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Original Research Article

To study the effect of topical clobetasol propionate cream 0.05% w/w on blood pressure, blood sugar and blood calcium level in patients requiring topical corticosteroids therapy

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Abstract
Corticosteroids are used to suppress the immune system and reduce inflammation in different conditions, ranging from skin diseases to brain tumors. Corticosteroids are administered by parenteral, oral and topical route. Topical corticosteroids are considered to have safer than oral corticosteroids. There are different topical corticosteroids preparations used in skin diseases. E.g. mometasone clobetasol, betamethasone, beclomethasone, fludrocortisone and desonide. Use of these steroids depends on anatomic location and strength of corticosteroids.
Clinical effectiveness of topically applied medications depends on the ability of the active ingredient to leave its vehicle and penetrate into the epidermis. Adverse effects of corticosteroids depend on duration of treatment, potency of corticosteroids and area of involvement. We have investigated effect of topical Clobetasole propionate on blood pressure, blood sugar level and blood calcium level after seven day application in patients requiring topical clobetasol therapy. Area of application measured by "Palmar method", blood pressure by sphygmomanometer, blood sugar by glucometer, calcium investigation by O – cresolphthalein complexone method, concentration of clobetasol propionate by HPLC method. After seven day application, clobetasol propionate had raised systolic blood pressure. The systolic blood pressure was raised more than the diastolic blood pressure. Blood sugar level was raised by clobetasol propionate. Clobetasol propionate after once daily application for seven days did not change blood calcium levels. As area of application of topical steroids increase there were increases in blood concentration of corticosteroids.
Keywords: Topical, Clobetasole propionate cream, blood pressure, blood sugar, blood calcium

Introduction

Corticosteroids are involved in a wide range of physiological processes, including stress response, immune response and regulation of inflammation, carbohydrate metabolism, protein catabolism, blood electrolyte levels, and behavior [1].
Corticosteroids are used to suppress the immune system and reduce inflammation. Corticosteroids are used in different conditions, ranging from skin diseases to brain tumors. They are used to treat allergic rhinitis, asthma, hay fever, chronic obstructive pulmonary disease (COPD), atopic eczema, painful and inflamed joints, muscles and tendons, lupus, ulcerative colitis, inflammatory bowel disease (IBD) – including Crohn's disease, giant cell arteritis, polymyalgia rheumatic arthritis and multiple sclerosis (MS). Corticosteroids used to replace certain hormones in Addison's disease that are not produced by the body.
Corticosteroids are administered by parenteral, oral and topical route. Topical corticosteroids are considered to have safer than oral corticosteroids. There are different topical corticosteroids preparations used in skin diseases. e.g. mometasone clobetasol,

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betamethasone, beclomethasone, fludrocortisone and desonide. Use of these steroids depends on anatomic location and strength of corticosteroids.

Clinical effectiveness of topically applied medications depends on the ability of the active ingredient to leave its vehicle and penetrate into the epidermis [2].

In the dermatological diseases, topical corticosteroids are used for few days to few weeks and different corticosteroids used according to location (site) of application, potency and severity of disease. More potent corticosteroids are used for longer duration in the treatment of diseases like discoid lupus erythematous, psoriasis etc. Percutaneous absorption of topical corticosteroids is determined by many factors such as anatomical site of application, formulation, vehicle, integrity of the epidermal barrier, concentration and frequency of application and use of occlusive dressing. Corticosteroids are known to cause multitude of adverse effects *viz.* elevation of blood pressure, derangement of blood sugar levels, perforation of peptic ulcer, *etc*., when used orally, parenterally depending on dose and duration. Likewise, the adverse effects of topical corticosteroids also depend on duration of treatment, potency of corticosteroids and area of involvement [3].

Thus, the study was undertaken to estimate the effect of clobetasol propionate on the blood pressure, blood calcium and blood sugar level and to estimate the blood concentration of topically applied corticosteroids in patients requiring topical corticosteroid therapy and to correlate these effect with the concentration of clobetasol in blood.

Material and Methods

This study was conducted in MGM Medical College and Hospital Kamothe, Navi Mumbai in patients from dermatology outpatient department (OPD). Total number of 10 healthy patients who were not using corticosteroid treatment for more than one month prior to inclusion in the study or they were freshly diagnosed and they required topical steroid therapy were included.

Study was carried out after the approval of Institutional Ethics Committee MGM Medical College, Kamothe Navi Mumbai and obtaining proper consents from each healthy volunteer and patients before enrolling in the study.

Before enrollment, patients were explained each and every parameter of study including use of study, procedure of blood pressure measurement, blood sugar and blood calcium level estimation and blood samples collection.

All details of patients were taken while proceeding the study, name of patient, age, sex, disease history, drug history, general examination, affected body surface area was measured by palmar method [4], blood pressure was measured before and after seven days of treatment by sphygmomanometer, blood sugar level was measured before and after seven days of treatment by glucometer, blood calcium level was measured by biochemical method by collection of blood sample in plain tube before and seven days after treatment, blood collected in EDTA tube for estimation of corticosteroid in blood by HPLC method seven days after drug treatment.

