

# Comparative Study of Oral Isotretinoin as Conventional, Intermittent, and Low Dose Regimen in Management of Acne Vulgaris

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## ABSTRACT

**Introduction:** Acne vulgaris causes scars when not treated for a long time. Oral isotretinoin, which is a widely used treatment modality, has adverse effects. New studies conveyed that low-dose Isotretinoin is a good option with fewer side effects than the conventional treatment regimen.

**Aim:** To evaluate the clinical efficacy of conventional, intermittent, and low-dose isotretinoin regimens in acne vulgaris using the Global Acne Grading System (GAGS).

**Objectives:** 1. To compare conventional, intermittent, and low-dose regimens of oral Isotretinoin in terms of efficacy, side effects, and compliance. 2. To evaluate the recurrence rates associated with Isotretinoin treatment regimens.

**Materials and Methods:** Prospective comparative interventional research was done in 72 patients diagnosed with acne vulgaris attending the department of dermatology, in a tertiary care teaching institute (IHEC-I/4179/25) and CTRI/2025/10/095515. Patients were randomly allocated into Group C (24): Conventional dose of Isotretinoin 0.5 mg/kg/day, Group I (24): Intermittent dose of Isotretinoin 0.5 mg/kg/day on alternate days, Group L (24): Low dose of Isotretinoin 0.2 mg/kg/day. After obtaining patients' consent, data were collected on patients' demographics, presenting complaints, findings of examination, including GAGS acne grading. Statistical analysis: Unpaired student t test, Chi-square/fisher exact test was used (P<0.05 considered as statistically significant).

**Results:** A significant decrease in the mean scores was noted among all three groups, with Group C showing the lowest score of  $4.30 \pm 0.17$  compared to groups I ( $12.5 \pm 1.64$ ) and L ( $8.13 \pm 1.25$ ), which was statistically significant. Also, 16.7% of participants in Group C and 20.8% of patients in Group L experienced recurrence, while Group I had a slightly higher recurrence rate of 25%. This difference was found to be statistically insignificant.

**Conclusion:** Overall, the treatment was effective in reducing acne severity across all three groups, with each group experiencing a significant decrease in mean acne scores. Due to its effectiveness and cost-benefit ratio in treating acne compared to other regimens, further use of low dose of Isotretinoin in the therapy for acne appears justified.

**Keywords:** Acne vulgaris, conventional dose isotretinoin, intermittent dose isotretinoin, low dose isotretinoin, comparative study, tertiary care, efficacy, adverse effects, recurrence.

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## Introduction:

Acne vulgaris is a chronic inflammatory disorder of the skin involving the pilosebaceous units, arising from increased sebum secretion, inflammatory processes, and colonization by microorganisms<sup>1</sup>. Typically face, upper trunk, and back of the chest were affected. While the disease itself may resolve on its own, the subsequent inflammatory alterations are pigmentation and scarring. Almost 20% of adolescents show facial acne scars<sup>2</sup>.

A frequently employed systemic treatment approach for acne involves the use of isotretinoin (13-cis retinoic acid) in conjunction with oral antibiotics. Isotretinoin is specifically indicated for severe nodulocystic forms of acne. In general, clinical practice, the usual daily dose of isotretinoin ranges from 0.5 to 1.0 mg per kilogram of body weight.<sup>3,4</sup> Nevertheless, excessive Isotretinoin dosages can have a number of negative effects, including systemic side effects. Research has shown that reducing dosages can effectively reduce cost and adverse effects. This means that the other therapeutic strategies may be taken into consideration.<sup>4</sup>

The recommended treatment regimen is 0.5 -2 mg/kg/day over a course of 20 weeks, with a 120 mg/kg maximum overall dosage in people with moderate to severe acne. Oral Isotretinoin is a highly potent teratogen, and it is associated with various side effects, including mucocutaneous, headache, musculoskeletal, and central nervous system effects<sup>5,6</sup>.

In addition to having a higher relapse rate, the researchers discovered that doses of 0.3 or 0.5 mg/kg/day for severe acne were just as effective as the typical dose of 1mg/kg/day. As a result, these doses were abandoned for treating.

However, current studies show that low doses of Isotretinoin can be an effective option in cases of mild and moderate acne. This treatment has fewer side effects than the conventional treatment regimen<sup>7,8</sup>. The longer the initial acne lesion goes untreated, the worse the scarring can be, hence early management is needed. Thus, this research wanted to evaluate the effectiveness of conventional, intermittent, and low-dose Isotretinoin treatment regimens for acne.

