



## Comparative Study of Desogestrel- Containing Oral Contraceptive and Levonorgestrel- Containing Oral Contraceptive in Dysfunctional Uterine Bleeding

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### ABSTRACT

Dysfunctional uterine bleeding is a type of abnormal uterine bleeding where vaginal bleeding occurs outside of the menstrual cycle in the absence of any known pelvic pathology. Dysfunctional uterine bleeding can be treated safely with hormone therapy. Combined oral contraceptives help in increased menstrual cycle regularity and decreased blood loss. In this study, a reliable drug for the dysfunctional uterine bleeding with maximum effectiveness and minimal side effects were assessed. This study was conducted on 120 cases of dysfunctional uterine bleeding. Patients who were diagnosed with dysfunctional uterine bleeding were randomly assigned into two groups. Group D and group L included patients who were given Ethinyl estradiol 0.02mg + desogestrel 0.15mg and Ethinyl estradiol 0.03mg + levonorgestrel 0.15mg respectively for the four consecutive 28- day cycles. Menstrual blood loss was assessed using the pictorial blood assessment chart (PBAC) score on 2<sup>nd</sup> and 4<sup>th</sup> months of recruitment. Side effects such as weight gain, acne and headache were assessed in both groups. This study shows 56.68% reduction in mean PBAC score in 2 months in desogestrel group whereas only 44.96% reduction in levonorgestrel group and 79.87% reduction in mean PBAC score in desogestrel group in 4 months whereas only 74.46% reduction in levonorgestrel group. Side effects like weight gain, acne and headache were more prominent in the levonorgestrel group than desogestrel group. Desogestrel containing combined oral contraceptive can be a useful and safe treatment for dysfunctional uterine bleeding.

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### INTRODUCTION

Dysfunctional uterine bleeding (DUB) is a type of abnormal uterine bleeding where vaginal bleeding occurs outside of menstrual cycle were structural pelvic pathology, pregnancy, iatrogenic causes and other systemic conditions are ruled out. Most of the dysfunctional uterine bleeding is caused due to anovulatory menstrual cycles which are due to dysfunction of hypothalamic-pituitary-ovarian axis rather than ovulatory menstrual cycles which are due to luteal or follicular phase dysfunction. Anovulatory DUB may result in menorrhagia, and ovulatory DUB may result in polymenorrhoea, oligomenorrhoea, spotting and dysmenorrhoea. Prevalence of

DUB is found to be more in adolescents immediately after menarche were the hypothalamic-pituitary-ovarian axis is not completely developed and in perimenopausal age.

Once the disease has been diagnosed with the aid of medical history, laboratory investigation, dilatation and curettage, then the usual next approach is medical management (Chithrangada *et al.*, 2014). A reliable drug for DUB should show large safety margins, minimal side effects, maximum effectiveness and should be cost-effective. The currently available treatment options for DUB include antifibrinolytics like tranexamic acid, nonsteroidal anti-inflammatory drugs like mefenamic acid, combined estrogen and progesterone pills, progesterone alone, high dose estrogens, danazol and levonorgestrel-releasing intrauterine system (Luthra and Dwivedi, 2018). Most of the DUB occurs due to endocrinological dysfunction, which responds well to hormone therapy and can be treated effectively by combined oral contraceptive pills (COC).

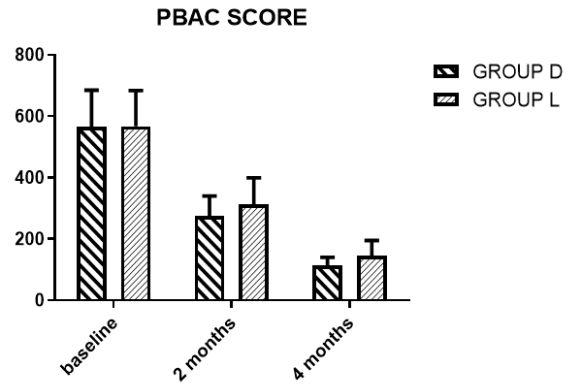
Oral contraceptives initially cause proliferation and further secretory changes in the endometrial lining of the uterus as in a regular menstrual cycle and thereby increasing cycle regularity and reducing the blood loss (Chauhan *et al.*, 2017). Progesterone causes a reduction in estrogen receptors and also a conversion of estradiol to estrone sulphate, which is less potent and thereby produces endometrial maturation and stromal matrix enhancement causing cessation of bleeding. Oral contraceptives can also alter the process of coagulation, fibrinolysis and prostaglandin synthesis, which ultimately results in changes in menstrual blood loss during menstruation (Larsson *et al.*, 1992). Low dose COC can cause cycle control which may increase the patient compliance and reduce the intra-cyclic bleeding (Endrikat *et al.*, 2001). Menstrual blood loss greater than 80ml per cycle can lead to complications, including iron deficiency anaemia and may also harm a patient's quality of life (Weisberg *et al.*, 2017).