Ten patients were enrolled those who required topical clobetasol propionate cream 0.05% w/w. Blood pressure, blood sugar and blood calcium level were measured before and 7 days after drug application. Three ml of blood was collected in plain tube after patients enrolled in study for calcium estimation and on the 7^{th} day after drug application, two ml of blood was collected in EDTA tube for clobetasol propionate concentration and three ml of blood was collected in plain tube blood calcium level estimation, four hours after drug application on the affected part.

Inclusion criteria

1. Human patients with skin diseases who required topical corticosteroid therapy & who were willing to participate in the study.
2. Vitiligo, eczema, psoriasis and lichen planus disease patients.
3. Age 18 to 50 years
4. Patients who did not use corticosteroid treatment before one month.
5. Freshly diagnosed patients.

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Exclusion criteria

1. Patients who took corticosteroids in previous one month.
2. Hypertensive and hypotensive patients.
3. Obese patients.
4. Diabetic patients

Measurement of body surface area

Affected body surface area were measured by palmar method[4] when patients for the first time attended skin OPD and after seven days of drug application also investigate severity of disease and affected site.

Palmar method

- Identified the affected site.
- Area of affected site was measured by study participant's hand including digits.
- One patients hand is nearly equal to 1% body surface area

Blood pressure measurement

Group B: Blood pressure was measured when study participant for the first time attended skin OPD and after seven days of drug application, on right hand in sitting position by using mercury sphygmomanometer.

Method of blood pressure measurement

- **Subject**
- **Position:** Seated.
- The flexed elbow on the table at the level of the heart.

Procedure

- The cuff was wrapped around the upper arm of right hand with the cuff's lower edge, one inch above the antecubital fossa.
- The stethoscope's bell was lightly pressed over the brachial artery just below the cuff's edge.
- The cuff was rapidly inflated to 180 mmHg. Released air from the cuff at a moderate rate (3mm/sec).
- The stethoscope sounds were heard and simultaneously observed the sphygmomanometer. The first knocking sound (Korotkoff) was the subject's systolic pressure and when the knocking sound disappears, that was the diastolic pressure.

Blood collection

- **Group B:** Blood samples were collected before and seven days after starting drug treatment.
- **Method:** 21 gauge needles and 10 ml syringes were used for blood collection, asked the study participant with the arm extended to form a straight-line form shoulder to wrist. Tourniquet was applied 3-4 inches above the collection site, the puncture site was cleaned with the 70% alcohol swab and venipuncture was performed. Blood samples were collected in EDTA tube (3 ml) and plain tube (2 ml) from group A volunteers and group B study participant for estimation of concentration of drug in blood and 3 ml of blood samples collected in EDTA tube from group C study participant for estimation of concentration of drug in blood.
- **Serum separation and storage:** Once the blood samples were collected quickly transferred them into tubes with tops or caps. The samples were centrifuged at 2000 rpm for 15 minutes at room temperature. After centrifugation, serum was removed and placed into a polypropylene microcentrifuge tube. The serum samples were stored in

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Pharmacology laboratory of MGM medical collegeat -4 degrees centigrade.

- **Drug standard collection and storage:** standard drug samples of Clobetasol propionate, Betamethasone dipropionate, Mometasone furoate were purchased from Sigma Aldrich and stored in refrigerator as directed by company

Blood sugar measurement

- **Group B:** Blood sugar levels were measured when patients first time attended skin OPD and after seven days by glucometer.

Procedure

- Middle finger was cleaned with the 70% alcohol swab
- The finger was pricked with lanc*et al*.lowed the sample of blood to flow right onto the glucose strip.
- Glucose strip then inserted into the glucometer.
- The reading appeared on the glucometer was recorded.

Blood calcium measurement: Serum samples stored in plain tube were used for calcium investigation. Estimation of calcium done by OCPC method (O – cresolphthalein complexone)

Principle: Calcium in alkaline medium combines with O- cresolphthaline complexone and forms a purple coloured complex. Intensity of the colour formed is directly proportional to the amount of calcium present in the sample.

Calcium + OCPC ⟶ Purple colour complex

Reagent: Buffer reagent (L1), colour reagent (L2), Calcium standard (10 mg/ml) (S) Reagents were ready to use.

Table 1: Procedureof O – cresolphthalein complexone method

Addition Sequence	Blank (ml)	Standard (ml)	Test (ml)
Buffer Reagent (L1)	0.5	0.5	0.5
Colour Reagent (L2)	0.5	0.5	0.5
Distilled Water	0.2	---	---
Calcium Standard (S)	---	0.2	---
Sample	---	---	0.2

Incubated at room temperature (25 0^{c}) for 5 min. measured the absorbance of standard (Abs S) and Test sample (Abs T) against the blank, within 60 min.
Wavelength/ filter: 570 nm (Hg 578) / Yellow
Temperature: R.T
Light path: 1 cm
Calculation: Calcium in mg/dl = (Abs T ÷ Abs S) × 10

Estimation of corticosteroids concentration in the blood

Instruments: Weighing balance, refrigerated centrifuge, glassware's were used from pharmacology laboratory. High performance liquid chromatography instrument from OMICS research laboratory in MGM medical college, Navi Mumbai.
Weighing balance**:** Weight balanced was standardised with standard weights before the use and mainly used to weight standard drugs.
Cooling centrifuge**:** Samples were centrifuged at – 6 °C and at 6000 rpm.

