

Oral Administration of Injectable Calcium Gluconate versus Intravenous Calcium Gluconate in Neonates with Asymptomatic Hypocalcaemia

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ABSTRACT

Background: Neonatal hypocalcaemia is a common metabolic abnormality requiring appropriate calcium supplementation. Intravenous calcium gluconate is frequently used for correction, whereas oral administration may offer a less invasive approach in clinically stable neonates with asymptomatic hypocalcaemia.

Aim: To compare the biochemical response and treatment-related outcomes of oral administration of injectable calcium gluconate versus intravenous calcium gluconate in neonates with asymptomatic hypocalcaemia.

Methods: This retrospective comparative study was conducted in the Department of Pediatrics, Tertiary Care Hospital in Dakshina Kannada, Karnataka from May 2025 to May 2026. Medical records of 60 eligible neonates were reviewed. Of these, 34 received oral administration of injectable calcium gluconate and 26 received intravenous calcium gluconate. Baseline and 72-hour serum calcium concentrations, treatment duration, neonatal intensive care unit (NICU) stay, recurrence, feeding intolerance, rescue therapy and documented adverse events were evaluated. Continuous variables were compared using Welch's independent-samples *t*-test, and categorical variables were assessed using Fisher's exact test.

Results: Mean baseline serum calcium concentrations were 6.80 ± 0.62 mg/dL in the oral group and 6.70 ± 0.68 mg/dL in the intravenous group ($p = 0.56$). At 72 hours, concentrations increased to 8.40 ± 0.54 and 8.50 ± 0.61 mg/dL, respectively. The mean calcium increase was 1.60 ± 0.60 versus 1.80 ± 0.65 mg/dL ($p = 0.23$). Differences in treatment duration and NICU stay were not statistically significant.

Conclusion: Both groups demonstrated improved serum calcium concentrations. Larger prospective studies are required to establish comparative effectiveness and safety.

Keywords: Neonatal Hypocalcaemia, Calcium Gluconate, Oral Administration, Intravenous Calcium, Neonates.

INTRODUCTION

Neonatal hypocalcaemia is a frequently encountered metabolic abnormality in newborns, particularly among preterm infants, low-birth-weight neonates and those with associated perinatal risk factors. It is characterized by a reduction in serum total or ionized calcium below the age- and gestation-specific reference limits.^[1,2] Although some neonates remain asymptomatic, significant hypocalcaemia may lead to neuromuscular irritability, jitteriness, apnoea, tetany, cardiac dysfunction and seizures. The severity of clinical manifestations depends on the degree

and rate of decline in serum calcium, the underlying cause and the overall clinical condition of the newborn. Early recognition and appropriate management are therefore essential to prevent complications and maintain metabolic stability during the neonatal period.^[3,4]

Calcium homeostasis in newborns depends on coordinated hormonal regulation, adequate nutritional intake and appropriate mineral metabolism. During intrauterine life, calcium is transferred from the mother to the fetus through the placenta, supporting fetal skeletal mineralization and maintaining calcium stores.

Following birth, the interruption of placental calcium transfer requires the newborn to establish independent calcium regulation. Changes in parathyroid hormone secretion and other mechanisms involved in mineral homeostasis may contribute to the development of hypocalcaemia during this transition.^[5,6] Other contributing factors include prematurity, low birth weight, magnesium abnormalities, excessive phosphate intake, vitamin D deficiency and disorders of parathyroid function. Hypocalcaemia may occur during the early neonatal period or develop later, depending on the underlying cause and associated clinical conditions. Recognition of these risk factors is important for identifying neonates who require biochemical assessment and appropriate intervention.^[7,8]

Management depends on the severity of the biochemical abnormality, the presence of symptoms, feeding tolerance and the overall clinical condition of the neonate. Intravenous calcium gluconate is commonly used when rapid calcium correction is necessary, particularly in symptomatic or severe hypocalcaemia.^[9-11] Its administration requires careful dose calculation, appropriate vascular access and monitoring of the clinical response. Rapid administration may produce bradycardia or cardiac arrhythmias, while extravasation can cause local tissue injury. Consequently, appropriate administration techniques and monitoring are essential during calcium replacement therapy. The choice of treatment route should be guided by the urgency of correction and the individual clinical requirements of the neonate.^[12,13]