## AIM:

- To evaluate the clinical efficacy of conventional, intermittent, and low-dose isotretinoin regimens in acne vulgaris using the Global Acne Grading System- GAGS.

## OBJECTIVES:

- To compare conventional, intermittent, and low-dose regimens of oral Isotretinoin in terms of efficacy, side effects, and compliance.
- To evaluate the recurrence rates associated with Isotretinoin treatment regimens.

## Materials and methods:

Prospective comparative interventional research was done in Patients diagnosed with acne vulgaris attending the department of dermatology, in a tertiary care teaching institute (IHEC-I/4179/25), and CTRI/2025/10/095515

## Inclusion

- Individuals who did not respond adequately to first-line treatment for acne vulgaris.
- Patients with moderate to severe acne showing frequent recurrence.
- Cases of moderate acne with a high risk of developing scars.
- Patients presenting with severe acne characterized by nodular and cystic lesions.
- Inflammatory acne associated with established scarring.

## Exclusion

- Individuals below 18 years of age.
- Pregnant women and married women planning conception.
- Acne resulting from medication use.
- Presence of abnormal liver function tests or a history of hyperlipidaemia.
- Existing musculoskeletal abnormalities.

**Sample size:** Based on the study conducted by Faghihi G et al., which compared low-dose isotretinoin with the conventional dosing regimen in acne management, the following statistical assumptions were adopted.<sup>9</sup> A two-tailed significance level (1- $\alpha$ ) of 95% was used, with a study power (1- $\beta$ ) of 80% to ensure adequate detection of differences. The sample size ratio between the unexposed and exposed groups was maintained at 1:1. The outcome was observed in 78% of the unexposed group and 22% of the exposed group.<sup>9</sup> The calculated odds ratio was 0.08, with a risk or prevalence ratio of 0.28, indicating a risk difference of -56%.

## Randomization and sampling method:

Randomization was done using computer generated random number table, into 3 groups.

Group C (24): Conventional dose of Isotretinoin/ 0.5 mg/kg/day,

Group I (24): Intermittent dose of Isotretinoin / 0.5mg/kg/day on alternate days.

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Group L (24): Low dose of Isotretinoin/ 0.2mg/kg/day.

**Methodology:** The study was done after obtaining institutional ethical committee clearance (IHEC-I/4179/25). Patients fulfilling inclusion criteria were randomized as per computer generated random number table, and included after obtaining written informed consent. Prior to treatment, patients underwent fasting lipid profile, liver function tests, complete blood picture, blood glucose, creatinine phosphokinase, renal function test, and ESR. Additionally, screening for cutaneous and ocular changes was done. Monitoring of lipid profile, kidney function, and liver function tests was done every 15 days for the first month and then every month for the next 5 months. All the groups were given topical clindamycin as a standard of care treatment. Data on patients in all the groups were collected. The questionnaire included items on patients' demographics (age, sex, occupation), detailed history on presenting complaint, precipitating factors, food and drug history, and coexisting illnesses. Findings of general examination and dermatological examination were noted, which included GAGS acne grading.

Withdrawal criteria from trial –

- Patients who did not respond to a low dose of isotretinoin for 2 months were withdrawn and managed appropriately.
- A patient who gets accidentally pregnant would be immediately withdrawn from the trial.

The Patients were reviewed every month for 6 months. After the end of treatment, patients were monitored for a period of two months to assess recurrence rates in each study group. At the completion of therapy, patient satisfaction was assessed using a visual analogue scale (VAS). A further follow-up was conducted six months after treatment completion to evaluate long-term recurrence rates in both groups.

**Global Acne Grading System:**

Acne severity is graded using the Global Acne Grading System (GAGS). It quantifies based on the type of lesion, like comedones, papules, pustules, and nodules on parts like the forehead (2), right cheek (2), left cheek (2), nose (1), chin (1), chest and back (3), as given in brackets. Lesions are assigned a grade based on severity. Additionally, each zone is assigned a factor ranging from 1 to 3, depending on its location. GAGS Score is given by adding up all scores across all the parts. GAGS was categorized into mild (1-18), moderate grade (19-300, severe (31-38), and very severe (39 and above)<sup>10</sup>.

VAS scale for patient satisfaction:

Patient satisfaction was scored using a visual analogue scale (VAS). The VAS was a straight line on which the patient marked their level of satisfaction, with descriptors representing the highest and lowest levels of satisfaction. The survey included two descriptors: no satisfaction (0 points) and extreme satisfaction (5 points).