Glassware: Glassware were washed with soap and rinsed with distilled water and dried in the oven at temperature 40 °C.

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HPLC instrument

Instrument and software: LC (liquid chromatography) – 2010CHT liquid chromatograph, Shimadzu. Software: Lab solution lite version 5.5. HPLC instrument was standardized as per guideline given by the manufacturer of HPLC in OMICS research laboratory in MGM medical college.

Chemicals

Mobile phase: HPLC grade methanol, water

Diluents: HPLC grade methanol and acetonitrite

Extracting solvent: Ethyl acetate used as protein precipitator, extractor same as diluents.

Clobetasol propionate

HPLC method standardization: 5 mg standard Clobetasol propionate dissolve in 50 ml methanol to get concentration of 100 µg/ml and then serially dilutions were made in the concentration of 10 ng/ml, 20ng/ml, 30ng/ml, 40 ng/ml, 50ng/ml, 60ng/ml.
0.4 ml of Clobetasol propionate from each dilution was added in 1 ml plasma in separate test tube and mixed properly.

Extraction procedure

Liquid Liquid Extraction: 100µl of plasma added in 1200µl of ethyl acetate (extracting solvent) in eppendorf tube and kept in vertex for proper mixing, then the eppendorf tube centrifuged at 6000 rpm at -6 °C for 10 minutes. The supernatant liquid was removed from eppendorf tube transferred into small test tube. Then small test tubes were kept on simple heater at 40 °C for evaporation of volatile solvent. Then remaining solid residue dissolved in 400 µl of methanol and run in HPLC.

HPLC parameter

Mobile Phase: Methanol: Water (80:20)
Flow Rate: 1 ml/min
Retention time of drug: 4.6 min
Column: C18
Wavelength: 254nm

After running different dilutions of Clobetasol propionate in HPLC at given HPLC parameter gives reading [area under curve (AUC)]. We plotted graph AUC Vs concentration, drown straight line.

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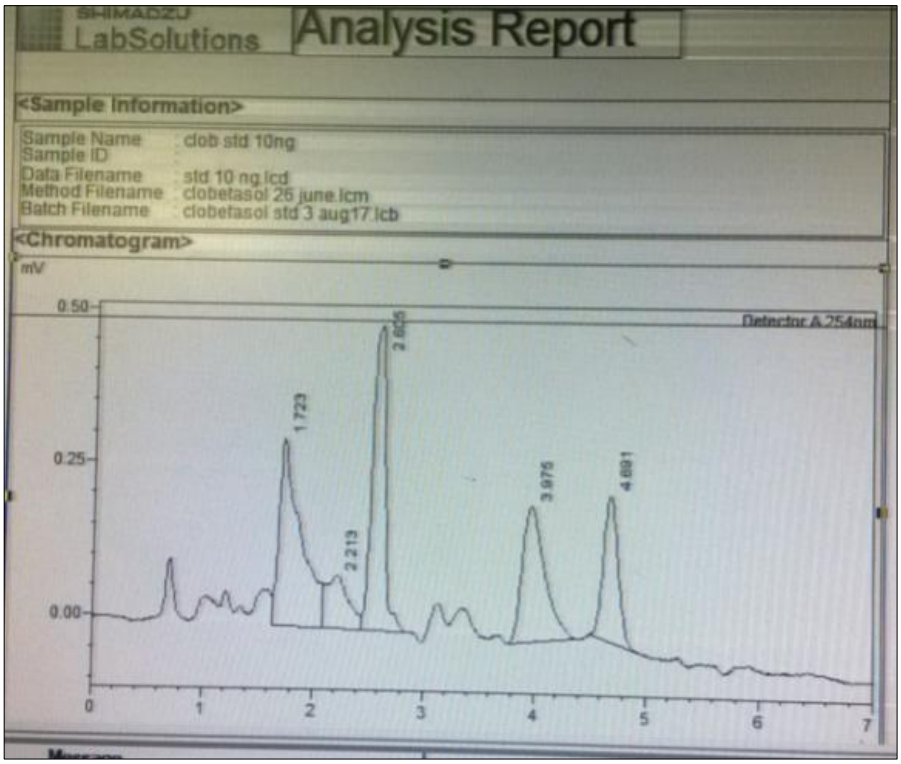
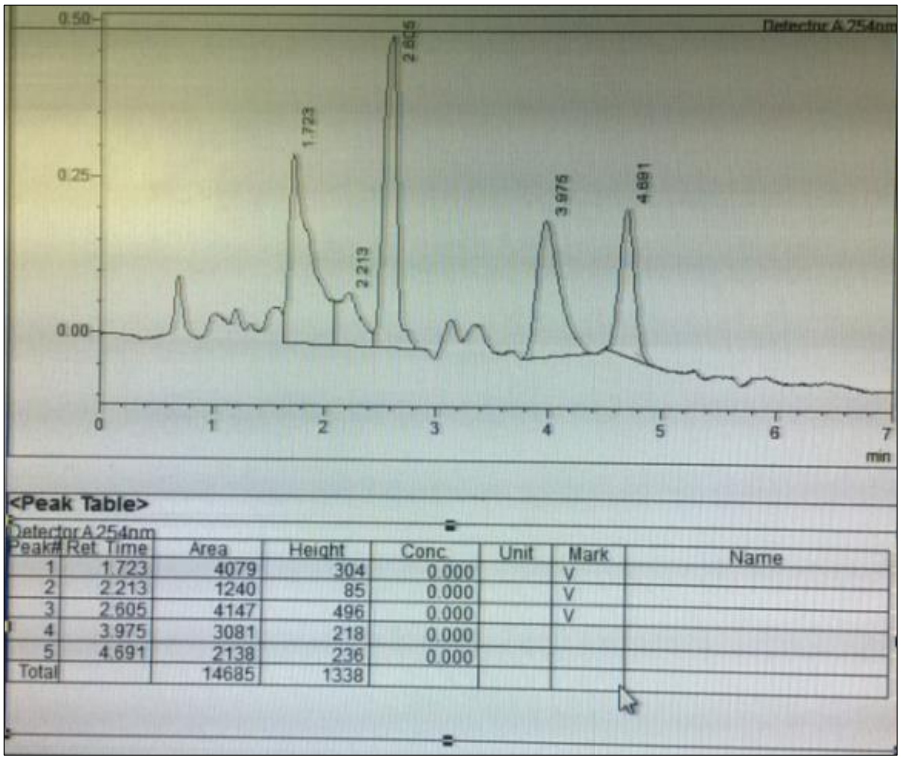
HPLC graph of Clobetasol propionate
Clobetasol propionate 10 ng/ml





