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Original Research Article

A Hospital Based Comparative Study Assessing Calcium Homeostasis Comparison in Thermal Burn Patients–Early Tangential Excision and Grafting versus Conservative Management

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Abstract

Aim: The aim of the present study was to identify whether early wound closure in the burnt state corrects the deranged parathyroid function, which is attributable to the proinflammatory state, thereby optimizing overall calcium homeostasis.

Material & methods: A prospective observational case control study was performed in Department of Surgery. A study cohort was formed composed of 50 burn patients admitted to the Burns Unit for the duration of 12 months.

Results: The average burn surface area under treatment in Group A was 35.82 percent and in Group B group was slightly higher at 37.72 percent. However, difference was not statistically significant. There was a significant improvement in serum calcium, magnesium and phosphorous levels in the tangential excision group. For serum calcium levels, p value became statistically significant on day 15 and at first and second month of follow-up. The serum magnesium improved in the tangential excision group compared with the conservatively managed group, which was statistically significant at day 15 of in-patient stay and at 1st and at 2nd month of follow-up. Serum phosphorus levels in the tangential excision group improved on day 12, 15 of admission and at 1st month and 2nd month and were statistically significant. The mean serum parathormone in Group B was significantly higher in Group A. It remained persistently high during admission and entire follow-up, which correlated with increase calcium loss in Group A at the end of follow-up period. The 24-hour urinary calcium levels were remarkably low in tangential excision group (Group A) as compared with the nonoperative group. This corroborated with the finding of low-parathormone levels, which were also found in Group A.

Conclusion: Early tangential excision and grafting in burns plays an important role in maintaining serum parathormone and calcium levels, leading to prevention of hypercalciuria and optimization of other factors affecting calcium homeostasis.

Keywords: Homeostasis, Hypercalciuria, Hypocalcemia, Parathormone, Tangential Excision

Introduction

Burn injury is damage to the skin or other body parts caused by extreme heat, flame, or contact with heated objects or chemicals. The World Health Organization estimated that 322000 people die each year from fire related burns with >95% of these occurred in developing countries. [1] The mortality rates were much greater at both ends of the age spectrum. Thirty-eight percent of all burn deaths were due to multiple organ failure and only 4.1% were due to burn wound sepsis. [2] The biggest factor in burn mortality was inhalation injury with increased mortality to 26.3% in the 6.5% of burn patients admitted with inhalation injury. [2] Painful and lengthy hospitalization, multiple stages of surgery, permanent disfigurement and disability, prolonged rehabilitation, loss of income and job and enormous financial burden are some of the horrors looming large over the burn victims. The success or failure of treatment of burn victim is difficult to measure. Similarly, survival without consideration of the functional and social rehabilitation of the victim should not be the only measure of success.

With the ever-improving burn care the world over, the frontier has shifted from improving rate of survival to improving quality of life following injury. Currently, multiple strategies exist for the management of burn wounds depending on both the depth and extent of the burn. Burn wound care strategies aim to modulate the inflammatory response, accelerate re-epithelialization, and improve overall wound healing. Furthermore, combinatorial approaches that incorporate cellular-based therapies, pharmacological agents, and

biomaterials are utilized to minimize infection and serve as burn wound coverage adjuncts with the goal of restoration of skin function (i.e., barrier, range of motion, sensation, hair and sweat generation, and pigmentation). [3]

As more patients survive the initial insult of thermal burns, the long-term metabolic consequences of burns are being brought to light. One of these is the derangement of calcium metabolism that occurs in burn patients. [4]

In a healthy person, calcium metabolism comes under the modifying influence of parathormone, with calcitonin playing an insignificant role in humans. Parathormone is, in turn, under the negative feedback of circulating serum calcium. There is evidence of disordered calcium homeostasis following burns, [4,5] which include upregulation of calcium sensing G protein coupled receptors on the chief cells of parathyroid gland. In the physiological state, low-serum calcium levels are responsible for sensitization of parathormone release. But this upregulation of receptors sensitizes the parathyroid gland to even the low levels of free serum calcium, thus setting the cutoff point of serum parathormone to a new nadir. [5,6]