For clinically stable neonates with asymptomatic hypocalcaemia who tolerate enteral feeding, oral calcium supplementation may be considered as an alternative approach in appropriately selected cases. Oral administration may reduce the need for venous access and avoid complications associated with intravenous delivery. However, its suitability depends on the severity of hypocalcaemia, clinical stability, feeding tolerance, formulation used and administered elemental calcium dose. The oral administration of an injectable calcium gluconate preparation requires particular attention to formulation suitability, dosing accuracy and safety.^[14,15] Evidence specifically comparing this approach with intravenous calcium gluconate in neonates with asymptomatic hypocalcaemia remains limited. A comparison of the two routes is therefore important to evaluate their biochemical

response and treatment-related outcomes. Relevant parameters include changes in serum calcium concentration, duration of treatment, length of neonatal intensive care unit stay, recurrence of hypocalcaemia, feeding intolerance, requirement for additional calcium therapy and documented adverse events. Such an assessment may help identify potential advantages and limitations of each treatment approach while highlighting areas requiring further investigation. The present study was undertaken to compare oral administration of injectable calcium gluconate with intravenous calcium gluconate in neonates with asymptomatic hypocalcaemia, focusing primarily on the change in serum calcium concentration from baseline to 72 hours and secondarily on treatment-related outcomes. The findings may contribute to the limited evidence concerning alternative calcium administration routes in clinically stable neonates, while providing a basis for larger prospective studies to establish appropriate treatment protocols and evaluate comparative safety and effectiveness.

MATERIALS AND METHODS

Study Design

The study was conducted as a retrospective comparative study.

Study Setting

The study was conducted in the Department of Pediatrics, Tertiary Care Hospital in Dakshina Kannada, Karnataka.

Study Duration

The study covered the period from May 2025 to May 2026.

Inclusion Criteria

- Neonates admitted to the neonatal unit during the study period.
- Biochemically documented hypocalcaemia.
- Absence of documented clinical manifestations attributable to hypocalcaemia.
- Treatment with either oral administration of injectable calcium gluconate or intravenous calcium gluconate.
- Availability of baseline and 72-hour serum calcium measurements.

Exclusion Criteria

- Neonates with symptomatic hypocalcaemia.

- Neonates requiring emergency calcium correction.
- Incomplete baseline or 72-hour serum calcium records.
- Documented contraindications to enteral administration, where applicable.

Study Sampling

A retrospective record-based sampling approach was used. Medical records satisfying the eligibility criteria were reviewed, and eligible neonates were included according to their documented treatment route. Participants were categorized into oral and intravenous calcium gluconate groups.

Study Sample Size

A total of 60 neonates were included. Of these, 34 received oral administration of injectable calcium gluconate and 26 received intravenous calcium gluconate. The sample comprised eligible records available for the specified study period.

Study Groups

Participants were divided into two groups according to the treatment documented in their medical records. Group A included 34 neonates who received oral administration of injectable calcium gluconate, while Group B included 26 neonates who received intravenous calcium gluconate according to the institutional treatment protocol.

Study Parameters

The primary parameter was the change in serum calcium concentration from baseline to 72 hours. Secondary parameters included serum calcium at 72 hours, treatment duration, NICU stay, requirement for rescue calcium

therapy, recurrence of hypocalcaemia, feeding intolerance and documented adverse events.

Study Procedure

Eligible medical records were reviewed, and neonates were classified according to their treatment route. Baseline serum calcium concentrations were recorded and compared with values measured after 72 hours of treatment. Treatment duration, clinical course and documented treatment-related outcomes were also assessed.

Study Data Collection

Data were extracted from existing medical records, including sex, birth weight, gestational age, small-for-gestational-age status, maternal diabetes history, baseline and 72-hour serum calcium concentrations, treatment route, treatment duration, NICU stay, recurrence, feeding intolerance, rescue therapy and adverse events.

Data Analysis

Data were summarized as frequencies and percentages for categorical variables and mean $\pm$ standard deviation for continuous variables. Welch's independent-samples t-test was used to compare continuous variables, while Fisher's exact test was used for binary outcomes. A p-value below 0.05 was considered statistically significant.

RESULTS

The study included 60 neonates with asymptomatic hypocalcaemia, of whom 34 received oral administration of injectable calcium gluconate and 26 received intravenous calcium gluconate.

Parameter	Oral group (n=34), n (%)	IV group (n=26), n (%)	p-value
Birth weight below 2.5 kg	18 (52.9)	13 (50.0)	1.00
Male sex	20 (58.8)	15 (57.7)	1.00
Preterm neonates	14 (41.2)	10 (38.5)	1.00
Small for gestational age	8 (23.5)	6 (23.1)	1.00

Table 1. Distribution According to Birth Weight, Sex and Gestational Age

Low birth weight was documented in 52.9% of neonates in the oral group and 50.0% in the intravenous group. Male neonates constituted

58.8% and 57.7% of the respective groups. Preterm neonates accounted for 41.2% of the oral group and 38.5% of the intravenous group.