## METHODS

This prospective observational study was conducted in the department of Obstetrics and gynaecology, Tertiary care hospital in Chennai, Tamil Nadu from October 2018 till April 2019.

### Inclusion criteria

Both female inpatient and outpatient with age from 18 to 45 years who had abnormal uterine bleeding with and without complaints of dysmenorrhoea, menorrhagia, polymenorrhoea and polymenorra-



Graph 1: Mean pre-treatment PBAC score and post-treatment scores (2<sup>nd</sup> and 4<sup>th</sup> month) in group D and group L

gia, comorbid with anaemia (menorrhagia associated with anaemia) were included in the study.

### Exclusion criteria

Women who had a suspected or verified pregnancy, lactating women, post-menopausal women, patients with moderate to severe hypertension, insulin-dependent diabetes mellitus, hyperlipidemia, thromboembolic, coronary and cerebrovascular diseases and existing hepatic or renal disease were excluded in the study.

Total 120 patients were selected according to inclusion and exclusion criteria, 60 patients were randomly assigned into two groups where the first group was comprised of patients who were prescribed COC containing Ethinyl estradiol 0.02mg and desogestrel 0.15mg (Group D) and the second group was comprised of patients who were prescribed COC containing Ethinyl estradiol 0.03mg and levonorgestrel 0.15mg (Group L) for 21 days starting from 5<sup>th</sup> day of menstruation followed by seven pill-free days. After the last pill-free day patient begins with a new regimen for the next cycle (Kaunitz, 2000), this is continued for four consecutive 28-day cycle. Informed consent from each patient was obtained. Each patient was followed up at 2<sup>nd</sup> month and 4<sup>th</sup> month from the commencement of the treatment.

The efficacy of drugs was assessed using the Pictorial Blood Loss Assessment Chart (PBAC) 10 (Higham *et al.*, 1990). Side effects such as headache, weight gain and acne along with DUB associated complaints such as dysmenorrhoea and menorrhagia were assessed subjectively during each follow-up and were noted.

All patients assigned to this study were instructed to use the same brand of the sanitary napkin, which