Burn injury is a state of net calcium, magnesium and phosphate loss. [7,8] This is evident from calciuria, despite low-circulating serum calcium, serum magnesium, serum phosphate, serum parathormone and serum vitamin D. [8,9] Unlike calcium, phosphorus absorption goes unabated across a healthy gut irrespective of serum levels. Thus, it comes down to the ingenuity of the Henle's loop and distal convoluted tubule (DCT) wherein phosphorus regulation occurs by virtue of being linked to calcium and ergo under the influence of parathyroid, which increases phosphorus excretion at the cost of calcium reabsorption. [7,8]

This study aims to identify whether early wound closure in the burnt state corrects the deranged parathyroid function, which is attributable to the proinflammatory state, thereby optimizing overall calcium homeostasis.

Material & Methods

A prospective observational case control study was performed in Department of Surgery, RDJM Medical College and Hospital, Muzaffarpur, Bihar, India. A study cohort was formed composed of 50 burn patients admitted to the Burns Unit for the duration of 12 months.

Inclusion Criteria:

Patients in the age group between 16 to 60 years with thermal burns of up to second degree depth and involving 20 to 40 percent total burn surface area (TBSA)

Exclusion Criteria:

Patients with associated systemic comorbidities like acute respiratory distress syndrome, head injury, abdominal or chest injury, inhalational component of burn, uncontrolled diabetes mellitus, pre-existing chronic kidney disease or new onset renal failure, chronic liver disease, and nonthermal burns were excluded from this study.

Methodology

The patients fulfilling the inclusion criteria were randomly allocated in either group, with Group A being the tangential excision group and Group B being the conservative management group. The randomization was done by random group allocation software. Each group was a cohort of 25 patients.

- **Tangential Excision Group (Group A)**

Humby's knife was used for tangential excision and grafting. All white, pinprick insensate wounds were considered for grafting between 3 to 7 days of burns with prior adrenaline solution infiltration. Excision was done till punctuate bleeding occurred and meticulous hemostasis was achieved with adrenaline solution (1 in 1 lac dilution) soaked gauze, bipolar cautery and compression as required by the operating surgeon.

Tourniquet Use: Limb exsanguinations and tourniquet application was done prior to excision. The capillary refill was constantly measured in the pulp of digits.

The wound was covered with thin split-thickness skin graft, and compressive dressing was done using mupirocin ointment-soaked paraffin gauze and dry gauze. The rest of the burn area was dressed with long-acting nanocrystalline silver dressing.

Postoperative dressing: Wound examined at 24 hours, replacing the primary dressing. First dressing was done on day 3 and subsequently every alternate day. Dressing was done with paraffin tulle, mupirocin ointment, saline-soaked gauze and appropriate splinting.

- **Conservative Management Group (Group B)**

Regular dressing with nanocrystalline silver-based dressing, as provided by the hospital surgical store. Splinting of appropriate part done, according to pattern of burns. Also, supportive treatment in the form of antibiotics like third generation cephalosporins, nonopioid analgesics and IV fluids constitute treatment, which was common in both groups. Dressing was done every 3 to 5 days, as per department's protocol. Exceptions to this rule were: a) soiled dressing, b) unexplained fever or pain, c) performing debridement/collecting wound swab of selective areas.

Dietary supplementation: All patients in either group having similar TBSA % burns received similar diet from the hospital dietary department and were routinely supplemented with oral calcium. All received daily supplementation with 500 mg calcium and 250 international units of vitamin D3 for the first 7 days, following which supplementation was done only when indicated.

Blood transfusion: Blood transfusion was done when analysed 412in levels < 8 mg/dl or per operatively during excessive blood loss. None required > or equal to 2 units within 24 hours, thereby affecting serum calcium levels.

Mobilization: All patients underwent daily in bed physiotherapy to mobilize all major joints. Assisted ambulation was started as soon as the general condition and wound status allowed.

