ISSN: 0975 -8542

Journal of Global Pharma Technology

Available Online at: www.jgpt.co.in

RESEARCH ARTICLE

Effect of Topical *Laportea Decumana* Leaves Extract on Labor Pain and Cortisol Level in the First Active Phase of Inpartu Condition

Sisma HL[1*], Ariawan Soejoenoes[2], Trilaksana Nugroho[3], Soeharyo Hadisaputro[4], Neni Susilaningsih[5], Syarif Taufik Hidayat[6], Melyana Nurul Widyawati[7]

[1]*Doctoral Program of Medical/Health Science, Faculty of Medicine, Diponegoro University Semarang, Indonesia.*

[2]*Department of Obstetric and Gynecology, Faculty of Medicine, Diponegoro University,Semarang, Indonesia.*

[3]*Division of Pharmacology & Therapeutic, Faculty of Medicine, Diponegoro University, Semarang, Indonesia.*

[4]*Faculty of Medicine Diponegoro University, Indonesia.*

[5] *Departement Anatomy-Histology, Faculty of Medicine Diponegoro University, Indonesia.*

[6] *Department of Obstetric and Gynecology, Faculty of Medicine, Diponegoro University,Semarang, Indonesia.*

[7] *Poltekkes Kemenkes Semarang*

***Corresponding Author: Sisma HL**

Abstract

This research aims to obtain the effect of *L. Decumana* extract toward labor pain and cortisol level in the first active phase of inpartu condition. This research used True Experimental with pre post test control group on the first active phase in inpartu condition. This research was combining pharmacology and non-pharmacology method. In choosing the research's subject, consecutive sampling and randomization were applied to divide the subject into four groups. To measure the pain level, Visual Analog Scale (VAS), and saliva liquid was applied to measure the level of cortisol. The smallest average of pain level before the treatment was KS+V group (6, 40) and the highest was LD+KS group (7, 70). After the treatment, the smallest level was in LD+KS (5, 60) group and the highest is in the SP+V group (7, 00). It meant that there was reduction in the pain level before and after treatment. *L. Decumana* as the medical medicine can be used as reducing the first active phase of labor pain in inpartu condition. However, the further research is needed to prove the effect of biomarker *L. Decumana* to initiate labor.

Keywords: *Cortisol, Laportea Decumana, Labor pain level, Medicinal plants, Inpartu condition.*

Introduction

The pain occurred along the birth process is physiological, complex, subjective, and multidimensional responses with the sensory stimulation, mainly produced by uterine contractions [1]. The pain will impact the psychological state of the mother, and also impact on the health of uterus [2].However, culture is also involving the way peoples cope with pain [3].Dehchesmes reports that 96% of women are experiencing labor pain, and 73% of them are using at least one therapy to reduce it [4]. Another researches dealing with labor pain shows that women are experiencing different levels of pain including are mild pain 15%, moderate pain 35%, severe pain 30% and worst pain 20% [5].

Due to the pain in birth process, the pregnant mother tend to avoid normal birth and choose to perform C-Section surgery [6]. Nevertheless, C-section without indication always increasing as related to the survey of Iran health demography which reported that

C-section without medical indication is happened about 35% [7]. The uncoordinated labor pain can cause adequate uterus contraction, thus will lead into uncorrected uterine inertia, labour dystocia, and hypoxia [8, 9]. The previous studies dealing with the labor pain is found that the cortisol level is increasing along the birth process [8, 10].

Afterward, the research conduct by Carpenter is found that there is relation between cortisol respond with the increasing of IL-6 in stressful condition. Cytokine IL-6 is an integral part of innate inflammatory response toward physical stress (infection and inflammation). Besides, psychosocial stress is initiated cytokine response as clinical consequent of stress [11]. It should be known that the principal of labor pain prevention is safe, simple and do not give impact on the mother and its uterus.

There are some method to manage the labor pain including pharmacology and non-pharmacology method [12].Non-pharmacology method helping to reduce the pain is known as complementary and alternative therapies. This technique is used to change the interaction between mind-body and affective component in pain perception. *L. Decumana* is a kind of herbaceous plants comes from *Urticaceae* family and contains of Acetamida/Acetaminophen (N-(4-Hydroxyphenyl) [13].