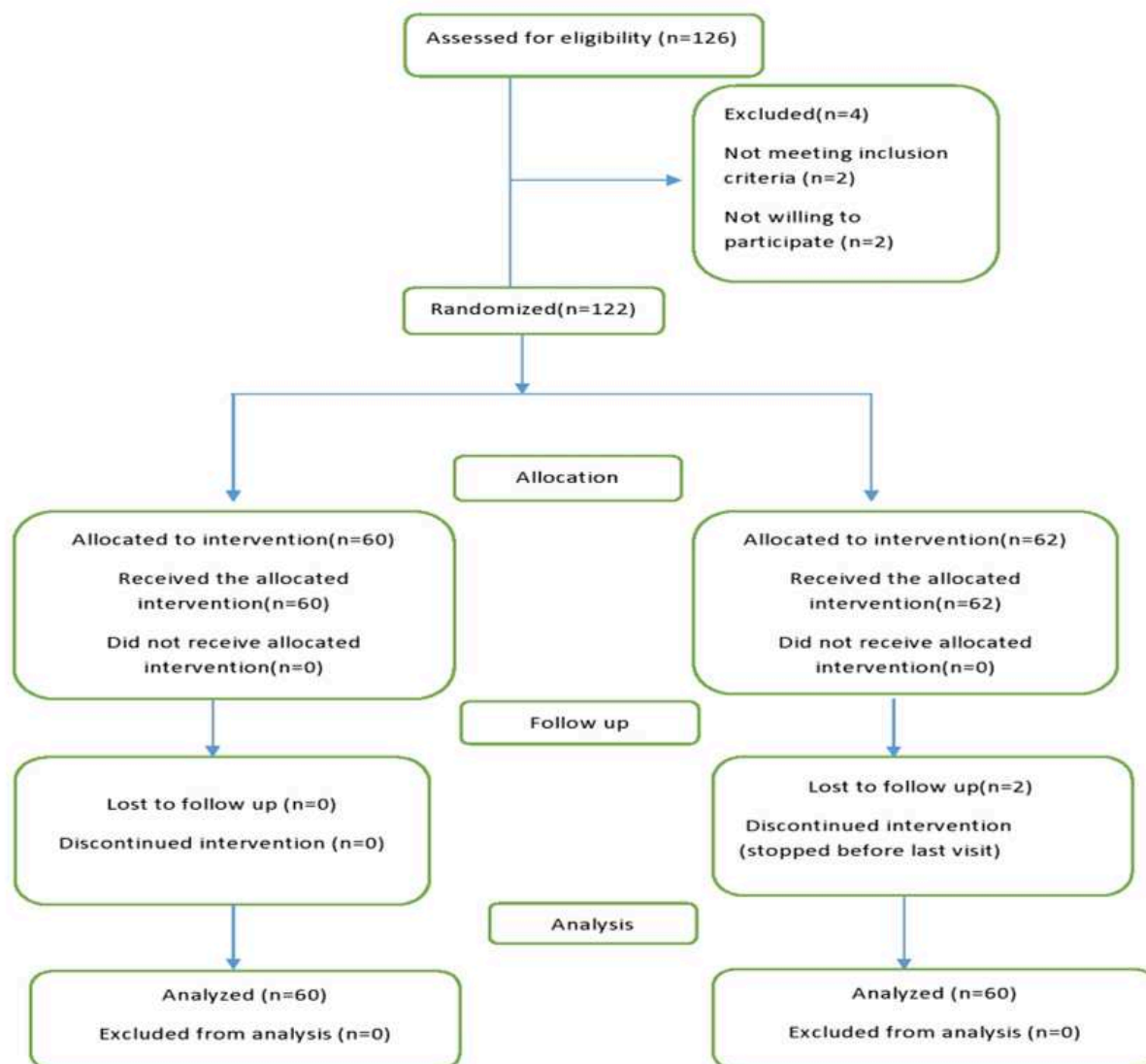


Chart 1: 2 subjects in group D lost to follow up and the efficacy data of the same was excluded considering the precision of the results

**Table 1: Pictorial Blood Loss Assessment Chart (PBAC)**

	Level of soiling	Score
Pads	Light	1
	Moderate	5
	Heavy	20
Clots	Size of a rupee coin or smaller	1
	Size larger than rupee coin	5
Staining or flooding	1 each episode	

**Table 2: Baseline clinical characteristics**

Characters	GROUP L(n=60)	GROUP D(n=60)
Age (yrs)	39.94±5.17	40.12±4.84
Thyroid disorders	21 (17.5%)	17(14.6%)
Weight(kg)	62.189 ± 12.77	63.465 ± 12.11
PBAC Score	567.10 ± 116.248	566.03 ± 118.937
Anemia	52(86%)	53(88%)
Uterine fibroids	21(35%)	18(30%)
Clots	39(65%)	41(68%)
Irregular cycles	41(68%)	37(61%)
Dysmenorrhoea	35(58%)	36(60%)

Data are shown as mean± standard deviation or number (%) as appropriate. Mann-whitney U test were used to determine significance

**Table 3: Comparison of PBAC score between 2 groups**

Characteristics	GROUP D (n=60)	GROUP L(n=60)	p value (intergroup)
PBAC score			
Baseline	566.03 ± 118.93	567.10 ± 116.24	0.8209
2 months	273.46 ± 66.95	312.10 ± 86.67	0.5546
4 months	113.91 ± 26.15	144.82 ± 50.12	0.5129
p value(within group)	<0.0001	<0.0001	