VAS > 8 - excellent, 5-8 = good, < 5 - poor.

**Analysis of data:** Analysis was done using SPSS version 26. Qualitative data represented in numbers and percentages (%) and Quantitative variables as mean ± SD. Graphical representation was in the form of bar diagrams and line diagrams. For quantitative variables with a normal distribution, the unpaired t-test was used. For qualitative variables, bivariate analysis was performed using the chi-square/Fisher's exact test, which was used (P<0.05 considered statistically significant).

**Results:** Group C participants' mean age was 20.22 ± 5.05 years, in Group I it while in group I was 19.52 ± 3.17 years, and in Group L it was 20.57 ± 1.56 years, which shows no statistically significant difference across the groups (p=0.829). The proportion of males were 54.1%, 41.7%, and 50% in group C, I, and L, whereas the proportion of females were 45.8%, 58.3% and 50% in group C, I, and L, with p= 0.4 (p=0.44). The initial mean acne severity scores were 110.14 in Group C, 119.04 in Group I, and 129.05 in Group L. The scores were statistically similar across all treatment groups (P>0.05). Thus, patients were comparable with respect to mean age, gender distribution, and baseline GAGS score across the three groups. (Table 1)

**Table 1: Baseline characteristics of patients across the groups**

variable	Sub Groups	Group C	Group I	Group L	p value
Mean Age ± SD		20.22 ± 5.05	19.52 ± 3.17	20.57 ± 1.56	0.829
Gender	Male	13(54.1%)	10(41.7%)	12(50%)	0.442
	Female	11(45.8%)	14(58.3%)	12(50%)	
Mean Acne severity at baseline ± SD		110.14 ± 5.22	119.04 ± 7.07	129.05 ± 3.42	0.858

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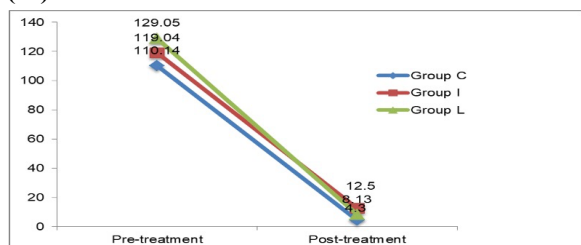
After completion of treatment mean acne score was significantly reduced across all the 3 groups, with Group C showing the lowest score of  $4.30 \pm 0.17$  compared to groups I ( $12.5 \pm 1.64$ ) and L ( $8.13 \pm 1.25$ ). (table 2, figure 1)

Table 2: Mean acne score reduction after treatment

Group	Pre (Mean $\pm$ SD)	Post (Mean $\pm$ SD)
Group C	110.14 $\pm$ 5.22	4.30 $\pm$ 0.17
Group I	119.04 $\pm$ 7.07	12.5 $\pm$ 1.64
Group L	129.05 $\pm$ 3.42	8.13 $\pm$ 1.25

\*- Significant

Figure 1: Change in mean acne score post treatment (%)



It was observed that side effects such as cheilitis were more among participants in Group C (91.7%) compared to Group I (66.7%) and Group L (54.2%), which was not statistically significant ( $p < 0.05$ ). Also, no significant difference in the proportion of patients with dry skin across the groups ( $p > 0.05$ ). The incidence of dry mouth and rashes was significantly lower in Group L (4.2%/8.3%) when compared to Group I (29.2%/25%), and even lower when further compared to Group C (58.3%/41.7%), which was statistically significant ( $p < 0.05$ ). (table 3, figure 2)

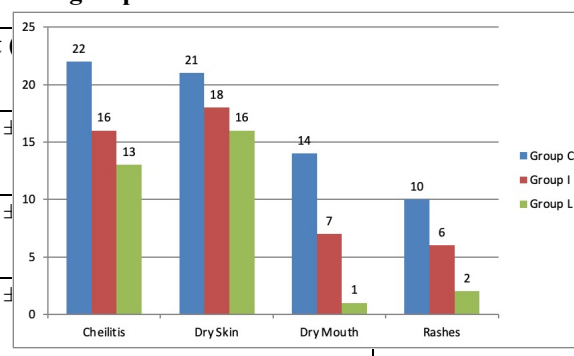
Table No. 3: Side effects to treatment

Side effects	Group C	%	Group I	%	Group L	%	P-Value
Cheilitis	22	91.7	16	66.7	13	54.2	0.014*
Dry Skin	21	87.5	18	75	16	66.7	0.231
Dry Mout	14	58.3	7	29.2	1	4.2	0.0002*