It has been beneficially used by Maluku, Papua, and Papua New Guinea peoples to treat any medical cases such as pain, stiff, headache, muscle ache, stomachache and others by rubbing on the sick body parts [14, 15].Acetamida/Acetaminophen (N-(4-Hydroxyphenyl) is a derivative p-aminofenol which has antipyretic/analgesic that can inhibit Cyclooxygenase in the central nerve [16, 17].The pain reduction using *L. Decumana* has been used from generation to generation and proven to be safe and efficacy. In addition, there are no reports of adverse effects using these plants [13, 18, 19].

The used of *L. Decumana* in reducing pain is not complemented with the science evidence, thus a research need to be conducted to provide additional evidence about its safety and beneficial. Due to the reason, this research is conducted by analyzing the effect of *L. Decumana* analgesic extract toward labor pain and cortisol level. In addition, this research has wider scope and the results will not limit in the maternal mother. But, it can be developed as a product in a form of gel/cream, so that the beneficial can be applied by societies in reducing the pain through *L. Decumana* cultivation.

Method

The scope of this research is obstetric field which specifically discuss the reproduction system dealing with labor pain. It has been approved by Health Research Ethics Commission of the Faculty of Medicine, Diponegoro University number 514/EC/FK-RSDK/VII/2018 and research recommendation from Political and National Unity Board of Mimika Regency number 070/368/209.4/2018.

This research is including into True Experimental with pretest-posttest control group design. True Experimental is usually known s Randomized Control Trial (RCT). Campbell & Stanley explain that the test unit in this type is allocated randomly to the experimental and control group. The two groups are measured before and after the experiment performed in the research [20]. This research is conducted in the Mitra Masyarakat Hospital in the first active phase of inpartu condition.

This form of research provides treatment to reduce labor pain by pharmacology and non-pharmacy methods. The research's subject is chosen by consecutive sampling by dividing the respondents into four groups, namely:

- Group I: 5 grams *L. decumana* and suppositoria placebo.
- Group II: 5 grams *L. decumana* and 2 grams kaltofren suppositoria
- Group III: 2 gram kaltofren suppositoria and vaselin
- Group IV: Vaseline and suppositoria placebo

The making of 5 grams of Vaseline and *L. Decumana* extract is conducted in Integrated Research and Testing Laboratory (LPPT), and suppositoria placebo is made from PG600 and conducted in Gadjah Mada University's pharmaceutical laboratory. *L. Decumana* is

given sedation acupressure technique in the SP6, SP8 and SP point. The minimum sample in each group is 10 mothers, thus the total sample from 4 groups are 40 mothers in inpartu condition.

The measurement is performed twice, before and after the treatment. The level of labor pain is measured using Visual Analog Scale (VAS), and the cortisol level is measured using saliva liquid in GAKI (Iodine Deficiency Disorder) Laboratory of Diponegoro National Hospital.

Results

Respondent Characteristics

L. Decumana as medical plants has been used from generation to generation and there are no adverse effect reported. The research subjects are involving 40 mothers in the first active phase of inpartu condition. It is performed 80 times for pain level reducing measurement using VAS and 80 times measurement of cortisol level using saliva liquid. The Table 1 below shows the respondent characteristics analysis based on the treatment group.