Data is shown as mean ± standard deviation. Mann-whitney U test was used to determine significance

**Table 4: Weight gain observed in the patients**

Weight(kg)	GROUP D	GROUP L	p value (intergroup)
Baseline	63.465 ± 12.11	62.189 ± 12.77	0.5600
4 months	64.155 ± 11.98	64.241 ± 12.24	0.9515
p value(within group)	0.7676	0.3002	

Data are shown as mean ± standard deviation or number (%) as appropriate. Mann-whitney U test were used to determine significance

**Table 5: Side effects assessed in the subjects**

Side effects	GROUP L(n=60)	GROUP D(n=60)
Weight gain	17 (28%)	9(15%)
Acne	22(36%)	13(22%)
Headache	7 (11%)	4(6.6%)

Data are shown as number (%).

showed similar absorbent capacities to standardize the results. This simple scoring method counts the number of sanitary napkins used and its degree of soiling, number and size of clots passed (Reid *et al.*, 2000) as shown in Table 1. PBAC scoring for a given cycle was done by adding up the scores obtained on each day of menstruation, thereby assessing MBL (Mandal *et al.*, 2014). A PBAC score greater than 100 signifies that menstrual blood loss is greater than 80ml (Srivaths *et al.*, 2015; Rani *et al.*, 2016; Hymavathi *et al.*, 2018). This scoring system

is not equivalent but is proportional to MBL (Maganay *et al.*, 2018).

### Statistical analysis

PBAC score was obtained from each recruited patients who were diagnosed with abnormal uterine bleeding before the commencement of therapy and at 2<sup>nd</sup> and 4<sup>th</sup> month after commencement of treatment. PBAC score being the statistical parameter was used as a mean ± standard deviation and was analyzed using the Mann-Whitney U test. Com-

parison between mean baseline PBAC score and 2<sup>nd</sup>, 4<sup>th</sup> month mean PBAC score was done using two-way ANOVA (Analysis of Variance). Weights of all recruited patients were checked before the start of therapy and were compared with weights measured after four months. Mean baseline weight in kilogram was compared with mean weight obtained at 4th month. A p-value of  $\leq 0.05$  was considered to be statistically significant. All analysis was carried out using graph pad prism with a 95% confidence interval.

## RESULT

One hundred and twenty healthy women of reproductive age, diagnosed with abnormal uterine bleeding, were recruited in this study. Each group consisted of 60 patients who were randomly assigned. Six patients were excluded from the study (2 were not willing to participate, two didn't meet the inclusion criteria; two were lost to follow up). The result of 2 patients who were lost to follow up was not included in statistical analysis considering the accuracy of the results Chart 1.

PBAC score showed a significant reduction in four months, proving clinical improvement in both groups. However, desogestrel containing third-generation COC showed significantly better improvement of menstrual abnormalities when compared to second-generation levonorgestrel containing COC.

Mean age of both groups (40.12-group D and 39.94-group L; p=0.777) did not show any significant statistical difference Table 2.

The mean PBAC score before the commencement of treatment was found to be above 550 in both the groups. Whereas the mean PBAC score in 2<sup>nd</sup> and 4<sup>th</sup> month after the start of therapy showed a significant improvement in menstrual abnormalities in both groups, but mean PBAC score was found to be significantly reduced in group D when compared to group L in 2<sup>nd</sup> month ( $273.46 \pm 66.95$  vs  $312.1 \pm 86.67$ ; p=0.5546) and 4<sup>th</sup> month ( $113.91 \pm 26.65$  vs  $144.82 \pm 50.12$ ; p=0.5129) as shown in Graph 1. Within each group, statistical analysis showed a significant reduction in mean PBAC score in post-treatment cycles (p<0.0001) Table 3.

The mean body weight in kilogram before the start of therapy was found to be above 60 in both groups. At the end of the study period, a 2.05 kg increase in mean body weight was observed in group L (p=0.3002) while there was only a 0.69 kg increase in mean weight in group D (p=0.7676). Within each group, statistical analysis showed a significant

increment in body weight (kg) in post-treatment cycles Table 4.