<Peak Table>
Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	1.723	4079	304	0.000		V	
2	2.213	1240	85	0.000		V	
3	2.605	4147	496	0.000		V	
4	3.975	3081	218	0.000			
5	4.691	2138	236	0.000			
Total		14685	1338				

Clobetasol propionate 30 ng/ml

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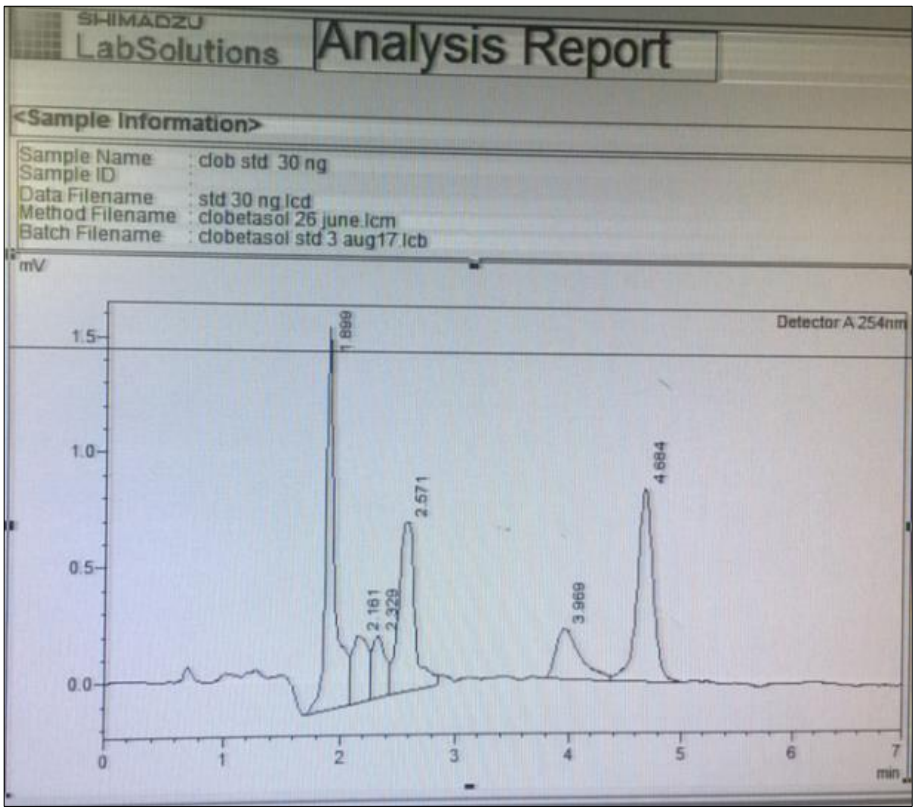

