Systemic Adverse Effects of Topical Clobetasol and Counterfeit Cosmetic Products on Iraqi Women

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Abstract

Background: Topical corticosteroids (TCs) are widely used for dermatologic diseases. Unfortunately, there exists many adverse effects (local and systemic). These adverse effects are comparable to those observed when glucocorticoids are administered systemically, but they are typically less severe. Aim: To assess the systemic adverse effects of topical clobetasol (TCL) and counterfeit cosmetic products (CCP) on Iraqi women. Methods and patients: This was a cross-sectional observational study; carried out from October 2022 to March 2023. Patients visited the outpatient clinic of the Department Dermatology and Venereology in Abu al Khasib Hospital in Basra City, Iraq. Patients may be categorized into two distinct groups: the first group of subjects utilized TCL (n=31), while the second group consisted of patients with CCP (n=32), and the remaining participants were designated as the control group (n=35). A specialized dermatologist conducted a clinical examination to make a diagnosis. A questionnaire was collected, and blood samples were obtained for laboratory investigations. Results: TCs suppressed vitamin D (Vit-D), INTERLUKIN-6 (IL-6), testosterone, and estrogen and reduced cortisol concentrations significantly. TCs elevated red blood cell counts significantly. TCs elevated red blood cells (RBC), neutrophils percent (NEU%), and hemoglobin (HB) levels significantly and prolong bleeding time. While not affecting WBCs, PLT, MPV, MCH, MCV, ACTH, or insulin levels. Accompanied with decreased in HCT, MCHC, Eos%, and Lym% for all groups in comparison to control group. Conclusion: Topical corticosteroids are extensively used, mostly for the treatment of dermatological conditions. However, they can be misused for their cosmetic effects as fairness creams. TCs misuse is a big problem in Iraq, resulting in massive skin effects and systemic deterioration, such as hematological and hormonal effects. Nevertheless, the general population remains ignorant of the systemic adverse effects. Educational activities targeting the general public are suggested to address the systemic deterioration.

1. Introduction

Topical corticosteroids (TCs) have a well-established and extensive historical background, making them very prevalent as therapeutic treatments for dermatological conditions. TCs are often used in clinical practice owing to their demonstrated effectiveness in relieving pruritus, suppressing cellular proliferation, diminishing inflammatory responses, and stimulating melanogenesis in the cutaneous tissue [1]. Unfortunately, there exists many side effects (local and systemic), systemic absorption of TCs may result in laboratory indications of systemic adverse effects, and risk factors include high-strength, inappropriate and chronic use corticosteroids (Cs), application in thin-skinned locations or extended treatment duration, and occlusive. These adverse effects are comparable to those observed when glucocorticoids(GCs) are administered systemically, but they are typically less severe. Based on their clinical activity and capacity for suppressing the Hypothalamus pituitary adrenal- axis (HPA axis), TCs can be categorized as super potent, potent, medium, and mild. Systemic side effects may include neuropsychiatric problems, musculoskeletal-metabolic-endocrine, and life-threatening...
infections in addition to minor and reversible HPA axis suppression (2, 3).

In hospitals and clinical settings, topical corticosteroid propionate (TCL) is most frequently used. TCL is a newly developed fluorinated topical corticosteroid, the most potent topical steroid (super potent) to date, and is roughly 1,800 times more potent than hydrocortisone (4).

TCL is an effective TCs that has shown potential for short-term and intermittent management of various inflammatory dermatoses that affect a large area of the skin. The adherence to limitations and safeguards is of utmost importance. TCL relieves inflammation (swelling, pain and itching) caused by irritation or allergic reaction by reduces the production of inflammatory molecules. TCL use for treatment eczema, psoriasis, lichen planus and lupus erythematosus (5).

Additionally, it may inhibit the production of new skin cells, which may help certain skin conditions (such as psoriasis) by reducing patches or scales. Finally, it reduces the body's immunological reaction, which might assist with certain skin issues brought on by a sensitive immune system (such as eczema) (6, 7).