Parameter	Oral group (n=34)	IV group (n=26)	p-value
Infants of diabetic mothers, n (%)	5 (14.7)	5 (19.2)*	0.73
Baseline serum calcium (mg/dL), mean $\pm$ SD	6.80 $\pm$ 0.62	6.70 $\pm$ 0.68	0.56

Table 2. Distribution According to Maternal Diabetes and Baseline Serum Calcium

The mean baseline serum calcium concentration was 6.80 ± 0.62 mg/dL in the oral group and 6.70 ± 0.68 mg/dL in the

intravenous group. The difference was not statistically significant ($p = 0.56$).

Serum calcium measurement	Oral group (n=34), mean $\pm$ SD	IV group (n=26), mean $\pm$ SD	p-value
Baseline calcium (mg/dL)	6.80 ± 0.62	6.70 ± 0.68	0.56
Calcium at 72 hours (mg/dL)	8.40 ± 0.54	8.50 ± 0.61	0.51

Table 3. Comparison of Serum Calcium Concentrations at Baseline and 72 Hours

The mean serum calcium concentration increased from baseline to 72 hours in both treatment groups. At 72 hours, the intravenous group had a mean serum calcium concentration

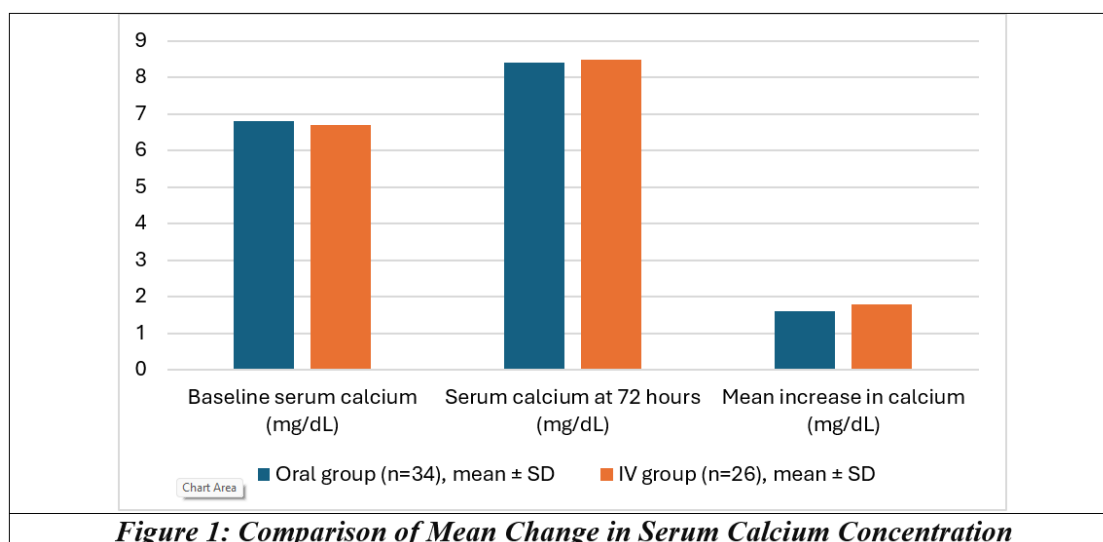
of 8.50 ± 0.61 mg/dL, compared with 8.40 ± 0.54 mg/dL in the oral group. The between-group difference at 72 hours was not statistically significant ($p = 0.51$).

Parameter	Oral group (n=34), mean $\pm$ SD	IV group (n=26), mean $\pm$ SD	p-value
Baseline serum calcium (mg/dL)	6.80 ± 0.62	6.70 ± 0.68	0.56
Serum calcium at 72 hours (mg/dL)	8.40 ± 0.54	8.50 ± 0.61	0.51
Mean increase in calcium (mg/dL)	1.60 ± 0.60	1.80 ± 0.65	0.23

Table 4. Comparison Of Mean Change in Serum Calcium Concentration

The mean increase in serum calcium was 1.60 ± 0.60 mg/dL in the oral group and 1.80 ± 0.65 mg/dL in the intravenous group. Although the

numerical increase was greater in the intravenous group, the difference was not statistically significant ($p = 0.23$).