Table 1: Respondent Characteristics

Respondent Characteristics	LD+SP	LD+KS	KS+V	SP+V	P value
	n (%)	n (%)	n (%)	n (%)	
Age	26,10 ±4,84	23,40 ±7,76	25,30 ±8,06	SP+V	0,815 [b]
p-value (normality)	0,432	0,131	0,347	0,265	
Race					
a. Indigenous Peoples of Papua	7 (70,7)	6 (60,0)	7 (70,0)	10 (100,0)	0,187[a]
b. Non Indigenous Peoples of Papua	3 (30,0)	4 (40,0)	3 (30,0)	0 (0,0)	
Education					
a. Not graduated from school	3 (30,0)	2 (20,0)	3 (30,0)	5 (50,0)	0,444[a]
b. Elementary School	2 (20,0)	5 (50,0)	2 (20,0)	1 (10,0)	
c. Junior High School	1 (10,0)	1 (10,0)	1 (10,0)	1 (10,0)	
d. Senior High School	2 (20,0)	0 (0,0)	2 (20,0)	3 (30,0)	
e. Diploma	0 (0,0)	1 (10,0)	2 (20,0)	0 (0,0)	
f. Bachelor	2 (20,0)	1 (10,0)	0 (0,0)	0 (0,0)	
Occupation					
a. Teachers	1 (10,0)	0 (0,0)	0 (0,0)	0 (0,0)	0,410[a]
b. Honorary Employee	0 (0,0)	1 (10,0)	0 (0,0)	0 (0,0)	
c. Housewife	8 (80,0)	9 (90,0)	10 (100,0)	10 (100,0)	
d. Private Employee	1 (10,0)	0 (0,0)	0 (0,0)	0 (0,0)	
Parity					
a. Primigravida	3 (30,0)	4 (40,0)	3 (30,0)	3 (30,0)	0,952[a]
b. Multigravida	7 (70,0)	6 (60,0)	7 (70,0)	7 (70,0)	

A Chi Square Test, (b) One-way Anova, Indigenous Peoples of Papua

The average age of the subjects' research is range from 23-26 years old. Most of the respondents are from indigenous peoples of Papua amounts 30 peoples (70%), meanwhile the rest are from non indigenous peoples of Papua (30%). Afterwards, 13 respondents are reported as not graduated from school.

The most occupation is housewife amounts 37 peoples (92, 5%). Some of the respondents are included as multigravida amounts 27 peoples with the percentage is 67,5%, while 32,5% is included as primagravida.

From the test, it is obtained that there are no significant difference in the age, race, education, occupation, and parity in each group (p value > 0, 05). Therefore, it shows that the characteristic can be controlled and do not cause bias effect in the analysis results.

The Effect of *L. Decumana* Toward Labor Pain and Cortisol Level in the First Active Phase of inpartu Condition

The Table 2 below will shows the distribution along with the effect of L. Decumana toward labor pain and cortisol level in the first active phase of inprtu condition

Table 2: The data distribution and the effect of L. Decumana toward labor pain and cortisol level in the first active phase of inpartu condition

Variable			Groups				*p-value* (Independent T-Test)
			LD+SP (n=10)	LD+KS (n=10)	KS+V (n=10)	SP+VP (n=10)	
Pain Level	Pre	$\bar{X} \pm SD$	7,60 ± 1,07	7,70 ± 0,67	6,40 ± 1,26	7,40 ± 1,26	0,106[b]
		Min - max	6,0-10,0	7,0-9,0	5,0-8,0	5,0-9,0	
		p-value (normality)	0,090	0,015	0,042	0,445	
	Post	$\bar{X} \pm SD$	5,70 ± 1,34	5,60 ± 0,97	6,10 ± 0,88	7,00 ± 1,05	0,035[b]
		Min - max	4,0-8,0	4,0-7,0	5,0-7,0	5,0-9,0	
		p-value (normality)	0,466	0,245	0,017	0,105	
	p-value (Independent T- Test)		0,000[a]	0,004[b]	0,317[b]	0,157[a]	
Cortisol Level	Pre	$\bar{X} \pm SD$	4,19 ± 3,65	4,09 ± 2,55	2,18 ± 1,45	3,61 ± 2,75	0,337[b]
		Min - max	0,10-11,20	1,30-8,50	0,40-4,50	0,50-9,40	
		p-value (normality)	0,078	0,255	0,413	0,100	
	Post	$\bar{X} \pm SD$	3,11 ± 2,37	3,16 ± 2,55	1,76 ± 1,58	3,62 ± 2,74	0,337[a]
		Min - max	0,50-8,10	Alanna 0,40-7,70	0,20-5,40	0,70-9,20	
		p-value (normality)	0,242	0,188	0,089	0,346	
	p-value (Independent T- Test)		0,062[a]	0,092[a]	0,436[a]	0,970[a]	

A superscirpt = oneway anova test, b superscript = kruskal wallis test, wlicoxon test

In the Table 2, it shows that the smallest average of pain level before the treatment is in the group KS+V (6, 40), and the highest average of pain level is in the group LD+KS (7,70).