The drug is available in many different formulations, including ointment or cream, in concentrations ranging from 0.05% to 0.1%. It is also available as, a shampoo, lotion, and spray combined with an antifungal and an antibiotic. Most formulations of clobetasol aren’t recommended to be used for more than two weeks at a time since they can cause serious side effects (8).

TCs have been shown to effectively brighten the skin tone. However, it is regrettable that a wide range of cosmetic products are being marketed under bogus names, sometimes without proper labeling including misleading information on the presence of natural or herbal ingredients, or with names that have been obscure or covered up. These products are found in the markets of Iraq, and a large proportion of them includes hydroquinone, corticosteroids (mostly clobetasol, betamethasone, and dexamethasone) and mercurial substances. Cosmetic formulations must be devoid of any corticosteroids. Nonetheless, several companies have been found to use such substances in the production of counterfeit cosmetic products (CCP). TCs are often used as a cosmetic cream by a large percentage of people. Many patients attribute the rapid and amazing effects of TCs as one of the primary factors influencing their decision to choose it for treating various skin-related concerns in their daily lives (7, 9).

A large number of individuals completely ignorant for the potential negative consequences of long-term TCs application. Because of the rebound phenomenon they experience when they attempt to stop using the medication, they continue to take TC even after they start to see the adverse effects it has on their skin. Since they are less costly than the conventional standard fairness and beauty creams on the market, several of the brands that are often used by patients are seen as low-income or poor (10, 11).

Accordingly, The main aim of this study was to assess the systemic adverse effects of TCL and counterfeit cosmetic products in Iraqi women.

2. Subjects and methods

2.1 Study design and ethical approval

This was a cross-sectional observational multicenter study carried out from October 2022 to March 2023. Patients visited the outpatient clinic of the Department of Dermatology and Venereology in Abou-al Khassib Hospital in Basra City, Iraq were included in this study. Informed consent was obtained according to the Helsinki Declaration, and the study was authorized by the ethical committee at the Basra University College of Pharmacy (EC 10 in 2022).

2.2 Patients

A total of ninety-eight females between the ages of 16 and 60 years are enrolled. Sixty-three patients may be categorized into two distinct groups: the first group of subjects utilized TCL (n=31), while the second group consisted of patients with CCP (n=32), and the remaining thirty-five participants were designated as the control group.

Patients with continuous application of TCL or CCP to any part of the body for at least 30 days were recruited. We selected females with cutaneous adverse effects from TCs. This usage should have continued until the day of presentation to the center, or if discontinued, no more than two weeks before.

A questionnaire was distributed to the patient, which covers several aspects of information, such as participants’ ages, levels of education, systemic adverse effects experienced, reasons for use or abuse, frequency and kind of drug utilized, and periods of usage of TCs.

A specialized dermatologist conducted the clinical examination to make the diagnosis. The researchers were given instructions to assess the appropriateness and Justification of using TCs in every given circumstance. The criteria used to identify inappropriate or unjustified use included instances of wrong indication (e.g., skin weighting), as well as cases of undiagnosed dermatitis, as determined by the investigator’s opinion. The study excluded participants who had previously taken oral steroids for whatever reason, those with a medical background of chronic illnesses, patients with endocrine, pulmonary, or cardiovascular disorders, pregnant women, and lactating mothers.

2.3 Blood investigation

The blood samples were draw between 8 and 10 a.m., one ml of whole blood in an EDTA then centrifuged to plasma to check ACTH by (Roche cobas e 411); 2 ml in a sodium citrate tube, plasma take to check PT and INR by (STAGO START MAX, France); 3 ml in a gel tube, take serum, and then stored in a cold setting to prevent any effects of the environment on the samples; they were then checked for other parameters. For all patients and control groups, hormonal and biochemical test was estimated by ELISA technology (cobas e 411), cortisol, international ratio (INR), prothrombin time (PT), interleukin-6 (IL6), vitamin D3 (Vit-D3), insulin, testosterone, and estradiol (E2).

