotherapy to increasing asthma control level with asthma standard therapy in both of uncontrolled or partial controlled psychogenic asthma patient. We observe 60 psychogenic asthma that divided into group A and group B. First, we evaluate asthma control levels for both of groups, then for group A, we give standard therapy and six sessions of hypnotherapy (for 6 weeks) continuing with reevaluation of asthma control level. Moreover, after 6 weeks we reevaluate asthma control level again. For group B, 6 weeks after the first evaluation, we reevaluate asthma control levels and continue to give standard therapy and six sessions of hypnotherapy (for 6 weeks) then evaluate asthma control level again. To evaluate variation of asthma control level variables, we use *Friedman statistic test*, then continue to *Marginal Homogeneity statistic test*. We found the higher asthma control level for both of groups after hypnotherapy that statistically significance. Group A (A1 vs A2; $p=0,001$) and group B (B2 vs B3; $p=0,004$). We found that age ($p=0,006$), smoking history ($p=0,02$), *BMI* ($p=0,026$), allergen triggers ($p=0,027$) is statistically significance influence asthma control level in this study where all of them have p value $< 0,05$. Hypnotherapy statistically significance to increasing asthma standard therapy response in psychogenic asthma patient.

Keywords: psychogenic asthma, hypnotherapy, and asthma control level.

INTRODUCTION

Asthma Bronchial is chronic airways inflammation. It is started by inflammation from hyper-responsive airways that leading to airways obstructions¹. Bronchial asthma is developed from unbalancing between *T-helper1 (Th1)* and *T-helper2 (Th2)* expressions, that signs by accumulations and also activation of inflammation cells, like *Mast Cell*, *Eosinophil*, and *Neutrophils* in bronchus and airways lumens. Inflammation cells activity regulated by humoral immunity like *interleukin-4 (IL-4)*, *IL-5*, *IL-9*, *IL-13*, *immunoglobulin E (IgE)* and also *IL-17*. *Lymphocyte*, *Th-17*, and also *Neutrophils* play roles in non-atypic asthma and also steroid resistant asthma^{1,2}. Asthma has bad effect to patient's Quality of Life. Recent asthma therapy is only depending in pharmacotherapy, but for a long time, it will raise side effect and also psychological stress. Psychological stress including social stress is predisposition factor that worsening both atypic and also non-atypic asthma patient conditions. Sympathics Nerve System Neuroendocrine activations through cortisol and catecholamine secretions, play roles

in the immune system by reserving the balance of *Th2* through supporting its responses. Increasing of endogen cortisol may give an advantage for the allergic disease because cortisol is very effective in allergy therapy, but there is still an opportunity of corticosteroid resistant caused by chronic stress³. Both of long physical and also psychological stress in asthma patient lead to activating *hypothalamic-pituitary-adrenocortical (HPA)* axis and also *sympathetic-adrenal-medullary (SAM)* axis that activate secretions of cortisol, adrenalin (epinephrine), and noradrenaline (norepinephrine) that decreasing immune protection functions and also increasing of *Th2*^{3,4}. Hypnosis has been applying clinically to treat many diseases that have no response to medical therapy, including in asthma patient, but clinical hypnosis applying as standard therapy of asthma still not be developed well⁵. Recently, there is no study that clearly describing the hypnotherapy mechanism to treat asthma. Brown studies have found that hypnosis have good efficacy in emotional stress controlling that cause obstructive airways exacerbation and also can stabilize