Furthermore, after the treatment is obtained the smallest average is in LD+KS group (5,60) and the highest average is in SP+V (7,00). Hence, it means that there is a reduction in the pain level before and after treatment.

The pain level in almost of the groups are reducing, but there are two groups that shows significant differences namely LD+SP (p=0,000) and LD+KS (p=0,004). The result analysis in a whole shows that the pain level has sign significance difference with the p value < 0,035. Afterwards, the smallest average of cortisol level is in the group KS+V (2,18) and the highest average is LD+SP group (4,19). After the treatment, it is obtained that the smallest average is in group KS+V (1, 76) and the highest is in group SP+V (3,62).

The results in a whole shows that only SP+V group that increasing after the treatment, while the others three groups (LD+SP, LD+KS and KS+V) are decreasing.

The result of independent t-test after the treatment shows that no different among the four groups with p value is 0,337. It means that the treatment given can decrease the cortisol level statistically not significantly.

The Mean Differences in the Change of Labor Pain and Cortisol Level in the First Active Phase of Inpartu Condition

The Table 3 here will shows the mean differences in the change of labor pain and cortisol level in the first active phase of inpartu condition:

Table 3: The Mean Differences in the Change of Labor Pain and Cortisol Level in the First Active Phase of Inpartu Condition

Variable	Group				p-value
	LD+SP (n=10)	LD+KS (n=10)	KS+V (n=10)	SP+VP (n=10)	Independent t-test
	$\bar{X} \pm SD$	$\bar{X} \pm SD$	$\bar{X} \pm SD$	$\bar{X} \pm SD$	
Pain Level	1,90 ± 1,10	2,10 ± 1,28	0,70 ± 0,67	0,60 ± 0,67	0,004
Cortisol Level	1,42 ± 1,27	1,29 ± 1,25	1,16 ± 1,17	0,61 ± 0,50	0,764

Kruskal Wallis Test

Based on the table 3, the p value of the significant difference in the pain level is 0, 004. The largest significant differences in the decrease of pain level is in the combination group LD+KS group (2,10±1,28), LD+SP group (1,90±1,10), KS+V group (0,70±0,67). Afterwards, the smallest significant difference in the decrease of pain level is in the SP+V group (0, 60±0, 67).

The largest difference in the decrease of cortisol levels is in LD+SP group (1, 42 ± 1,27) and the smallest is in the group KS+V (1,16 ± 1,17). Meanwhile, the SP+V group is increasing with the significant amounts (0, 61 ± 0, 50). The results in a whole shows that the treatment given to the all groups has no significance influences by the value is 0, 764. It means that statistically, the treatment given does not influence the cortisol level.

Discussion

Historically, the medical plants often used for reproduction health and is amounted that 79,9% people are using these plants in the birth process [21]. *L. Decumana* mostly found in Papua used as medicine from generation to generation. This research has combining pharmacology approach topically and non-pharmacological approach with acupressure techniques in the SP6, SP8, SP9 meridian point. The respondents' age in this research is range in 23 to 26 years old. These ages are chosen due to the majority of these reproductive age group physiologically able to hold the labor pain [22].

From the respondents' race which comes from indigenous people of Papua and non-indigenous people of Papua shows that mostly *L. Decumana* plants are used by the indigenous peoples of Papua. According to Perry and Potter, the cultural background influences individual believes, values, and customs. Race factor is also having important role for individual respond to the pain. It is in line with the theory which mentions that every person has difference respond based on the race and culture [23]. Afterwards, the research conducts by Nergard et al. dealing with the used of medical plants on pregnant mother in Mali, West Africa, shows that the cultural belief influences the used of traditional medicines [21].