2.4 Statistical analysis

This work was statistically evaluated using the Chi-square method for analysis and Fisher exact tests with the Koopman asymptotic score and the method of Katz to
evaluate the relative risk and correlations. One-way analysis of variance with Bartlett’s post hoc analysis for multiple comparisons was utilized by GraphPad Prism for Windows (version 8.0).

3. Results

In total, 98 women were involved in this research. Among them, 31 women had a defined skin condition resulting from the use of TCL, whereas 32 women used CCP. The other 35 participants were chosen as the control group. The research included individuals with ages ranging from 16 to 60 years.

The majority of patients had a low level of education and were within the age range of 18 to 45 years, as seen in Table 1. Moreover, a significant proportion of patients used TCs for a duration exceeding 40 days, whereas only a few patients utilized TCs for a period less than 40 days. No statistically significant variation was seen between the TCL and CCP groups with regards to age, education level, or period of usage. Among the 63 patients included in the study, a significant number of TCL users (28 out of 31) reported applying the treatment more than once daily. In contrast, the majority of CCP users (27 out of 32) reported applying the treatment once daily.

Table 1. A Comparison of the demographic characteristics of females who used topical clobetasol (TCL) with cosmetic counterfeit products (CCP) users: represents the duration of use, graduation, and ages

<table>
<thead>
<tr>
<th>Demographic information</th>
<th>TCL (n=31)</th>
<th>CCP(n=32)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily frequency use</td>
<td>Once</td>
<td>More</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Graduation</td>
<td>2</td>
<td>29</td>
</tr>
<tr>
<td></td>
<td>&lt;40 days</td>
<td>&gt;40 days</td>
</tr>
<tr>
<td>Duration of use</td>
<td>5</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>&lt;18</td>
<td>18-45</td>
</tr>
<tr>
<td>Ages( years)</td>
<td>5</td>
<td>19</td>
</tr>
</tbody>
</table>

The differences between abuse groups are not statistically significant. The frequency of daily application showed a significant difference between study groups. Reveals that there has been no significant difference among the study groups in (age, education level, and duration of use) (P>0.05).

As shown in Table 2, testosterone levels were evaluated in the current study. The table summarizes the considerable and statistically significant decline in testosterone levels seen in patients who had TCL (0.1903± 0.039) and CCP (0.1920± 0.02) compared to the control group (0.3637± 0.037). To get comprehensive knowledge of the cause and adverse effects of TCs misuse, serum estrogen levels were assessed in the TCL (59.35± 13.11) and CCP (59.55± 6.56) groups as well as in the control group (143.1± 18.7). Significant differences were noticed across the groups (P<0.01), as seen in Table 2.

Table 2. Serum cortisol concentration, levels, testosterone level, and estrogen level of the subjects in the study (n=98)

<table>
<thead>
<tr>
<th>Serum hormone concentration</th>
<th>Control (n=35)</th>
<th>TCL (n=31)</th>
<th>CCP(n=32)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortisol nmol/L</td>
<td>277.0± 24.21</td>
<td>196.2± 20.25*</td>
<td>169.3± 22.03**</td>
<td>0.0023</td>
</tr>
<tr>
<td>ACTH pg/ml</td>
<td>3.876± 0.37</td>
<td>2.883± 0.544</td>
<td>3.259± 0.54</td>
<td>0.3225</td>
</tr>
<tr>
<td>Insulin uU/mL</td>
<td>28.75± 3.78</td>
<td>45.90± 12.5</td>
<td>44.69± 8</td>
<td>0.2116</td>
</tr>
<tr>
<td>Testosterone ng/ml</td>
<td>0.3637± 0.037</td>
<td>0.1903± 0.039**</td>
<td>0.1920± 0.02**</td>
<td>0.0004</td>
</tr>
<tr>
<td>Estrogen pg/ml</td>
<td>143.1± 18.7</td>
<td>59.35± 13.11**</td>
<td>59.55± 6.56**</td>
<td>0.0010</td>
</tr>
</tbody>
</table>

The results are given as Mean ±SEM, with * indicating a significant differences from the control (P<0.05). ** represent highly significant difference among groups P<0.01. Plasma Adrenocorticotropic Hormone (ACTH) and serum insulin level no significant changes were observed among study groups.

