ORIGINAL ARTICLE

Effect of Topical Mometasone Furoate Cream (0.01 % w/w) on Blood Pressure, Blood Sugar and Blood Calcium Level

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Abstract:

Background: Corticosteroids are commonly administered for skin diseases over short durations, typically ranging from a few days to a few weeks. The choice of corticosteroid is based on its potency, which is determined by the application site and the severity of the condition. The adverse effects associated with corticosteroid use are influenced by their strength, the length of the treatment, and the extent of the affected area. *Material and Methods:* This study examined the impact of topical mometasone furoate on blood pressure, blood sugar, and blood calcium levels after seven days of application. Additionally, the study assessed the relationship between the absorbed concentration of corticosteroids and their effects on blood pressure, blood sugar, blood calcium, and the extent of the body surface area involved. *Result:* After seven days of mometasone furoate use, no significant changes were observed in blood pressure, blood sugar, or blood calcium levels. The extent of the drug-absorbing surface area was found to be directly proportional to the blood concentration of corticosteroids. The effects on blood pressure, blood sugar, and calcium levels were dependent on the absorbed concentration, which, in turn, was influenced by the drug-absorbing surface area. *Conclusion:* The application of Mometasone Furoate to skin lesions does not result in significant absorption into the bloodstream at measurable levels and absorb concentration of corticosteroids in the blood increases in proportion to the extent of the area treated with topical steroids. Mometasone Furoate did not cause any changes in either systolic or diastolic blood pressure, blood sugar or calcium levels after seven days.

Keywords: Topical, Mometasone Furoate cream, blood pressure, blood sugar, blood calcium.

Introduction:

Corticosteroids are primarily used for their anti-inflammatory properties and to suppress immune responses. They are prescribed for a wide range of conditions, from brain tumours to dermatological disorders. Common routes of administration include oral, parenteral, and topical, with topical corticosteroids generally considered safer than oral forms. Various topical corticosteroids, such as clobetasol, mometasone, beclomethasone, betamethasone, desonide, and fludrocortisone, are used in dermatological treatments. The choice of steroid is influenced by its potency and the anatomical site of application. In skin disorders, corticosteroids are typically prescribed for short periods, lasting from a few days to several weeks, with potency and treatment duration adjusted according to the severity and location of the condition. The adverse effects of corticosteroids are linked to their potency, duration of use, and the size of the treatment area. Higher potency corticosteroids are often used for extended periods in treating conditions like psoriasis and discoid lupus erythematous. The absorption of topically applied corticosteroids is influenced by several factors, including the formulation, type of vehicle, site of application, condition of the skin barrier, use of occlusive dressings, and frequency of application. Short-term use is generally associated with mild side effects such as skin reactions, electrolyte imbalances, and hyperglycaemia, while prolonged use can result in more severe issues like osteoporosis, hypertension, adrenal insufficiency, and other systemic effects.[1] This study aimed to evaluate the impact of Mometasone Furoate on blood pressure, blood calcium, and blood sugar levels, while also measuring the concentration of the drug absorbed into the bloodstream, and correlating these findings with the extent of topical application..

Material and Methods:

This study was an Observational Pilot Study conducted

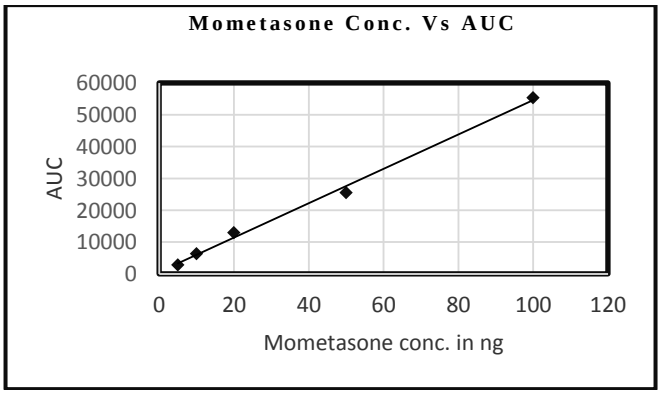
at the dermatology outpatient department (OPD) of MGM Medical College and Hospital, Kamothe, Navi Mumbai. The study was initiated following approval from the Institutional Ethics Committee, with informed consent obtained from all participants. Prior to enrolment, the patients were thoroughly briefed on all aspects of the study, including the procedures for measuring blood pressure, blood sugar, and blood calcium levels, as well as the process for collecting blood samples. Detailed information was recorded for each patient, including their name, age, sex, medical history, and the extent of the affected body surface area, which was measured using the palmar method.[2] Blood pressure was assessed before and after seven days of treatment using a sphygmomanometer, blood sugar levels were monitored using a glucometer, and blood calcium levels were measured using OCPC (O-cresolphthalein complexone) methods with samples collected in plain tubes. Corticosteroid levels were analysed through HPLC from blood samples collected in EDTA tubes seven days post-treatment. The study enrolled 10 patients whom had either not used corticosteroid treatment for at least one month prior to the study or were newly diagnosed and required topical steroid therapy and who required topical treatment with 0.01% w/w Mometasone Furoate cream. Blood pressure, blood sugar, and blood calcium levels were recorded both before treatment and seven days after application. For calcium estimation, 3 ml of blood was collected in plain tubes at the time of enrolment. On the 7th day, after the topical application of the cream, 2 ml of blood was drawn in EDTA tubes to determine Mometasone Furoate concentration, while another 3 ml was collected in plain tubes to reassess blood calcium levels, four hours after the cream was applied to the affected areas. Patients suffering from dermatological conditions necessitating the application of topical corticosteroids and expressing an interest in partaking in the study, diagnosed cases of vitiligo, eczema, psoriasis, or lichen planus, aged between 18 and 50 years, and who have refrained from corticosteroid use for a minimum of one month prior to the commencement of the study, as well as individuals newly diagnosed with such conditions were included in the study. Patients who have utilized corticosteroids within the previous month, individuals with hypertension or hypotension, obese patients, and those with diabetes were excluded from the study. Blood samples were drawn before and seven days after treatment initiation. 2ml blood in plain tubes was collected and serum was used for calcium. Three ml venous blood was collected in EDTA tubes and plasma was used for estimation of Mometasone Furoate by HPLC method as follows - A standard solution of 5 mg of Mometasone Furoate was dissolved in 50 ml of methanol to achieve a concentration of 100 µg/ml. Serial dilutions were then prepared, resulting in concentrations of 5 ng/ml, 10 ng/ml, 20 ng/ml, 50 ng/ml, and 100 ng/ml. For each dilution, 0.4 ml of Mometasone Furoate was added to 1 ml of plasma in separate test tubes and mixed thoroughly. Liquid-liquid extraction was done for standard curve as follows - 100 µl of plasma was mixed with 1200 µl of ethyl acetate, the extracting solvent, in an Eppendorf tube. The mixture was vortexed for proper blending and centrifuged at 6000 rpm at -6°C for 10 minutes. The supernatant was collected and transferred to small test tubes. These tubes were heated at 40°C to evaporate the volatile solvent, and the remaining solid residue was dissolved in 400 µl of methanol, which was then injected into the HPLC. After analyzing different dilutions of Mometasone Furoate using HPLC under the specified parameters, the area under the curve (AUC) was recorded. A graph of AUC versus concentration was plotted, resulting in a straight-line relationship (Table 1 and Graph 1). The same procedure was followed for estimation of Mometasone Furoate in patient's Serum samples. Statistical analysis was done by standard methods by calculated mean, standard deviation and applied paired t-test. Correlation was done by Karl Pearson test.

Results:

Table 1: Concentration of mometasone furoate Vs Area Under Curve

Concentration of mometasone furoate in ng	Area Under Curve
5	2836
10	6342
20	12946
50	25566
100	55311

Graph 1 : Concentration of mometasone Vs AUC



The same procedure was followed for estimation of Mometasone Furoate in patient's Serum samples. Statistical analysis was done by standard methods by calculated mean, standard deviation and applied paired t-test. Correlation was done by Karl Pearson test.