Hosseinzadeh also adds that even the modern medicines are quite advanced but the rural plant is still being maintained due to cultural and historical reason [24]. Referring to the results above, the group which has significant influence from the treatment given is LD+SP and LD+KS group (p = 0,000; 0,004), the most significance decreasing in the labor pain is LD+KS group (2,10 ± 1,28) and LD+SP group (1,90 ± 1,10). LD+KS group is a combination between L. Decumana and Ketoprofen Supp. L. Decumana contains Acetamida / Acetaminophen (N- (4-Hydroxyphenyl) which is a p-aminophenol derivate.

It has antipyretic or analgesic that has been used from generation to generation in Papua. Ketroprofen Supp. is non-steroid anti-inflammation drugs that have been proven to be used. Meanwhile, LD+SP group is combination between *L. Decumana* and *Suppositoria placebo* so that this group is clearly testing the anti pain effect from *L. Decumana.* The pain during the birth process will impact on mother condition such as feeling tired, fear, and stress. Stress can cause uncoordinated uterine contraction and labour dystocia.

In the normal state, the stress hormone is released only in small amount, but it will increase in stressful condition [25]. The body's respond to the physical stress or psychological stress can increase the Adrenocorticotropic hormone (ACTH) secretion and will increase the cortisol level as well. The initial release of stress hormones begins with the secretion of corticotrophin releasing factor (CRF). CRF is first released from the hypothalamus in the brain into the

bloodstream, thus reaching the pituitary gland located below the hypothalamus. CRF stimulates the release of pituitary adenocorticotrophin hormone (ACTH), which in turn stimulates the adrenal glands to release various hormones. One of them is cortisol [26].

Cortisol which circulates in the body has role as coping mechanism. If the stressor received by the hypothalamus is strong enough, then secreted CRF will increase as well. Thus, the stimulation received by the pituitary and cortisol secretion by the adrenal gland will increase too. If the condition has been stable, then coping mechanism become positive and the brain's signal will inhibit the released of CRF and hormonal stress cycle will repeat. In the fear and depressed condition, the secreted cortisol will increase.

Thus, cortisol secreted stress will increase to 20 times [25]. Referring to the largest mean difference in cortisol reduction is LD+SP (1,42 ± 1,27), LD+KS group (1,29 ± 1,25), and KS+V (1,16 ± 1,17). Meanwhile, SP+V group is increasing (0,61± 0,50). Therefore, it can be said that the treatment of LD+SP group combination is the most effective treatment to decrease the cortisol level of labor pain in the first active phase of inpartu condition.

Conclusion

L. Decumana as medical plants has benefit as pain relieving for the birth process in the first active phase of inpartu condition. The used of *L. Decumana* can be recommended to provide obstetric care for maternal mother. However, the further research is needed to be conducted to prove the effect of *L. Decumana* biomarker.

Abbreviation

Visual Analog Scale (VAS), Corticotrophin Releasing Factor (CRF), Adenocorticotrophin hormone (ACTH), Randomized Control Trial (RCT).

Ethical Approval and Consent to Participate

It has been approved by Health Research Ethics Commission of the Faculty of Medicine, Diponegoro University number 514/EC/FK-RSDK/VII/2018 and research recommendation from Political and National Unity Board of Mimika Regency number 070/368/209.4/2018.