In comparison to the control group, treatment with TCL or CCP resulted in substantial reductions in MCHC, Eos%, Mon%, and Lym%. WBCs, PLT, MPV, MCH, and MCV were similar in the study groups. The current study’s findings show that the TCL group and CCP group had significantly higher RBCs, HB and NEU% than those in the control group as a showing in Table 3.

The present finding showed a significant increase in RBCs and LYM% in females using the TCL and CCP groups P-values (≤ 0.05) and compared with the control group (Table 3). The results showed a highly significant increase in HB concentration and the TCL and CCP groups, comparisons with the control group had a p-value less than (0.01). The study shown no significant difference (p-value > 0.05) in WBCs, PLT, MPV, MCH, or MCV for all groups. This finding showed a significant decrease in HCT, MCHC, Eos%, and Lym% for patient groups, as documented in Table 3.
Table 3: Comparison of hematological parameters between topical clobetasol (TCL) or counterfeit cosmetic products (CCP) and control group

<table>
<thead>
<tr>
<th>Haematological parameters</th>
<th>Control (n=35)</th>
<th>TCL (n=31)</th>
<th>CCP (n=32)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RBCs 10^6/µl</td>
<td>4.890± 0.406</td>
<td>5.181± 0.7027</td>
<td>5.202± 0.5711*</td>
<td>0.0219</td>
</tr>
<tr>
<td>Hb g/dl</td>
<td>11.76± 1.290</td>
<td>12.40± 1.72**</td>
<td>12.72± 1.17**</td>
<td>0.0097</td>
</tr>
<tr>
<td>WBCs 10^3/µl</td>
<td>7.269± 1.957</td>
<td>8.395± 3.114</td>
<td>8.008± 2.569</td>
<td>0.1423</td>
</tr>
<tr>
<td>PLT 10^3/µl</td>
<td>309.2± 61.37</td>
<td>274.8± 71.86</td>
<td>295.5± 59.64</td>
<td>0.0748</td>
</tr>
<tr>
<td>MPV (fl)</td>
<td>9.076± 1.154</td>
<td>8.681± 1.710</td>
<td>10.24± 5.837</td>
<td>0.1728</td>
</tr>
<tr>
<td>EOS%</td>
<td>4.656± 1.278</td>
<td>2.790± 1.312</td>
<td>3.424± 1.280</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>NEU%</td>
<td>39.24± 7.231</td>
<td>48.49± 11.90</td>
<td>46.44± 11.05</td>
<td>0.0013</td>
</tr>
<tr>
<td>MON%</td>
<td>4.544± 1.427</td>
<td>2.5± 1.15**</td>
<td>3.382± 1.57**</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LYM%</td>
<td>29.08± 6.613</td>
<td>21.9± 7.88**</td>
<td>24.21± 9.029*</td>
<td>0.0004</td>
</tr>
<tr>
<td>HCT%</td>
<td>40.43± 4.053</td>
<td>42.8± 5.26**</td>
<td>42.36± 5.297*</td>
<td>0.0662</td>
</tr>
<tr>
<td>MCV(fl)</td>
<td>79.28± 7.754</td>
<td>82.55± 7.235</td>
<td>80.86± 6.444</td>
<td>0.1552</td>
</tr>
<tr>
<td>MCH (pg)</td>
<td>24.62± 2.773</td>
<td>25.34± 2.382</td>
<td>24.81± 3.015</td>
<td>0.5265</td>
</tr>
<tr>
<td>MCHC (g/dl)</td>
<td>31.00± 2.099</td>
<td>29.2± 1.88**</td>
<td>29.40± 2.697**</td>
<td>0.0011</td>
</tr>
</tbody>
</table>