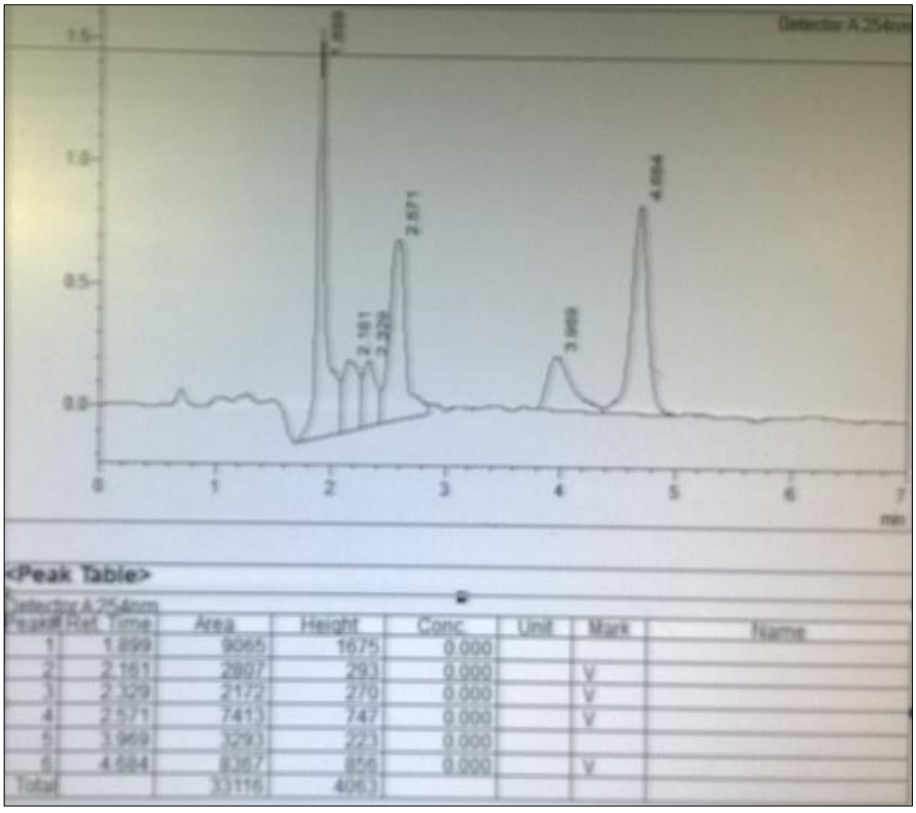

Table 2: Concentration of Clobetasol Vs AUC

Concentration of clobetasol in ng	AUC
10	2138
20	5311
30	8367
40	10678
50	13943
60	14159

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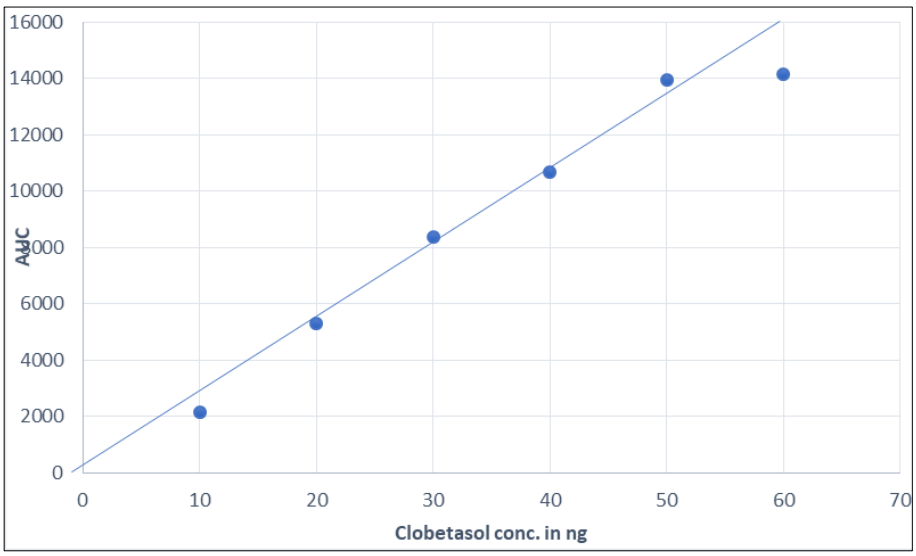

Fig 1: Concentration of clobetasol Vs AUC

Serum samples
Extraction procedure

Liquid liquid extraction: 100 µl of serum sample added in 1200 µl of ethyl acetate (extracting solvent) in eppendorf tube and kept on the vertex for proper mixing, then the eppendorf tube centrifuged at 6000 rpm at -6 ^{0}c for 10 minutes. The supernatant liquid was removed from eppendorf tube transferred into small test tube. Then small test tubes were kept on simple heater at 40 0c for evaporation of volatile solvent. Then remaining solid residue dissolved in 400 µl of methanol and run in HPLC.
HPLC gave reading (AUC), we compared AUC with plotted standard graph gave unknown concentration of Clobetasol propionate in serum sample.

Recovery experiment

The recovery of clobetasol propionate determined by comparing the peak area of the extracted plasma samples of six dilutions with control samples. As control equivalent amount of Clobetasol propionate was added directly into the mobile phase and injected.
Recovery was assessed by comparing the chromatographic peak area of clobetasol propionate of the extracted the plasma standard to those obtained from equivalent amount of the clobetasol propionate directly into the mobile phase.
The extraction recovery of each concentration was calculated using the following equation.
Recovery = (Peak area of extracted analyte/Peak area of non-extracted analyte) × 100

Table 3: Recovery experiment of clobetasol propionate

Concentration (ng/ml)	AUC extracted analyte	AUC non-extracted analyte	Percentage
10	2138	2394	89.3%
20	5311	6119	86.7%
30	8367	9856	84.9%
50	10678	12052	88.6%
70	13943	15339	90.9%
100	14159	17059	83.0%

Mean recovery: 86.9%
Statistical analysis: Calculated mean, standard deviation and applied paired t-test.