Method

Biochemical Analysis

1. Fasting sample for serum calcium, magnesium and phosphorus studied every third day, starting from first sample on day of admission to burn ward till 15th day and then at 1 month and 2 months, respectively.
2. Fasting sample for serum parathormone and 24-hour urine sample for urinary calcium collected every 10th day of in-hospital stay, starting from first sample at day of admission (before starting supplementation) till 1month and then at 2 months, respectively.

Parenteral supplementation: If a patient was symptomatic for hypocalcemia or routine serum calcium levels were < 7.0 mmol/dl, (after correction), additional supplementation with 10% calcium gluconate intravenous was given. Total calcium levels were calculated for observation. The serum calcium was corrected to serum albumin, using the following formula:

- Corrected calcium = serum calcium (mg/Dl) + 0.8 × (normal albuminemia [g/Dl]–patient albuminemia [g/Dl]).

For serum phosphorus and serum magnesium, no regular supplementation was done unless indicated.

All biochemical parameters were analysed as follows:

- Serum Ca, Mg, P and urinary calcium analysed on fully automated clinical chemistry analysed.
- Serum levels parathormone estimated on chemiluminiscence Immuno assay (CLIA) system.

Statistical Analysis

The data was entered in MS Excel spreadsheet and analysis was done using Statistical Package for Social Sciences (SPSS) version 22.0. Normality of the data was checked with the help of Kolmogorov–Smirnov and Shapiro–Wilk test. All categorical variables were analysed with the help of Chi square test. *A p* value of < 0.05 was considered statistically significant.

Results

Table 1: Age and gender distribution of burns patients in both groups along with the average TBSA %

Age group	Group A			Group B		
	Males	Female	Average %TBSA	Male	Female	Average TBSA %
16–25 years	6	2	38.22%	7	00	37.63%
26–35 years	10	3	39.63%	10	4	36.34%
> 35 years	2	2	29.61%	2	2	39.21%

The average burn surface area under treatment in Group A was 35.82 percent and in Group B group was slightly higher at 37.72 percent. However, difference was not statistically significant.

Table 2: Comparison of serum calcium, magnesium and phosphorus levels over time

Comparative analysis of various serum electrolytes for calcium homeostasis									
		Day 0	Day 3	Day 6	Day 9	Day 12	Day 15	1 month	2 months
S. Ca	Group A	7.2243	7.3728	7.5630	7.7824	7.7735	8.0345	8.1388	8.3946
	Group B	7.1622	7.3186	7.3960	7.4244	7.5186	7.6246	7.5730	7.75
S. Mg	Group A	1.5328	1.6630	1.7735	1.8890	2.0079	2.1630	2.3260	2.4646
	Group B	1.58	1.6535	1.7430	1.8228	1.9243	1.9330	1.9430	2.0432
S. Ph	Group A	2.9743	3.0743	3.2890	3.3630	3.5344	3.5946	3.9078	4.1079
	Group B	2.7828	2.8244	2.9228	2.9686	3.0186	3.0248	3.0229	3.0848

There was a significant improvement in serum calcium, magnesium and phosphorous levels in the tangential excision group. For serum calcium levels, p value became statistically significant on day 15 and at first and second month of follow-up. The serum magnesium improved in the tangential excision group compared with the conservatively managed group, which was statistically significant

at day 15 of in-patient stay and at 1st and at 2nd month of follow-up. Serum phosphorus levels in the tangential excision group improved on day 12, 15 of admission and at 1st month and 2nd month and were statistically significant.

Table 3: Comparison of parathormone levels in both groups

	Groups	Mean	SD	*p* value
PTH-0	Group A	30.0036	7.8664	< 0.001
	Group B	49.4244	12.2308	
PTH-10	Group A	30.1128	6.66846	< 0.001
	Group B	50.3360	9.75614	
PTH-20	Group A	30.0730	6.28731	< 0.001
	Group B	49.7246	8.99162	
PTH-1m	Group A	26.9430	5.78832	< 0.001
	Group B	47.93	8.02222	
PTH-2m	Group A	25.7764	5.70428	< 0.001
	Group B	46.44	7.8970	

The mean serum parathormone in Group B was significantly higher in Group A. It remained persistently high during admission and entire follow-up, which correlated with increase calcium loss in Group A at the end of follow-up period.