HB: hemoglobin, RBCs: red blood cell count, HCT: hematocrit, MCV: mean corpuscular volume, MCH: mean corpuscular hemoglobin, MCHC: mean corpuscular hemoglobin concentration, WBCs: white blood cell count, Neut%: neutrophil percentage, Lym%: lymphocyte percentage, Mon%: monocyte percentage, Eos%: eosinophil percentage, Baso%: basophil percentage, MPV: mean platelet volume. The results are given as Mean±SD, with * indicating a significant difference from the control (P<0.05). ** represent highly significant difference, *** represent very highly significant difference.

In the current study, there was a significant reduction in the blood levels of IL6 in both the TCL and CCP groups as compared to the control group. A substantial decrease (P<0.0001) in blood IL6 levels has been seen in patients with TCL and CCP misuse when compared with the control group. This value relates to the systemic anti-inflammatory impact of topical corticosteroid (TCS) usage, as seen in Figure 1. The data’s most striking finding is that the TCL and CCP groups have lower vitamin D blood concentrations. Figure 2 illustrates a significant change from the control group.

**Figure 1.** Serum Interleukin-6 level of the participants in the study groups. * considered a significantly decrease in the topical clobetasol (TCL) group . *** very highly significant decrease in counterfeit cosmetic products (CCP) group

**Figure 2.** Serum vitamin D3 levels of the participants in the study (n=68). *** represents a very highly significant difference P<0.0001
4. Discussion

The phenomenon of using TCs for aesthetic purposes within the social context may be traced back to the increased recognition of some TCs as aesthetic creams. These creams are seen to be very effective, providing immediate benefits, and are also affordable, readily accessible, and socially endorsed. However, TCs are available for the asking in urban and rural areas. The disturbing part is that even the most potent TCs, like clobetasol propionate, especially in mixed creams, are available over the counter and are among the most popular brands in Iraq. Regrettably, a lack of knowledge of the potential side effects of TCs contributes to the occurrence of severe local and systemic adverse effects (12-14). An optimal topical medication should exhibit efficacy at the site of administration while minimizing the occurrence of adverse effects. The substance should not undergo systemic absorption or should undergo deactivation upon absorption into the circulatory system, thereby preventing any systemic effects. Nevertheless, the existing TCs now available are not considered optimal and have often been associated with systemic and local adverse effects. These consequences are mostly seen when the TCs are used inappropriately or for an extended period (15).

In the collection of patients included in this study, a majority of participants utilized TCs for prolonged periods that might potentially result in the development of laboratory markers indicating systemic adverse effects. To reduce the potential for adverse effects, it is generally advised that the utilization of topical corticosteroids should not exceed two weeks without further guidance from a medical professional (3). The prolonged use of topical steroids might lead to the development of tolerance and tachyphylaxis. It is not advisable to use ultra-high-potency steroids continuously for a duration beyond three weeks. If prolonged therapy is required, it is advisable to gradually reduce the dosage of the steroid to prevent the occurrence of rebound symptoms. Additionally, it is recommended to wait a minimum of one week after discontinuing the steroid before resuming treatment. The intermittent schedule has the potential to be repeatedly implemented over a prolonged period or until the situation is resolved. Adverse effects are infrequent when using low- to high-potency steroids for three months or less, with except in intertriginous regions, the face and neck, and areas subjected to occlusion (7). In our result, the majority of the patients used CCP once daily. This finding agrees with the results of studies by Jacob et al. The current results are consistent with the results of Varshney I et al., which demonstrated that a large proportion of participants used TCL twice daily (16).