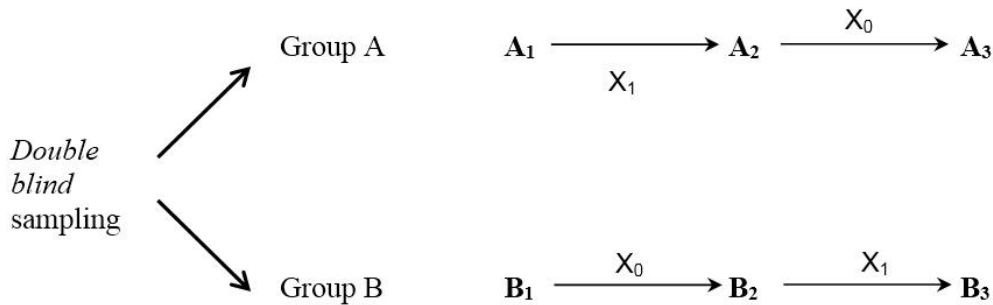


Figure 1: Crossover study design. Note: O = observation (Clinical Measurement), X₀ = without hypnotherapy, X₁ = hypnotherapy for 6 sessions.

Table 1. Description characteristic of asthma.

S. No	Characteristic	Controlled	Partly Controlled	Uncontrolled
1.	Daytime symptoms	None (twice or less/week)	More than twice/week	Three or more features of partly controlled asthma
2.	Limitations of activities	None	Any	
3.	Nocturnal symptoms/awakening	None	Any	
4.	Need for reliever/rescue treatment	None (twice or less/week)	More than twice/week	
5.	Lung function (PEF or FEV1	Normal	<80% predicted or personal best (if known)	

hiper-responsive airway in many asthma patients. Freeman and Welton' study found impairment of asthma status after *imagery hypnosis* therapy, although this study still not formally recommended in asthma therapy^{6,7}. This study aims is to know hypnotherapy effectiveness to increasing asthma control level patients both in controlled and also partial controlled psychogenic asthma patients.

MATERIAL AND METHODS

Our study design is experimental randomized control trial crossover group. We use double-blind sampling method to choose control and treatment groups (Figure 1). This Study started in September 2014 until May 2015 in Pulmonology Division Sebelas Maret University / Dr Moewardi Hospital Surakarta. Subjects are non-atypic psychogenic asthma patients that completed full inclusion criteria, that are: (a) Control and uncontrolled asthma patient⁸; (b) more than 18 years old; (c) willing to follow studies procedures and agreed to sign informed consent; (d) last formal education is more than Junior High School; (e) well understand Indonesians language; (f) not smoking; (g) not including in *asthma-COPD overlap syndrome (ACOS)* criteria. Exclusion criteria are (a) Severe psychological stress disorders with measurement by clinical interview; (b) Severe physical disorders; (c) severe hearing disorders that disturb verbal communications. Hypnotherapy described as unconsciousness induction that followed by some suggestions that can change general observations in conscious subjective minds (including the change of sensations, perceptions, emotions, minds, and also behaviors). We use short hypnotherapy procedures for 6 sessions with sensory imagery hypnotherapy methods. Psychogenic asthma described as asthma that initiated by

psychological stress factors. Peak Expiratory Flow (PEV) is measured by peak expiratory flow meter (PEF meter) devices. Descriptions of controlled asthma, partial controlled asthma, and uncontrolled asthma⁸, through over 4 weeks. Assessment of current clinical control which criteria are (Table 1): We use *sensory imagery* hypnotherapy methods for this study. Hypnotherapy application to controlling asthma use 3 important target areas, there are : (1) Anxiety component : patients lead to hypnotic state and ask to their imaginations to initiate full relaxations phase; (2) Conditional response to predisposition factors that lead to asthma exacerbations: Patients down to hypnotic state and use pleasant suggestions to create nice response to specific conditions; (3) Physiological response to predisposition factor to initiate asthma exacerbations: patient guided to deeper hypnotic state and focus on suggestions that change breathing activity that can initiate asthma exacerbation, it is useful to re-frame all things that can trigger asthma exacerbation to normal things for patient^{6,9}. To analyze asthma level variable differences that more than 2 categories pairing data (uncontrol, partly control, and full control) with more than two repetitions (before treatment, pre-crossover, and post-crossover) we use *Friedman* statistic test, continue to Marginal Homogeneity test. To compare asthma control characteristic variables, we use Cochran test, then continue to McNemar test. To analyze external variables that may influence hypnotherapy result, we perform multivariate analysis Ordinal Regression and also Logistic Regression test. All the result is significant if p-value < 0,05.