Side effects	Group C	%	Group I	%	Group L	%	P-Value
Rashes	10	41.7	6	25	2	8.3	0.028

\*-Significant

Figure 2: Frequency of side effects in each group

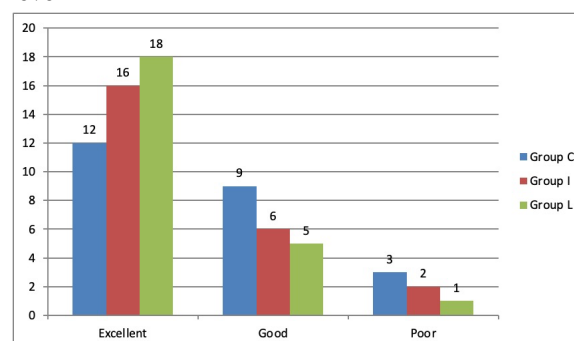


Though the excellent satisfaction scores were more frequently observed in group L (75%) and good satisfaction scores were seen in group C (25%), these findings were not significant ( $p > 0.05$ ) (table 4, figure 3)

Table No. 4: Distribution based on patients' satisfaction levels

Patient satisfaction	Group C	%	Group I	%	Group L	%	X <sup>2</sup> / P-Value
Excellent	12	50.0	16	66.7	18	75	3.517/ 0.475
Good	9	36.7	6	25	5	20.8	
Poor	3	13.3	2	8.3	1	4.1	
Total	24	100.0	24	100.0	24	100.0	

Figure 3: Comparison of Patient satisfaction level



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It was observed that 16.7% of participants in Group C and 20.8% of patients in Group L experienced recurrence, while Group I had a slightly higher recurrence rate of 25%, which was not found to be statistically significant ( $p=0.505$ ). (Table 5)

**Table No. 5:**  
**Distribution based on recurrence rates**

Recurrence	Group C	%	Group I	%	Group L	%
Yes	4	16.7	6	25	5	20.8
No	20	83.3	18	75	19	79.2
Total	24	100.0	24	100.0	24	100.0
Chi-square = 0.505, P=0.77, (P>0.05, not significant)						

### Discussion:

Acne is an inflammation of the pilosebaceous apparatus and is most frequently encountered during adolescence. Beyond its physical manifestations, the condition can exert considerable psychological distress and negatively influence social interactions. The advent of isotretinoin, a first-generation synthetic retinoid, for managing moderate to severe acne vulgaris is widely considered a landmark development in dermatologic therapy. Isotretinoin has adverse effects when administered at the conventional recommended dosage of 0.5–1 mg/kg/day. Since these unwanted effects are largely dose dependent, the use of lower daily doses ranging from 0.3–0.4 mg/kg has emerged as a potentially appealing alternative. Nevertheless, evidence regarding the long-term safety and therapeutic effectiveness of this low-dose regimen remains limited<sup>8</sup>.

In this study, the mean age was comparable across groups, with patients in Group C having an age of  $20.22 \pm 5.05$  years, in Group I it was  $19.52 \pm 3.17$  years, and in Group L mean age was  $20.57 \pm 1.56$  years. Sardana K et al documented in their research that the majority (60%) of patients were within the age limit of 21–30 years.<sup>7</sup> Hermes B et al study reported that the mean of age of participants was found to be 22.4 years.<sup>11</sup> Congruent with these observations,

majority of the participants in the current study are found to be in the range between 20 and 35 years.

The distribution of males and females in the three groups was similar, with a slightly higher frequency of males observed in group C (56.7%) and group L (53.3%), which was not statistically significant ( $P > 0.05$ ). Sardana K et al in their study also reported a similar result.<sup>7</sup> Agarwal U et al also mentioned a similar number of males across 4 different groups in their study (59%, 57%, 64%, 55%), congruent with the current study findings.<sup>12</sup>