Our findings revealed a highly significant decrease in cortisol levels compared to the normal control group. On the other hand, no significant effect was observed regarding ACTH. Inhibition of the hypothalamus, pituitary, and adrenal axis. It is widely known that TCs have the tendency to be absorbed in large enough doses to inhibit HPA-axis activity. If a sufficient amount is applied, a wide surface area is covered, occlusion is employed, or parts of the treated skin are thin or scraped, almost any topical steroid may produce suppression. The more inherently potent a steroid, the more likely it is to suppress the HPA-axis (8). Exogenous TCs molecules have the potential to inhibit the production of CRH and ACTH, which would limit the stimulation of the adrenal glands and lower levels of naturally occurring cortisol (30). Allenby and colleagues studied the impact of TCL on the HPA-axis in thirty-nine patients. They found that the application of more than 50 g per week of TCL results in adrenal suppression (6). In the same scenario, Rahila S. et al. conclude the same finding (17).

These results demonstrated that no significant variation in insulin level between groups. The prolonged use of glucocorticoids leads to an increase in hepatic gluconeogenesis, a reduction in peripheral glucose utilization, and an elevation in insulin levels and fasting insulin levels. The observed phenomenon is associated with a metabolic reaction of the pancreatic beta cells to elevated blood glucose levels, leading to a decrease in the body's responsiveness to insulin in peripheral tissues (18-20).

Additionally, the present data revealed that serum testosterone level was examined in patients and control groups. There was highly significant decrease in patient groups compared with control groups. These results match those of Alison S et al. (2019) measured testosterone blood levels after the administration of glucocorticoids, which were concluded to lower testosterone blood levels (21). High circulating glucocorticoid inhibits testosterone level reported by Whitlette et al. (2010) (22).

The most interesting aspect of our findings was the highly significant decrease in serum levels of estrogen in patient groups. The finding is consistent with the results of Danisova et al. (23). In contrast, Yahi D et al. showed that GCs treatment groups had no significant (p > 0.05) effect on estrogen concentrations (24). The inhibition of corticotrophin release mediated by GCs will result in adrenal atrophy and a decrease in the generation of adrenal androgens. GCs have been shown to have inhibitory effects on the synthesis and secretion of sex steroids, including luteinizing hormone (LH), follicle-stimulating hormone (FSH), testosterone, and growth hormone (GH). The suppression of pituitary gonadotropin production leads to a decrease in gonadal activation. In women, the release of luteinizing hormone (LH) in response to gonadotropin-releasing hormone (GnRH) is diminished. GCs were shown to induce a decrease in testosterone levels. Additionally, there is a reduction in follicle-stimulating hormone, which stimulates the synthesis of estrogen, ultimately resulting in a drop in estrogen levels (25, 26).

Regarding hematological markers, Table 3 presents an increase in RBCs and HB concentration. Ami Ballin’s also found similar results (27). Corticosteroids may increase the amount of hemoglobin and red blood cells (RBCs) in the peripheral circulation, possibly by stopping...
erythrophagocytosis (28). However, these results were contradicted by the findings of Larsen MK, in 2020, who found that there is no statistically significant variation seen in the hematological parameters with the administration of glucocorticoids (29).

GCs generally improve erythropoiesis (induce stress erythropoiesis) directly by activating glucocorticoid receptor (GR). Erythropoiesis refers to the biological process by which fully developed red blood cells are generated from pluripotent hematopoietic progenitor cells. This intricate process leads to the generation of around two million erythrocytes per second (30). Also, elevation of erythropoietin hormone (EPO) is a glycoprotein cytokine that is recognized for its pleiotropic effects on many cellular and tissue types, secreted by the kidney, stimulant production of bone marrow to RBCs and HB (31).

Data from Table (3), also showed that increase in the levels of circulating WBCs. Several mechanisms leads to an elevation in the number of polymorphonuclear leukocytes in the bloodstream, which occurs due to an accelerated entrance from the bone marrow and a reduced rate of elimination from the vascular compartment. Multiple mechanisms have been suggested to elucidate the underlying pathophysiology of the systemic corticosteroid-induced increases in white blood cell count. These mechanisms include an augmented release of neutrophils from the bone marrow, a delay in the process of apoptosis, a decrease in the migration of neutrophils into tissues, and a redistribution of neutrophils from the marginal to the circulating pool. On the other hand, the population of lymphocytes, eosinophils, monocytes, and basophils exhibits a decline after the administration of glucocorticoids (28, 32).