There was an increment in a number of acne lesions in 22 patients (36%) in group L. In contrast, only 13 patients (22%) showed an increase in the number of acne lesions in group D. Other side effects of the drug included mild to moderate headache. 7 out of 60 patients (11%) of group L had complaints of mild to moderate headache during the study period whereas only 4 out of 60 patients (6.6%) of group D had same complaints. There was an increment in weight in 17 patients (28%) in group L, whereas only nine patients (15%) in group D Table 5.

## DISCUSSION

Most of the recruited patients in this study (>50%) were in the age group of 35-45 years, where the median age of cases was 41 years, which is the premenopausal period and this is probably because of any dysfunction in the hypothalamic-pituitary-ovarian axis which may result in anovulatory dysfunction rather than a dysfunction of follicular phase that may result in ovulatory dysfunction.

In previous studies, it has shown that COC containing newer progestogens have low androgenic activity and shows lesser androgenic side effects (Halbe *et al.*, 1998). Moradan Sanam in their study compared the complications of third [(desogestrel (DSG) + Ethinyl estradiol (EE)] and second-generation [(levonorgestrel (LNG) + Ethinyl estradiol (EE)] of combined oral contraceptive pills and observed a 2.5 kg increase in mean weight in LNG + EE group. At the same time, there was no change in mean body weight (kg) in the DSG + EE group at the end of the study. Similarly, it was also found that the mean reduction of a number of acne lesion in DSG + EE group is 3. In contrast, there was a mean increment of 0.4 in a number of acne lesions in LNG + EE group at the end of the study and this difference was statistically significant (p=0.001) (Sanam and Ziba, 2011). The results of Mordan Sanam are comparable to the results of our study.

Other studies on the efficacy of desogestrel containing third-generation oral contraceptive for DUB are limited. A prospective trial was conducted by A. Kriplani to find the effectiveness and acceptability of combined oral contraceptive containing desogestrel and Ethinyl estradiol for management of DUB. A significant reduction (p<0.0001) in the mean number of bleeding days was observed, similarly a high mean PBAC score of 224 and 250 reduced to 70 and 55 (p<0.0001) in group I (cases with heavy menstruation) and group II (cases with heavy and irregular bleeding) respectively in three consecu-

tive cycles. Cycle pattern also was found to be regularized in group II and III (cases with irregular bleeding only) (Agarwal and Kriplani, 2001). These results are agreeable with our results. However, no comparative study between levonorgestrel containing OCP and desogestrel containing OCP is there to prove the efficacy for evaluating our results.

Our study shows 56.68% reduction in mean PBAC score in 2 months in group D whereas only 44.96% reduction in group L and 79.87% reduction in mean PBAC score in group D in 4 months whereas only 74.46% reduction in group L. Our study also showed a significant increase in body weight in both groups. Still, the increment in mean body weight was more significant in group L. Other side effects like headache and acne were found to be prominent in group L than in group D.

### Limitations of the study

Due to the short duration of the study, we were unable to find evidence regarding long term side effects of the drugs. Long term follow up was required to find the efficacy of the drug in some subjects and to justify the recurrence.

### Implications for Practice and Policy

The use of COC has a high potential for facilitating quality of life in women with DUB. Studies have shown that COCs are useful in the treatment of irregular menstrual cycles and menorrhagia. In our research, we have observed that desogestrel containing COC, which falls under the third generation COC are more safe and effective for treating DUB than levonorgestrel containing COC that falls under second-generation COC. These results may improve patient care for DUB by making an appropriate therapeutic decision in the treatment of DUB. Future researches can improvise these results by applying it to a larger proportion of women diagnosed with DUB and thereby improving the quality of life for women with DUB.

### CONCLUSION

From the above results and observations, it can be concluded that desogestrel containing the third generation combined oral contraceptive is superior to levonorgestrel containing the second generation combined oral contraceptive in efficacy, safety and compliance and can be a better option in increasing cycle regularity and decreasing MBL in any reproductive age, especially in peri-menopausal age and adolescence.

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### Conflict of Interest

The authors declare that they have no conflict of interest for this study.

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