Table 4: Trend of 24-hour urinary calcium levels in both the groups

	Groups	Mean	SD	*p* value
UCa-0	Group A	224.26	5.18228	< 0.001
	Group B	240.70	10.72834	
UCa-10	Group A	196.04	6.34000	< 0.001
	Group B	235.45	11.34536	
UCa-20	Group A	171.59	11.80943	< 0.001
	Group B	228.92	11.35040	
UCa-1m	Group A	136.44	17.96128	< 0.001
	Group B	228.82	13.81126	
UCa-2m	Group A	105.15	15.86890	< 0.001
	Group B	220.50	17.80120	

The 24-hour urinary calcium levels were remarkably low in tangential excision group (Group A) as compared with the nonoperative group. This corroborated with the finding of low-parathormone levels, which were also found in Group A.

Discussion

With the ever improving burn care the world over, the frontier has shifted from improving rate of survival to improving quality of life following injury. The questions we now face are how best to prevent the horrific scarring that has classically been associated with burns and to preserve function. Both these questions are more evident in the care of the burned hand than in burns over other parts of the body. [10-12] Our hands are so instrumental in maintaining one's independence that even simple tasks take on a new level of complexity with hand disabilities. [13,14] A burn injury to the hand, whether in isolation or associated with a major systemic burn injury, continues to be a challenge to the treating surgeon, as correct clinical judgment and decision regarding management thereof can affect the final outcome both aesthetically and functionally. [15,16]

The average burn surface area under treatment in Group A was 35.82 percent and in Group B group was slightly higher at 37.72 percent. However, difference was not statistically significant. There was a significant improvement in serum calcium, magnesium and phosphorous levels in the tangential excision group. For serum calcium levels, p value became statistically significant on day 15 and at first and second month of follow-up. The serum magnesium improved in the tangential excision group compared with the conservatively managed group, which was statistically significant at day 15 of in-patient stay and at 1st and at 2nd month of follow-up. There are two surgical approaches for patients with deep partial-thickness and full thickness burns to the hand an early tangential excision and skin grafting within the first few days

of injury or an initial topical treatment followed by late eschar excision and grafting. Both techniques have advantages and limitations, as brought out in various studies. [15-18]

In a study conducted by Klein et al [19] titled, "Where has all the Calcium gone," they have shown that despite adequate supplementation, children with burns continue to lose supraphysiological amounts of calcium through urine even in a state of low-serum calcium, which continues up to 6 months postburn. In another study by Klein et al [20], this calcium loss was linked to a proinflammatory state generated by the raw burn wound. They suggested that immobilization and endogenous corticosteroid production was responsible for the same. There is acute stimulation by proinflammatory cytokines of existing osteoblasts and osteoclasts, leading to both bone resorption and brittle bone formation. Adynamic bone, then, would not be conducive to mineralization and will further delay early rehabilitation and increase risk of osteoporosis in burn patients. [21] Serum phosphorus levels in the tangential excision group improved on day 12, 15 of admission and at 1st month and 2nd month and were statistically significant.

The mean serum parathormone in Group B was significantly higher in Group A. It remained persistently high during admission and entire follow-up, which correlated with increase calcium loss in Group A at the end of follow-up period. The 24-hour urinary calcium levels were remarkably low in tangential excision group (Group A) as compared with the non-operative group. This corroborated with the finding of low-parathormone levels, which were also found in Group A. The link between increased proinflammatory cytokines and an increased synthesis of the calcium sensing receptor on the chief cells of parathyroid was suggested by Murphy et al [22] opining that it is this state that leads to deranged intestinal absorption and increased urinary calcium loss. They established that tangential excision and prompt cover with split-thickness skin graft successfully decreased the circulating levels of proinflammatory mediators. In the study by Berger et al [23] mean magnesium remained low for patients who had burn surface areas more than 30 percent TBSA and the hypomagnesemia persisted until the second week. None of these underwent excision and grafting.

Conclusion

Early tangential excision and grafting in burns plays an important role in maintaining serum parathormone and calcium levels, leading to prevention of hypercalciuria and optimization of other factors affecting calcium homeostasis.

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