GCs prolong neutrophil survival by inhibiting their apoptosis (33). GCs may increase apoptosis in the eosinophil, this effect may lead to a reduction of eosinophil when exposed to corticosteroids (34).

Additionally, they observed a significant decrease in platelet counts in Patients’ groups who used TCS. Similarly, Royer et al. found that dexamethasone causes drug-induced thrombocytopenia (DITP) (35). However, Vogel et al. prednisolone and methylprednisolone have been reported to cause DITP (36, 37). In contrast, Praituan et al. concluded This use of steroids has been seen to result in a reduction in the synthesis of antibodies against platelets. Within two to four weeks of beginning steroid treatment, if it is successful, there will be an increase in the platelet count (38).

The most amazing finding, we can get from our research is that, when compared to the control group, blood levels of IL-6 in the patient groups have considerably decreased. This was in line with the findings of Gras MP et al., who reported that pro-inflammatory cytokines were down-regulated as TCS increased (39). Glucocorticoids prevent or decrease the whole inflammatory response to viral, physical, or immunologic stimuli by reducing both early and late inflammatory processes. The suppression of neutrophil and monocyte recruitment is a significant impact of glucocorticoids on the inflammatory process (28). The anti-inflammatory impact is also shown via the production of lipocortin, which acts as an inhibitor of phospholipase A2. This inhibition leads to a reduction in the generation of prostaglandins and leukotrienes. Topical corticosteroids exert their effects by directly modulating DNA activity, leading to an up-regulation of genes associated with anti-inflammatory responses. Additionally, they indirectly impede the activity of inflammatory transcription factors, such as NFkb, resulting in a down-regulation of genes associated with pro-inflammatory processes (40).

The results of our data was a very highly significant reduction of serum vitamin D levels in patient groups. Vitamin D insufficiency shown in control group, we considered both vitamin D insufficiency and Vit-D sufficiency as normal Vit-D states in this research (41). However, there are several factors that may affect the level of Vit-D including (Financial situation, weekly milk consumption, and time spent in the sun, using hijabs for social , and cultural considerations) (42-44). The present finding also supports the study of Sanchez-Armendariz . study which concluded that the use of TCS is correlated with a reduction in blood vitamin D levels (45). TCS has been shown to elevate the excretion of calcium in the urine and reduce the absorption of calcium in the intestines, leading to a net reduction in calcium levels via its anti-vitamin D mechanism (45, 46).

5. Conclusion
Topical corticosteroids are extensively used pharmaceutical agents, mostly for the treatment of dermatological conditions. However, they can be misused for their cosmetic effects as fairness creams. The majority of women are aware that TCS may result in cutaneous adverse effects. Nevertheless, the general population remains ignorant of the systemic adverse effects. Educational activities targeting the general public are suggested to address the systemic deterioration, including its hematological and hormonal implications. Since general practitioners (GPs) and pharmacists often operate as the initial point of contact between the majority of patients and TCS, these activities must be focused on them.

6. Acknowledgment
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7. Funding
We were not funded by anyone.

8. Conflicts of Interest
No think declared.

9. Ethics Statements
This was a cross-sectional observational multicenter study carried out from October 2022 to March 2023.
Patients were admitted to outpatients dermatology clinics at Abu-al Khasib Hospital in Basra City, Iraq. Informed consent was obtained according to the Helsinki Declaration, and the study was authorized by the ethical committee at the Basra University College of Pharmacy (EC 10 in 2022).