RESULT

Total subjects for this study are 30 psychogenic asthma

Table 2: Subject characteristic in asthma patients.

Characteristic	Group A (n= 15)		Group B (n=15)		p-value
	Means	SD	Means	SD	
Old	56,9	14,3	40,4	12,4	0,002*
BMI (kg/m ²)	25,10	5,83	23,83	3,37	0,475*
	n	%	n	%	
Sex					0,123**
Male	3	20,0	7	46,7	
Female	12	80,0	8	53,3	
Asthma Level					0,311**
Controlled asthma	0	0,0	2	13,3	
Partial Controlled asthma	7	46,7	5	33,4	
Uncontrolled asthma	8	53,3	8	53,3	
Daytime symptoms >twice /week					0,759**
Existed	14	93,3	14	93,3	
None	1	6,7	1	6,7	
Nocturnal symptoms/awakening					0,645**
Existed	9	60	9	60	
None	6	40	6	40	
Need for reliever/rescue treatments >twice/week					0,659**
Existed	11	73,3	11	73,3	
None	4	26,7	4	26,7	
Limitations of activities					0,650**
Existed	5	33,3	5	33,3	
None	10	66,7	10	66,7	
Lung function (PEF or FEV1)	67,05	19,05	69,42	17,75	0,727*
	n	%	n	%	
Smoking History					0,500**
Smoking	4	26,7	3	20,0	
Not Smoking	11	73,3	12	80,0	
Family Asthma History					0,195**
Existed	13	86,7	10	66,7	
None	2	13,3	5	33,3	
Allergen Triggers					0,674**
Existed	12	80,0	12	80,0	
None	3	20,0	3	20,0	
Weather Triggers					0,225**
Existed	7	46,7	4	26,7	
None	8	53,3	11	73,3	
Activity triggers					0,500**
Existed	4	26,7	3	20,0	
None	11	73,3	12	80,0	

Note: *Independent-samples T-test; **Chi-square test

patients. Subjects randomly divided to 2 groups, groups A and groups B. Subjects characteristics between group A and group B statistically similar, where is p value > 0,05 for sex (20% male vs 46,7% male; p= 0,123), BMI (25,10±5,83 kg/m² vs 23,83±3,37 kg/m²; p = 0,475), smoking history (26,7% vs 20,0%; p= 0,500), family asthma history (86,7% vs 66,7%; p= 0,195), allergen triggers (80,0% vs 80,0%; p= 0,674), weather triggers (46,7% vs 26,7%; p= 0,225) and also physical activity triggers (26,7% vs 20,0%; p= 0,500) (Table 2). We found higher asthma control level in both of groups after hypnotherapy sessions compare to before hypnotherapy given. It is statistically significance for both of groups that p-value is less than 0,05. For group A (A1 vs A2), we found p=0,001 (p<0,05). For group B (B2 vs B3), we

found p=0,004 (p<0,05), so the higher asthma control level after hypnotherapy in both of groups is statistically significance. To analyze external variables that may influence the result, we perform multivariate analysis. After we adjust all external variables, that are age, sex, Body mass index (BMI), education level, family asthma history, stress trigger, allergens trigger, weather trigger, occupation trigger, activity trigger, the result is asthma control level still higher in both of groups after hypnotherapy sessions compare to before hypnotherapy given, and It is statistically significance for both of groups that p-value is less than 0,05. From multivariate analysis we found that age (p = 0,006), smoking history (p = 0,02), BMI (p = 0,026), allergen triggers (p = 0,027) is statistically significance influence asthma control level