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Results

This study was conducted in MGM Medical College and Hospital Kamothe, Navi Mumbai in patients from Dermatology OPD. This study included total number of 10 patients who were not using corticosteroid treatment for more than one month or they were freshly diagnosed were included.

Ten patients were enrolled in test subgroup 4. Patients with age ranging between 26 years and 48 years, there were 9 males and 1 female those who required topical clobetasol propionate cream 0.05% w/w. Blood pressure, blood sugar and blood calcium were measured before and 7 days after drug application. 3 ml of blood was collected in plain tube after patients enrolled in study for calcium estimation. On the 7^{th} day four hours after drug application on the affected part two ml of blood was collected in EDTA tube for clobetasol propionate concentration and three ml of blood was collected in plain tube for blood calcium level estimation.

Table 4: Blood pressure (mm Hg)

Sr. No.	Age in year	ABSA%	Sex	Baseline BP (mm Hg)		7^{th} day BP (mm Hg)		Concentration of clobetasol propionate in ng/ml
				S	D	S	D	
1	37	30	F	126	86	138	90	17
2	35	20	F	128	80	136	80	15
3	49	04	M	130	86	134	88	12
4	37	0.5	M	134	88	138	90	09
5	37	10	M	132	86	140	86	11
6	20	10	M	126	82	134	82	17
7	32	10	M	118	76	126	80	13
8	24	40	M	116	82	128	88	22
9	32	12	M	128	82	134	82	11
10	42	08	F	124	86	130	90	10
Mean (mm Hg)				126.2 ± 5.69	83.4 ± 3.66	133.8 ± 4.57	83.6 ± 4.20	13.7 ± 4.03

S = Systolic blood pressure; D = Diastolic blood pressure
ABSA: Affected body surface area

The baseline systolic blood pressure ranged from 113 mm Hg to 134 mm Hg (mean 126.2 mm Hg, SD = 5.69). The diastolic blood pressure was between 76 mm Hg and 86 mm Hg (mean 83.4 mm Hg, SD = 3.66) on first day. Seven days after clobetasol propionate cream application, the systolic blood pressure was raised on an average by 7.6 mm Hg whereas rise in diastolic blood pressure was 0.2 mm Hg. After seven days of application of Clobetasol propionate the systolic blood pressure was increased significantly over baseline value. While diastolic blood pressure was not increased significantly.

Clobetasol propionate concentration in blood after seven days of drug application was in range between 09 ng/ml to 17 ng/ml and mean blood concentration was 13.7 ± 4.03.

Table 5: Blood sugar (mg/dl)

Sr. No.	Age in year	ABSA%	Sex	Blood sugar (mg/dl)		Concentration of clobetasol propionate in ng/ml
				Before	After	
1	37	30	F	83	98	17
2	35	20	F	87	105	15
3	49	04	M	78	90	12
4	37	0.5	M	81	86	09
5	37	10	M	94	110	11
6	20	10	M	87	96	17
7	32	10	M	90	102	13
8	24	40	M	76	104	22
9	32	12	M	84	96	11
10	42	08	F	92	100	10
Mean (mg/dl)				85.2 ± 5.9	98.7 ± 7.15	13.7 ± 4.03

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ABSA: Affected body surface area

The baseline blood sugar level ranged from 76 mg/dl to 94 mg/dl (mean 85.2 mg/dl, SD = 5.9) on first day. Seven days after clobetasol propionate cream application, the blood sugar level ranged from 86 mg/dl to 110 mg/dl (mean 98.7 mg/dl, SD = 5.9) Blood sugar level was raised on an average by 13.5 mg/dl. There was significant increase in blood sugar level.
Clobetasol propionate concentration in blood after seven days of drug application was in range between 09 ng/ml to 17 ng/ml and mean blood concentration was 13.7 ± 4.03.

Table 6: Blood calcium (mg/dl)

Sr. No.	Age in year	ABSA%	Sex	Blood calcium (mg/dl)		Concentration of clobetasol propionate in ng/ml
				Before	After	
1	37	30	F	8.1	8.2	17
2	35	20	F	9.3	9.4	15
3	49	04	M	8.7	8.7	12
4	37	0.5	M	8.5	8.6	09
5	37	10	M	10.5	10.5	11
6	20	10	M	8.9	9.0	17
7	32	10	M	9.1	9.1	13
8	24	40	M	8.5	8.6	22
9	32	12	M	7.9	7.9	11
10	42	08	F	8.9	8.9	10
Mean (mg/dl)				8.8 ± 0.7	8.9 ± 0.7	13.7 ± 4.03

ABSA: Affected body surface area

The baseline blood calcium level ranged from 7.9 mg/dl to 10.5 mg/dl (mean 8.8 mg/dl, SD = 0.7) on first day. Seven days after clobetasol propionate cream application, the blood calcium level ranged from 7.9 mg/dl to 10.5 mg/dl (mean 8.9 mg/dl, SD = 0.7). There was minor change in the blood calcium level. This change was not significant clinically. No patients developed frank hypercalcemia.
Clobetasol propionate concentration in blood after seven days of drug application was in range between 09 ng/ml to 17 ng/ml and mean blood concentration was 13.7 ± 4.03.