Table 2: Showing details of affected body surface area, blood pressure, blood sugar, serum calcium and concentration of mometasone furoate

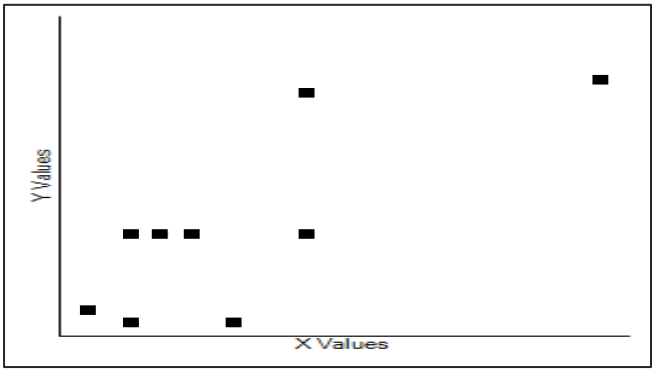
Sr. no.	Age in year	ABSA %	Sex	Baseline BP (mm Hg)		7th day BP (mm Hg)		Blood sugar (mg/dl)		Blood calcium (mg/dl)		Concentration of mometasone furoate (ng/ml)
				S	D	S	D	Before	After	Before	After	
1	29	05	F	126	82	126	82	92	94	7.9	7.9	02
2	21	20	F	116	78	120	80	111	114	8.5	8.4	19
3	42	20	M	110	70	115	74	84	88	8.6	8.8	08
4	25	10	F	126	82	130	82	94	100	9.3	9.3	08
5	29	40	M	118	80	124	82	92	96	9.0	9.0	20
6	52	08	M	124	84	126	84	84	82	8.5	8.6	01
7	35	15	M	132	86	136	88	86	90	9.4	9.5	01
8	53	10	M	126	82	130	82	76	78	8.3	8.3	08
9	38	08	M	122	84	124	84	88	92	8.5	8.5	08
10	52	12	M	134	86	140	88	82	90	7.8	7.9	08
Mean (mm Hg)				123.4± 7.28	81.4 ± 4.72	127.1 ± 7.31	82.6 0 ± 4.01	88.8 ± 9.20	92.4 ± 9.92	8.6 ± 0.5	8.6 ± 0.5	92.4 ± 9.92

S = Systolic blood pressure; D = Diastolic blood pressure ABSA: Affected body surface area The baseline systolic blood pressure ranged from 110 mm Hg to 134 mm Hg (mean 123.4 mm Hg, SD = 7.28). The diastolic blood pressure was between 70 mm Hg and 86 mm Hg (mean 81.4 mm Hg, SD = 4.72) on first day. The baseline blood sugar level ranged from 76 mg/dl to 110 mg/dl (mean 88.8 mg/dl, SD = 9.20) on first day. The baseline blood calcium level range from 7.4 mg/dl to 9.4 mg/dl (mean 8.6 mg/dl, SD = 0.5). After application of mometasone furoate cream for seven days, mean systolic blood pressure of 127.1 mm Hg (SD = 7) and diastolic blood pressure of 82.6 mm Hg (SD = 4.01) which were not higher than baseline value, mean blood sugar level 92.4 mg/dl (SD = 9.92)and mean blood calcium level mean 8.6 mg/dl(SD = 0.5).There is no significant statistically and clinically between blood pressure, blood sugar and blood calcium level. Mometasone furoate concentration in blood after seven days of drug application was in range between 01 ng/ml to 20 ng/ml and mean blood concentration was 8.3 ± 6.65mg/dl.

Table 3: Comparison of blood pressure, blood sugar and blood calcium before and after mometasone furoate administration in patients

		Mean	SD
SBP (mm Hg)	Before	123.4	7.28
	After	127.1	7.31
DBP (mm Hg)	Before	81.4	4.72
	After	82.6	4.01
Blood Sugar (mg/dl)	Before	88.8	9.20
	After	92.4	9.92
Blood Calcium (mg/dl)	Before	8.6	0.5
	After	8.6	0.5
significant at P < 0.05 ; Name of test : t-test (paired)			

Graph 2: Correlation between affected body surface area (X axis) and blood concentration(Yaxis)



Value of correlation(R) is 0.7629. This shows strong positive correlation between Affected body surface area and blood concentration of corticosteroid, which means that high affected body surface area scores go with high blood concentration of corticosteroid.