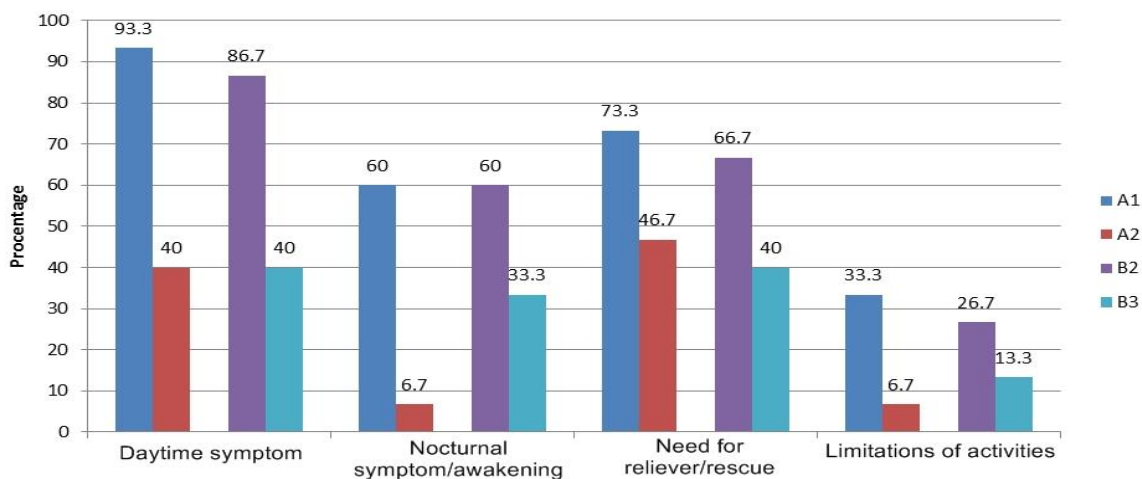


Figure 2: Asthma clinical control characteristics.