After completion of treatment mean acne score was significantly reduced across all the 3 groups, with Group C showing the lowest score of  $4.30 \pm 0.17$  compared to groups I ( $12.5 \pm 1.64$ ) and L ( $8.13 \pm 1.25$ ) in this study. Agarwal U et al. showed the same response. Their effect was earliest in group C (continuous dosing). Group I (intermittent) performed the worst, whereas Group L (low dose) showed equivalent results by the end of the 16-week therapy.<sup>12</sup> Sardana K et al. in their study reported that low-dose isotretinoin is equally effective as the standard dose.<sup>7</sup> Amichai B et al. demonstrated a lower incidence of severe adverse effects with low-dose isotretinoin at a reduced cost compared to higher doses; the findings are similar to this study.<sup>13</sup> Mandekou-Lefaki et al, in their study, reported that the low-dose treatment had a 69% success rate, while the high-dose treatment, with a total dose of up to 120 mg/kg, had a higher success rate of 91% and helped in preventing relapses.<sup>14</sup> Congruent observations were made in the present study. Akman A et al showed that acne scores significantly decreased by completion of the study with each follow-up ( $P < 0.05$ ).<sup>15</sup> However contrastingly low-dose regimen was better in efficacy compared to the conventional and intermittent regimen. Strauss JS et al, in their research, documented that both intermittent and conventional treatments cause a similar decrease in acne on the face and trunk. Additionally, an equivalent percentage of patients in both groups achieved a 90% reduction in the number of nodules. Plewig G et al in their investigation reported that a decrease in lesions by 87%–95% and others by 81%–88% in Group L (10mg) – Group C (20 mg) is noted.<sup>16</sup>

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This study shows that side effects such as cheilitis were more common among participants in Group C (91.7%) compared to Group I (66.7%) and Group L (54.2%). This variation was observed to be highly significant ( $p < 0.05$ ). Also, no significant difference in the proportion of patients with dry skin across the groups ( $p > 0.05$ ). The incidence of dry mouth and rashes was significantly lower in Group L (4.2%/8.3%) when compared to Group I (29.2%/ 25%), and even lower when further compared to compared to Group C (58.3%/ 41.7%) with statistical significance. Mucocutaneous side effects (cheilitis, dry mouth, dry skin) started to show up sooner in Group C (conventional) at two weeks and got worse over time, according to the study by Agarwal U et al. These negative effects started to show up in the other groups four or six weeks later. The most frequent side effects in group C (29.6%) were facial redness/rashes, followed by cheilitis and dry skin<sup>12</sup>. Amichai B et al also reported a low frequency of severe adverse effects in the low-dose treatment group.<sup>13</sup> Sardana K et al reported that a standard dose of 1mg/kg/day resulted in increased side effects.<sup>7</sup> Mandekou-Lefaki et al indicated in their study that the low-dose treatment resulted in lesser side effects and had a positive impact on previous scarring.<sup>14</sup> Akman A and colleagues reported that both the frequency and intensity of isotretinoin-associated adverse effects were reduced in groups L and I when compared with group C. Their findings suggest that intermittent isotretinoin therapy can serve as a useful alternative, particularly for patients with moderate acne, as it is associated with fewer side effects. This regimen may be especially suitable for individuals who are unable to tolerate standard dosing schedules.<sup>15</sup>

In the current study, it was observed that 16.7% of participants in Group C and 20.8% of patients in Group L experienced recurrence, while Group I had a slightly higher recurrence rate of 25%, which was insignificant ( $p = 0.505$ ). In their study, Lee JW et al documented the highest recurrence rates in Group I (intermittent), followed by Group L (low dose) and Group C (conventional), with Group L being comparable to Group C. They noted that the intermittent

regimen requires a higher cumulative dose to achieve fewer recurrences.<sup>17</sup> These observations align with current study findings.

### CONCLUSION:

In conclusion, with similar baseline characteristics like age, gender, and baseline acne severity score being ensured, all the 3 groups exhibited a significant decrease in acne severity after treatment. Low-dose isotretinoin was associated with fewer adverse effects, better tolerability, lower treatment cost, and thereby improved patient compliance. In contrast, higher-dose regimens were linked to increased side effects like cheilitis and higher cost, without offering substantial additional clinical benefit in moderate to severe acne. In intermittent dose isotretinoin, though the cost of treatment was reduced due to alternate-day dosage, side effects were still present. The favourable risk–benefit ratio observed with low-dose isotretinoin supports its use as an effective therapeutic option. The findings of this study suggest that low-dose isotretinoin regimens can achieve comparable clinical efficacy to standard-dose therapy with minimal adverse effects.