Table 7: Comparison of blood pressure, blood sugar and blood calcium before and after clobetasol propionate administration in patients

		Mean	SD
SBP (mm Hg)	Before	126.2	5.69
	After	133.8	4.57
DBP (mm Hg)	Before	83.4	3.66
	After	83.6	4.20
Blood Sugar (mg/dl)	Before	85.2	5.90
	After	98.70	7.15
Blood Calcium(mg/dl)	Before	8.8	0.7
	After	8.9	0.7

Significant at $p < 0.05$; Name of test: t-test (paired)

Comparison of systolic blood pressure and diastolic blood pressure before and after clobetasol propionate topical application in patients

Mean systolic and diastolic blood pressure before the clobetasol propionate application was 126.2 ± 5.69 mm Hg and 83.4 ± 3.66 mm Hg and after the clobetasol propionate cream application was 133.8 ± 4.57 mm Hg and 83.6 ± 4.20 mm Hg respectively.
There was significant increase in systolic blood pressure (P = 0.0040) and there was no

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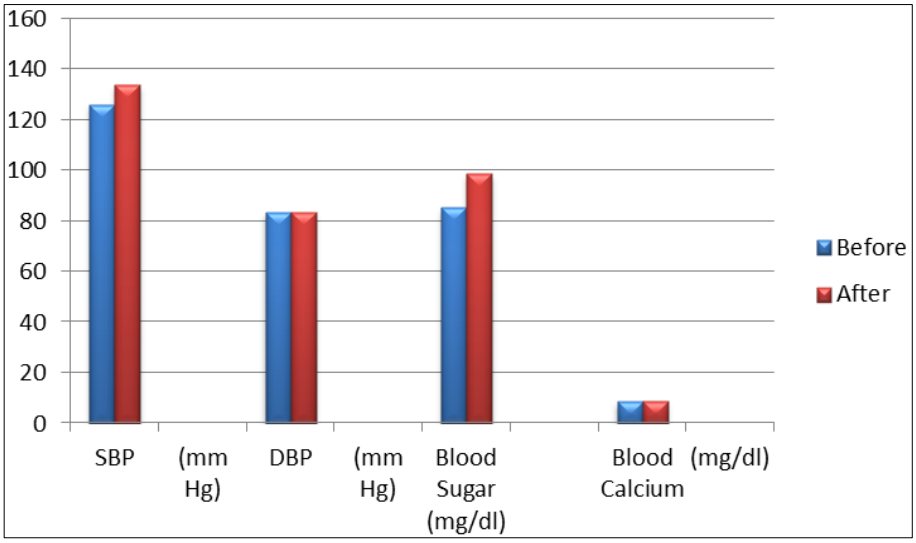
significant difference in diastolic blood pressure (P = 0.2273) after the clobetasol propionate application in patients

Comparison of blood sugar level before and after clobetasol propionate topical application in patients

Mean blood sugar level before the clobetasol propionate application was 95.20 ± 5.90 mg/dl and after the clobetasol propionate application was 98.7 ± 7.15 mg/dl.
There was significant increase in blood sugar level (P = 0.002) after the clobetasol propionate application in patients.

Comparison of blood calcium level before and after clobetasol propionate topical application in patients

Mean blood calcium level before the clobetasol propionate application was 8.8 ± 0.7 mg/dl and after the clobetasol propionate application was 8.9 ± 0.7 mg/dl respectively.
There was no significant difference in blood calcium level (P = 0.9026) after the clobetasol propionate application in patients



Significant at $p< 0.05$; Name of test: t-test (paired)

Fig 2: Comparison of blood pressure, blood sugar and blood calcium before and after clobetasol propionate administration in patients

Discussion

This study was conducted in MGM medical college and hospital Kamothe, Navi Mumbai. In this study, we have investigated effect of topical corticosteroids on systolic blood pressure, diastolic blood pressure, blood sugar level and blood calcium level after four hoursin healthy volunteers, seven days in patients who were not using corticosteroid treatment for more than one month and they were freshly diagnosed and more than one-month drug application in patients who were on topical corticosteroids for at least one month.

Blood pressure

In our study Clobetasol once daily for seven days has raised systolic blood pressure while diastolic blood pressure was normal. This is not surprising as clobetasol propionate is ultrahigh potent corticosteroid and get absorbed after single application also.
Clobetasol propionate concentration in blood after seven days application was 13.7 ng/ml respectively.
Whether it is applied once, daily once for seven days or daily once for continuous one month. Clinically, potency of steroid, concentration of steroid, area of application and how many

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times it is applied is very important. In long term local steroid therapy, doctor must keep watch on blood pressure and blood sugar level.

Clinical trial conducted in Australia by department of health and ageing of Australian government investigated that after clobetasol propionate shampoo application there were no difference in blood pressure after 4 weeks of application while after 6 weeks follow up blood pressure increases from 110/80 mm Hg to 132/104 mm Hg, irrespective of blood concertation of clobetasol propionate below lower limit of quantification. (< 0.20 ng/ml) [5].

In 1983 animal experiment conducted by Häusler A and coworkers on spontaneously hypertesive rat and normotensive wister rat, concluded that both rats responded with a significant elevation in average blood pressure after seven weeks of oral betamethasone treatment [6].

Koenen SV and co-workers conducted animal experiment in 2002 on pregnant baboon investigated that fetal blood pressure increased significantly after intramuscular betamethasone treatment [7].