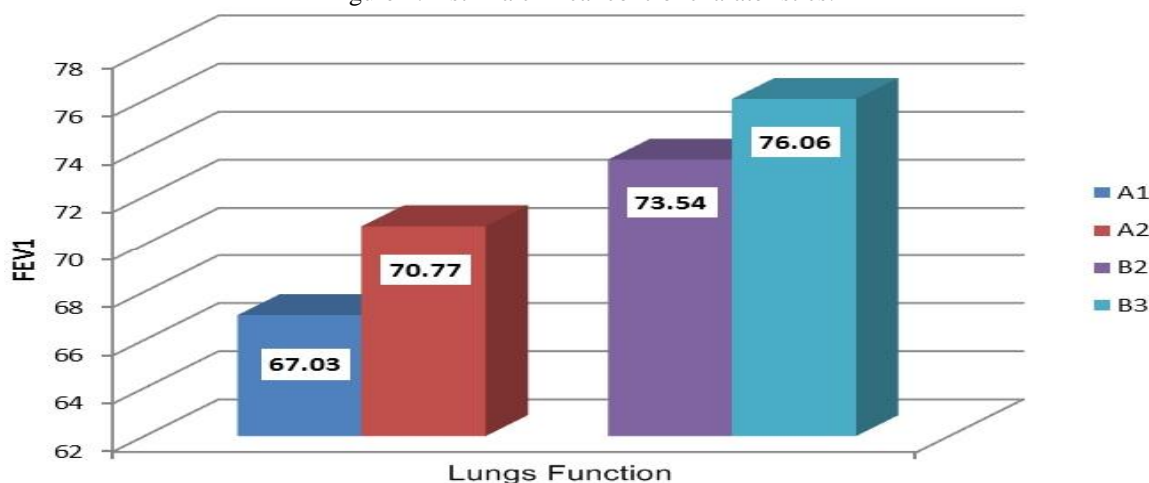


Figure 3: FEV1 result for both of groups

in this study where all of them have p -value $< 0,05$. Figure 2 shows that hypnotherapy increasing asthma clinical control in both of groups (A1 vs A2) and also (B2 vs B3) and statistical significance where are $p < 0,005$ for all. FEV1 result shows that hypnotherapy also increasing lungs function significantly where is $p < 0,05$ (Figure 3). Clinical asthma assessment result in group A and group B show that hypnotherapy is have been proven to increasing asthma standard therapy response in a psychogenic asthma patient⁸. This study found that pharmacotherapy alone without hypnotherapy is not significance in increasing asthma control level. Psychosocial stress is one of predisposition factors for asthma, and the mechanism is through multidimensional systems like endocrine, neural, immunity and behavioral systems. Emotional factors like stress can bother physiology pathways like airways autonomy control systems, endocrines systems, and also immunity systems that initiate asthma exacerbations⁹. Psychosocial stress change inflammation response that increasing Th-2 lymphocyte that appropriates to asthma characteristics. Hypnotherapy makes patient down to hypnotize that it can slow down allergy response (3,7), and also bronchus inflammation process in asthma⁶. Hypnotherapy will affect *non-adrenergic* and *non-cholinergic* nerve systems in airway

smooth muscle that leads to bronchodilatation in long periods¹⁰. Norepinephrine is primary catecholamine that released by sympathetic nervous systems that have meaningful influences in lymphocytes, including *T-cell*, *B-cell*, and also *Natural Killer Cell (NK-Cell)*, that play roles in asthma pathogenesis. Norepinephrine bonded by an adrenergic receptor that expressed in all immune cell. *Beta-2 adrenergic receptors* that expressed by primer receptors in *T-cell* and also *B-cell* through *Norepinephrine* have directly effect to modulate cellular activity¹¹, this signal is one of nerve systems ways to regulating immunity systems¹². *Norepinephrine* can generate both of stimulating effects and also step down effects in an immune cell, depends on immune cell type, cell activity status, the long to exposure, and also the dose. *Beta-2 adrenergic receptors* expressed by *Th-1 cells*, but it is not expressed by *Th-2 cells* (11). Increasing of *Norepinephrine* level in both of group (group A and B) after hypnotherapy showing that our body trying to response *Th-2 cells* dominations in asthma pathogenesis to *homeostatic* condition, re-balancing *Th-1/Th-2* through *TH-2* cells modulations. Our study is parallel with Zhu et al¹³ which found that *Th-1* and *Th-2 cells* are activated to be balanced in peripheral blood circulation. *Th-1 cell* modulation will increase and secretion of IFN- γ . IFN- γ

will increasing *Th-1 cell* proliferation and initiate *IgG2a* production through *B cell*. The balancing of *IL-4* and *IFN- γ* play a role in regulated *IgE* synthesis in asthma patients. *IFN- γ* can inhibit *Th2 cells* proliferation, induced eosinophil apoptosis, and also increasing mucous cell apoptosis¹⁴. Asthma immune response is a complex process that started by *Th-2 cells* following by proliferations of they, cytokines productions and raising of *memory cells*. The pathological response that produced such as lung eosinophil inflammation, airways smooth muscle contractions, and mucous production increment, that all of it lead to airways obstructions and lungs damage. Many experimental and clinical study support the theory of *Th-2 cells* that play roles to a specific allergen in asthma pathological response that leads to airways hyperreactivity^{2,15}. Otherwise, cytokines that secreted by other cells like *Th1*, *Th17* and *Tregs* may suppress *Th-2 cells*². *Th-1 cells* play a role in decreasing airways hyperreactivity, so to controlling asthma, it must focus on balancing of *Th-1* and *Th-2 cells*¹⁵. In our study, we also treat all patients with asthma standard therapy including corticosteroid and also xanthine, which have bronchodilator effect and anti-inflammation¹⁶. Theophylline mechanism in anti-inflammation is through activating histone deacetylases (HDAC) that lead to suppressing inflammation transcriptions genes. Steroid reduces histone deacetylases (HDAC) directly that will slow down the activation of inflammation transcriptions genes¹⁷. Overall, hypnotherapy increasing psychogenic asthma standard therapy responses such as impairment in daily symptoms, natural awakening, reliever requirement, and also lungs function (*PEV* and also *FEV-1*).

CONCLUSION

Hypnotherapy effective to increasing response of asthma standard therapy in psychogenic asthma patients.

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