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التأثيرات الظاهرة الجهازية للكلوبيتازول الموضعي ومستحضرات التجميل المزيفة على النساء العراقيات

الخلاصة

تستخدم الكورتيكوستيرويدات الموضعية على نطاق واسع لعلاج الأمراض الجلدية. نمو الحظ، هناك العديد من الأثر السلبي (المحيطي والجهازي). هذه الأثر الظاهرة قابلة للمقارنة مع تلك التي لوحظت عند إعطاء الجلايكورتيكوريدات بشكل جهادي، ولكنها عادة ما تكون أقل حدة. الهدف: تقييم الأثر الظاهرة الجهازية للكلوبيتازول الموضعي (TCL) ومستحضرات التجميل المزيفة (CCP) على النساء العراقيات. التطور والعرض: كانت هذه دراسة رصدية متقطعة؛ تم إجراؤها في الفترة من إبريل 2022 إلى مارس 2023. علاج النساء المصابات بمرض الجلد الجراحي الفعال والمثالي في مدينة عراق، العراق. يمكن تصنيف العلاج إلى مجموعتين: المجموعة الأولى من الأشخاص الذين استخدموا TCL الموضعية (ن = 31)، بينما تتألف المجموعة الثانية من المرضى الذين عُدِّلوا من CCP (ن = 32)، وتم تعيين المشاركين المتبقيين كمجموعة مراقبة (ن = 32). يتم طبب جلدية متخصص بالإجراء TCs (Vit-D) وYLyt-D (بالإنترلوكون 6 - IL6). عد عدد عينات الدم لإجراء الفحوصات المخبرية. النتائج: قام بعض الفيتامينات (Vit-D) وYLyt-D (بالإنترلوكون 6 - IL6) ومستويات الليمفوجلوبين (HB)، ومتوسطات المريضين، والإستروجين وتقليل تركيزات الكورتيزول بشكل ملحوظ. قامت برفع مستوى كلوبيتازول بشكل ملحوظ، وتقليل تركيزات الكورتيزول بشكل ملحوظ. حيث ينخفض مستوى كلوبيتازول بشكل ملحوظ، وتقليل تركيزات الكورتيزول بشكل ملحوظ. حيث ينخفض مستوى كلوبيتازول بشكل ملحوظ، وتقليل تركيزات الكورتيزول بشكل ملحوظ. حيث ينخفض مستوى كلوبيتازول بشكل ملحوظ، وتقليل تركيزات الكورتيزول بشكل ملحوظ. حيث ينخفض مستوى كلوبيتازول بشكل ملحوظ، وتقليل تركيزات الكورتيزول بشكل ملحوظ. حيث ينخفض مستوى كلوبيتازول بشكل ملحوظ، وتقليل تركيزات الكورتيزول بشكل ملحوظ. حيث ينخفض مستوى كلوبيتازول بشكل ملحوظ، وتقليل تركيزات الكورتيزول بشكل ملحوظ. حيث ينخفض مستوى كلوبيتازول بشكل ملحوظ، وتقليل تركيزات الكورتيزول بشكل ملحوظ. حيث ينخفض مستوى كلوبيتازول بشكل ملحوظ، وتقليل تركيزات الكورتيزول بشكل ملحوظ. حيث ينخفض مستوى كلوبيتازول بشكل ملحوظ، وتقليل تركيزات الكورتيزول بشكل ملحوظ. حيث ينخفض مستوى كلوبيتازول بشكل ملحوظ، وتقليل تركيزات الكورتيزول بشكل ملحوظ. حيث ينخفض مستوى كلوبيتازول بشكل ملحوظ، وتقليل تأثيرات الجانبية والجهازية. ومع ذلك، لا يزال عناية الناس بجهل الآثار الظاهرة الجهازية. وتشير النتائج إلى أن استخدام الكورتيكوستيرويدات الموضعية يمكن أن يكون مفيدًا في معالجة المشاكل الجلدية. ومع ذلك، لا يزال عناية الناس بجهل الآثار الظاهرة الجهازية. وتشير النتائج إلى أن استخدام الكورتيكوستيرويدات الموضعية يمكن أن يكون مفيدًا في معالجة المشاكل الجلدية.