Conflicts of Interest - None



BEFORE  
Figure 4-7: Improvement with low-dose Isotretinoin

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BEFORE  
Figure 8-9-Improvement with conventional dose Isotretinoin

BEFORE

Figure 10-11: Improvement with intermittent dose Isotretinoin

AFTER



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### References:

1. Williams HC, Dellavalle RP, Garner S. Acne vulgaris. *The lancet*. 2012 Jan 28;379(9813):361-72.
2. Hay RJ, Johns NE, Williams HC, Bolliger IW, Dellavalle RP, Margolis DJ, Marks R, Naldi L, Weinstock MA, Wulf SK, Michaud C. The global burden of skin disease in 2010: an analysis of the prevalence and impact of skin conditions. *Journal of Investigative Dermatology*. 2014 Jun 1;134(6):1527-34.
3. Bagatin E, Costa CS. The use of isotretinoin for acne—an update on optimal dosing, surveillance, and adverse effects. *Expert review of clinical pharmacology*. 2020 Aug 2;13(8):885-97.
4. Costa CS, Bagatin E, Martimbianco AL, da Silva EM, Lúcio MM, Magin P, Riera R. Oral isotretinoin for acne. *Cochrane Database of Systematic Reviews*. 2018(11).
5. Khalil S, Bardawil T, Stephan C, Darwiche N, Abbas O, Kibbi AG, Nemer G, Kurban M. Retinoids: a journey from the molecular structures and mechanisms of action to clinical uses in dermatology and adverse effects. *Journal of Dermatological Treatment*. 2017 Nov 17;28(8):684-96.
6. Dhir R, Gehi NP, Agarwal R, More YE. Oral isotretinoin is as effective as a combination of oral isotretinoin and topical anti-acne agents in nodulocystic acne.
7. Sardana K, Garg VK. Efficacy of low-dose isotretinoin in acne vulgaris. *Indian Journal of Dermatology, Venereology and Leprology*. 2010 Jan 1;76:7.
8. Rao PK, Bhat RM, Nandakishore B, Dandakeri S, Martis J, Kamath GH. Safety and efficacy of low-dose isotretinoin in the treatment of moderate to severe acne vulgaris. *Indian Journal of Dermatology*. 2014 May 1;59(3):316.
9. Faghihi G, Mokhtari F, Fard NM, Motamedi N, Hosseini SM. Comparing the efficacy of low dose and conventional dose of oral isotretinoin in treatment of moderate and severe acne vulgaris. *Journal of Research in Pharmacy Practice*. 2017 Oct 1;6(4):233-8.
10. Alsulaimani H, Kokandi A, Khawandanh S, Hamad R. Severity of acne vulgaris: comparison of two assessment methods. *Clinical, cosmetic and investigational dermatology*. 2020 Sep 28;711-6.
11. Hermes B, Praetel C, Henz BM. Medium dose isotretinoin for the treatment of acne. *Journal of the European Academy of Dermatology and Venereology*. 1998 Sep;11(2):117-21.
12. Agarwal US, Besarwal RK, Bhola K. Oral isotretinoin in different dose regimens for acne vulgaris: a randomized comparative trial. *Indian journal of dermatology, venereology and leprology*. 2011 Nov 1;77:688.
13. Amichai B, Shemer A, Grunwald MH. Low-dose isotretinoin in the treatment of acne vulgaris. *Journal of the American Academy of Dermatology*. 2006 Apr 1;54(4):644-6.
14. Mandekou-Lefaki I, Delli F, Teknetzis A, Euthimiadou R, Karakatsanis G. Low-dose schema of isotretinoin in acne vulgaris. *International journal of clinical pharmacology research*. 2003 Jan 1;23(2-3):41-6.
15. Akman A, Durusoy C, Senturk M, Koc CK, Soyurk D, Alpsoy E. Treatment of acne with intermittent and conventional isotretinoin: a randomized, controlled multicenter study. *Archives of dermatological research*. 2007 Dec;299(10):467-73.
16. Plewig G, Dressel H, Pflieger M, Michelsen S, Kligman AM. Low dose isotretinoin combined with tretinoin is effective to correct abnormalities of acne: Niedrig dosierte Isotretinoin-Therapie ist wirksam zur Behandlung der Acne conglobata und Acne papulopustulosa. *JDDG: Journal der Deutschen Dermatologischen Gesellschaft*. 2004 Jan;2(1):31-45.
17. Lee JW, Yoo KH, Park KY, Han TY, Li K, Seo SJ, Hong CK. Effectiveness of conventional, low-dose and intermittent oral isotretinoin in the treatment of acne: a randomized, controlled comparative study. *British Journal of Dermatology*. 2011 Jun 1;164(6):1369-75.