References

1. Huntley AL, Coon JT, Ernst E (2004) Complementary and alternative medicine for labor pain: A systematic review. Am J. Obstet. Gynecol.
2. Mello LF, Nobrega LF, Lemos A (2011) Transcutaneous electrical stimulation for pain relief during labor: a systematic review and meta-analysis. Rev. Bras. Fisioter., 15(3):175-84.
3. Halder A, Agarwal R (2013) Butorphanol in labour analgesia: A prospective cohort study. J Turkish Ger Gynecol Assoc., 14(4):221-4.
4. Dehchesmeh FS, Hossein Rafiei (2015) Complementary Therapies in Clinical Practice Complementary and alternative therapies to relieve labor pain : A comparative study between music therapy and Hoku point ice massage, 21: 2013-6.
5. Simavli S, Kaygusuz I, Gumus I, Usluogullar B (2014) Effect of music therapy during vaginal delivery on postpartum pain relief and mental health. J. Affect Disord., 156: 194-9.
6. Rahnama P, Mohammadi K, Montazeri A (2016) Salient beliefs towards vaginal delivery in pregnant women: A qualitative study from Iran. Reprod Health.
7. Loke AY, Davies L, Li S (2015) Factors influencing the decision that women make on their mode of delivery: the Health Belief Model. BMC Health Serv. Res., 15: 274.
8. Newton ER (2014) Cortisol as a Biomarker of Stress in Term Human Labor: Physiological and Methodological Issues. Biol. Res. Nurs., 16(1):64-71.
9. Rosaeg OP, Campbell N, Crossan M Lou (2002) Epidural analgesia does not prolong the third stage of labour. Can J. Anesth.
10. Asadi N, Maharlouei N, Khalili A, Darabi Y, Davoodi S, Raeisi Shahraki H, et al (2015) Effects of LI-4 and SP-6 Acupuncture on Labor Pain, Cortisol Level and Duration of Labor. JAMS J Acupunct Meridian Stud.
11. Carpenter LL, Gawuga CE, Tyrka AR, Lee JK, Anderson GM, Price LH (2010)

Association between plasma IL-6 response to acute stress and early-life adversity in healthy adults. Neuropsychopharmacology.

12. Hanjani SM, Tourzani ZM, Shoghi M (2015) The effect of foot reflexology on anxiety, pain, and outcomes of the labor in primigravida women. Acta Med. Iran,.
13. Simaremare ES (2014) Skrinig Fitokimia Ekstrak Etanol Daun Gatal (Laportea decumana (Roxb.) Wedd). Pharmacy.
14. Simaremare ES, Holle E, I Budi M, Yabansabra YY (2015) Perbandingan Efektifitas Anti nyeri Salep Daun Gatal dari Simplisia Laportea Decumana dan Laportea SP. Pharmacy, 12(01):1-10.
15. World Health Organization regional office for the WP (2009) Medicinal plants in Papua New Guinea.
16. Aribawa IGNM (2017) Dasar Manajemen Nyeri Dan Tata laksana Multi Teknik Patient Controlled Analgesia. 1. Cetakan. Jakarta: Sagung Seto; 315.
17. Ansel H (2005) Pengantar Bentuk Sediaan Farmasi. 4th ed. Jakarta, 244-251.
18. Simaremare ES, Holle E, Budi IM, Yabansabra Y (2015) Analisis Perbandingan Efektivitas Anti nyeri Salep Daun Gatal dari Simplisia Laportea decumana dan Laportea sp. J. Farm. Indones.
19. La Basy L, Soamole I, Bugis A (2016) Faktor Kejadian Congestive Heart Failure (CHF) di Ruang ICU di RSUD Masohi Kab. Maluku Tengah 2015. Glob. Heal. Sci., 1(HKN):11-4.
20. Campbell DT, Stanley JC (2015) Experimental and quasi-experimental designs for research. Ravenio Books.
21. Nergard CS, Ho TPT, Diallo D, Ballo N, Paulsen BS, Nordeng H (2015) Attitudes and use of medicinal plants during pregnancy among women at health care centers in three regions of Mali, West-Africa. J. Ethnobiol. Ethnomed., 11(1):73.
22. Access O (2018) Labour pain perception: experiences of Nigerian mothers, 8688: 1-7.
23. Potter A, Perry AG (2005) Buku ajar fundamental keperawatan: Konsep, proses, dan praktik. 4th ed. EGC, editor. Jakarta.
24. Hosseinzadeh S, Jafarikukhdan A, Hosseini A, Armand R (2015) The application of medicinal plants in traditional and modern medicine: a review of Thymus vulgaris. Int. J. Clin Med., 6(09):635.
25. Stocker (2012) Studies Link Stress and Drug Addiction. NIDA Res Find. 14: 1-4.
26. Lisdiana (2012) Regulasi kortisol pada kondisi stres dan addiction. J. Biol. Biol. Educ., 4(1):18-24.