A comparative animal study conducted by Derks J B *et al*. in 1997 concluded that prenatal betamethasone and dexamethasone treatment of late-gestation fetal sheep, in doses similar to those employed clinically, is associated with fetal cardiovascular, endocrine and behavioural effects. Both betamethasone and dexamethasone induce similar increases in fetal blood pressure [8].

Bartorelli A and co-workers in 1984 explained that 9-year-old boy suffering from exzematous dermatitis who was treated for 6 years with a daily dose of 100 mg of a dermatological ointment containing 9 alpha-fluoroprednisolone-21-acetate. At examination the patient's blood pressure was persistently 230/160 mm Hg [9].

In april 1986, Judith A. Whitworth and coworkers told that systolic blood pressure (SBP) was increased by both ACTH and hydrocortisone treatment, but more by ACTH [10].

In another study by Krishnankutty Sudhir and coworkers in 1989 showed that Oral hydrocortisone increases blood pressure, diastolic blood pressure remained unchanged, systolic blood pressure increased from 119 to 135 mm Hg [11].

A study conducted by Marinis Pirpiris and coworkers in 1992, also showed increase mean arterial pressure from 82±3 to 91 ±3 mm Hg by dexamethasone [12].

Another study conducted by Atsuhisa Sato and coworkers in 1995 showed glucocorticoid-induced hypertensionin elderly patients and/or in those with positive family history of essential hypertension [13].

In 1999 Dodic M and coworkers concluded that foetal exposure to maternal dexamethasone during defined developmental stage or 'window' programmes elevated blood pressure, which persists later in life [14].

From our results and from literature, it showed that corticosteroids increases blood pressure and change in blood pressure was more after oral administration than topical application. Ultra high potent corticosteroids increase only systolic blood pressure.

Blood sugar

In our study after seven days application raised the blood sugar level from 85.2% to 98.7 mg%. As area of drug application increases, blood concentration of corticosteroids also increases. This shows that continuous application of clobetasol propionate cream result in increased blood concentration that may increase blood sugar.

In 2009 study conducted by Peter Gonzalez and coworkers in patients with Diabetes mellitus they showed that Lumbosacral transforaminal and caudal epidural betamethasone injections are associated with statistically significant elevations in blood glucose levels in diabetic subjects [15].

Ramírez-Torres MA and co-workers in 2011 reported that betamethasone induced hyperglycemia was greater in insulin treated women with gestational or type 2 diabetes [16].

Study conducted by Jolley JA and coworkers in 2016 on pregnant women of diabetic and without diabetic, administration of betamethasone for threatened preterm delivery they find

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out that both subjects with and without diabetes demonstrate significant hyperglycemia after receipt of antenatal betamethasone [17].

Iwamoto T and co-workers in 2004 investigated that Steroid-induced diabetes mellitus was diagnosed if the patient had either a fasting glucose concentration of 126 mg/dl or greater, or a random glucose concentration of 200 mg/dl or greater [18].

In 2006 study conducted by Angela A and co-workers on diabetic patients, reported that blood glucose level increased in diabetic patients who received methylprednisolone injection [19].

Van Raalte DH and co-workersin 2013 investigated that prednisolone-induced impairment of insulin-stimulated capillary recruitment was paralleled by insulin resistance, increased postprandial glucose levels, hypertension and increased circulating resistin concentrations in healthy men [20].

From our study and most of literature shows absorbed concentration of corticosteroids affect blood sugar level mostly it's on higher side there is proportionate relation between blood concentrations of corticosteroids with sugar level.

Blood calcium

In our study clobetasol propionate hasn't changed the blood calcium level. Though there were absorption of clobetasol in blood but there was no effect on blood calcium.

Study conducted by C. Gennari, in 1993 revealed that low and high doses of betamethasone and high doses of prednisone induced a significant decrease in intestinal calcium absorption [21].

In 1981 Theodore J. Hahn *et al*. investigated that intestinal calcium absorption reduced by 31% after prednisone administration [22].

YasuoSuzuki and coworkers in 1983 studied Parathyroid function and calcium metabolism in 44 patients under glucocorticoid therapy conclude that urinary calcium excretion increased in patients under glucocorticoid therapy [23].

Most of the literature explained that corticosteroids decreases calcium absorption and increases excretion of calcium but not a single study corelated blood concentration of Clobetasol propionate with calcium level in the blood.

Conclusion

- Clobetasol propionate after once daily application for seven days did not change blood calcium levels.
- Blood sugar level was raised by clobetasol propionate
- After seven day application, clobetasol propionate had raised systolic blood pressure. The systolic blood pressure was raised more than the diastolic blood pressure.
- As area of application of topical steroids increase there were increases in blood concentration of corticosteroids.
- Topical corticosteroid preparations on application to skin get adsorbed substantially into systemic circulation and produced systemic adverse effects. Absorbed blood concentration of corticosteroids after topical application of corticosteroids depends on affected body surface area.
- After prolonged application of topical corticosteroid, there is increase in the blood pressure and blood sugar levels.
- For those patients, who are using dermal corticosteroids for prolonged periods and for larger area, there blood sugar and blood pressure must be checked periodically.

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