Discussion:

The study aimed to evaluate the effects of topical Mometasone Furoate on systolic and diastolic blood pressure, blood sugar levels, and blood calcium levels in patients who had not used corticosteroids for at least one month and were recently diagnosed. Our findings indicated that the application of Mometasone Furoate over seven days did not significantly alter systolic or diastolic blood pressure in the patients. This lack of change might be attributed to the drug's low potency and its rapid metabolism within the skin. The concentration of Mometasone Furoate in the blood after seven days was 8.3 ng/ml. Previous studies support the idea that corticosteroids can raise blood pressure, though the extent of this effect varies depending on the route of administration. For instance, an animal study conducted by Häusler and colleagues demonstrated that rats treated with oral betamethasone for seven weeks experienced a notable increase in blood pressure[3]. Similarly, Koenen et al. found a significant rise in fetal blood pressure after intramuscular betamethasone administration in pregnant baboons[4]. Other research, such as the work by Derks et al., showed that prenatal administration of corticosteroids in fetal sheep increased fetal blood pressure and had cardiovascular effects[5].Clinical studies, like Bartorelli's report in 1984 of a 9-year-old treated with a potent corticosteroid ointment, showed extremely elevated blood pressure (230/160 mm Hg) after long-term use[6].In april 1986, Judith A. Whitworth and co-workers told that systolic blood pressure (SBP) was increased by both ACTH and hydrocortisone treatment, but more by ACTH.[7]In another study by Krishnankutty Sudhir and co-workers showed that Oral hydrocortisone increases blood pressure, diastolic blood pressure remained unchanged, systolic blood pressure increased from 119 to 135 mm Hg.[8]A study conducted by Marinis Pirpiris and co-workers also showed increase mean arterial pressure from 82±3 to 91 ±3 mm Hg by dexamethasone.[9]Another study conducted by Atsuhisa Sato and coworkers showed glucocorticoid-induced hypertension in elderly patients and/or in those with positive family history of essential hypertension.[10]Dodic M and co-workers concluded that foetal exposure to maternal dexamethasone during defined developmental stage or 'window' programmes elevated blood pressure, which persists later in life.[11]Case-control study conducted by Marie-Josée Martel and coworkers explained that, there was no significance dose-response relation was observed between inhaled corticosteroids and pregnancy induced hypertension or pre-eclampsia. Oral corticosteroids were significantly associated with the risk of pregnancy induced hypertension.[12] 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. Molecular weight of mometasone furoate is 521.4 respectively. Weight for weight there will be lessor number of molecules of mometasone and plus it is the least potent hence mometasone does not produced effects on blood pressure.However, in our study, the low systemic absorption and potency of Mometasone Furoate may explain the absence of such changes in blood pressure. Mometasone Furoate also had no effect on blood sugar levels after seven days of application. This contrasts with studies on other corticosteroids, such as the one by Gonzalez et al. which demonstrated significant blood glucose increases in diabetic patients after betamethasone injections[13]. Similarly, Ramírez-Torres and colleagues reported hyperglycemia in insulin-treated women after betamethasone administration[14]. Jolley et al. also noted that betamethasone raised blood glucose levels in both diabetic and non-diabetic pregnant women[15].Iwamoto T and co-workers 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.[16]Other studies have linked corticosteroids like prednisolone and methylprednisolone to increased glucose levels, particularly in diabetic patients[17,18]. Our study did not replicate these findings with Mometasone Furoate, likely due to its minimal systemic absorption. There was no observed change in blood calcium levels after the application of MometasoneFuroate. The drug did absorb into the bloodstream, but the levels were not sufficient to cause any changes in calcium homeostasis. This contrasts with findings from studies on other corticosteroids. Gennari demonstrated that both low and high doses of betamethasone, as well as prednisone, reduced intestinal calcium absorption[19]. In another study, Hahn et al. reported a 31% reduction in calcium absorption following prednisone administration[20]. Suzuki and colleagues further found that glucocorticoid therapy increased calcium excretion in patients[21] Despite these findings on other corticosteroids, no previous research directly correlates corticosteroid blood concentration with calcium levels. In our study, MometasoneFuroate did not impact calcium levels after seven days of

application, possibly due to its low systemic absorption and potency.

Conclusion:

The application of Mometasone Furoate to skin lesions does not result in significant absorption into the bloodstream at measurable levels. Mometasone Furoate did not cause any changes in blood sugar or calcium levels. There were no significant changes in either systolic or diastolic blood pressure after seven days of Mometasone Furoate application. The concentration of corticosteroids in the blood increases in proportion to the extent of the area treated with topical steroids.

Sources of supports: Nil
Conflicts of Interest: Nil

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