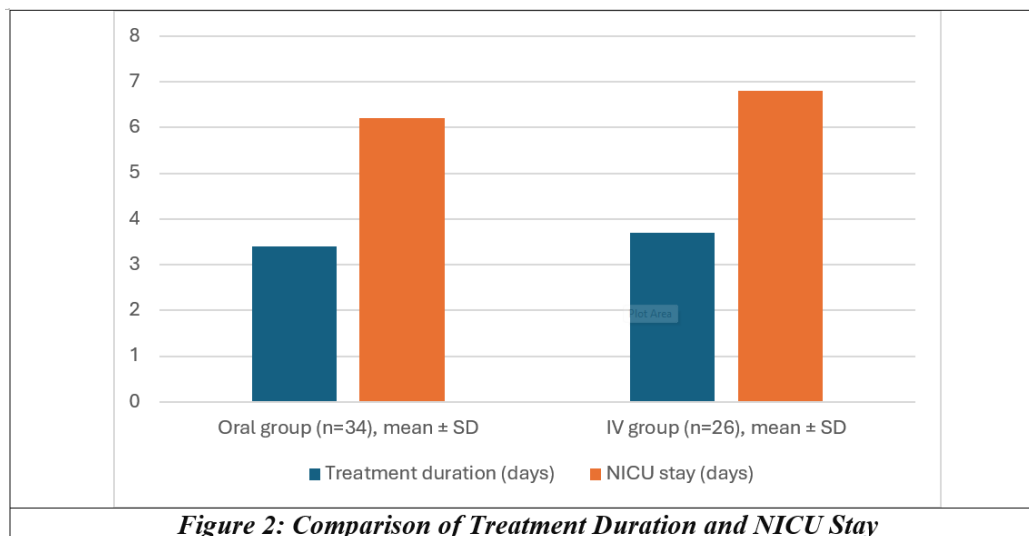
Outcome	Oral group (n=34), mean $\pm$ SD	IV group (n=26), mean $\pm$ SD	p-value
Treatment duration (days)	3.4 ± 0.8	3.7 ± 0.9	0.19
NICU stay (days)	6.2 ± 2.1	6.8 ± 2.4	0.32

Table 5. Comparison of Treatment Duration and NICU Stay

The mean treatment duration was 3.4 ± 0.8 days in the oral group and 3.7 ± 0.9 days in the intravenous group. The mean NICU stay was

6.2 ± 2.1 days and 6.8 ± 2.4 days, respectively. Both outcomes were numerically lower in the oral group, but the differences were not

statistically significant ($p = 0.19$ for treatment duration and $p = 0.32$ for NICU stay).



Outcome	Oral group (n=34), n (%)	IV group (n=26), n (%)	p-value
Recurrence of hypocalcaemia	2 (5.9)	0 (0.0)	0.50
Feeding intolerance	1 (2.9)	0 (0.0)	1.00

Table 6. Comparison of Recurrence and Feeding Intolerance

Recurrence of hypocalcaemia was documented in two neonates (5.9%) in the oral group, whereas no recurrence was recorded in the intravenous group. Feeding intolerance was documented in one neonate (2.9%) in the oral group and none in the intravenous group.

DISCUSSION

Neonatal hypocalcaemia is an important metabolic abnormality, particularly among preterm and low-birth-weight neonates and requires appropriate management to restore serum calcium concentrations and prevent associated complications. The present retrospective comparative study evaluated the biochemical response and treatment-related outcomes of oral administration of injectable calcium gluconate versus intravenous calcium gluconate in 60 neonates with asymptomatic hypocalcaemia. Of these, 34 neonates received oral calcium gluconate and 26 received intravenous calcium gluconate. The mean baseline serum calcium concentration was 6.80 ± 0.62 mg/dL in the oral group and 6.70 ± 0.68 mg/dL in the intravenous group, with no statistically significant difference ($p = 0.56$). These findings indicated comparable baseline calcium concentrations between the groups. The distribution of low birth weight, prematurity, male sex and small-for-gestational-age status was also broadly similar,

although the retrospective design and limited sample size restricted the assessment of potential confounding factors.

The principal finding was an increase in serum calcium concentration in both treatment groups after 72 hours. The mean serum calcium concentration increased to 8.40 ± 0.54 mg/dL in the oral group and 8.50 ± 0.61 mg/dL in the intravenous group. The corresponding mean increases were 1.60 ± 0.60 mg/dL and 1.80 ± 0.65 mg/dL, respectively, with no statistically significant difference between the groups ($p = 0.23$). These observations suggested that biochemical improvement occurred with both treatment approaches in the study population, although they did not establish equivalence or non-inferiority of oral administration. A relevant comparison was provided by Brown et al. (1976),^[16] studied eight matched pairs of premature and asphyxiated infants receiving oral calcium supplementation at 75 mg/kg/24 hours between 12 and 72 hours of age. Their supplemented infants had significantly higher serum calcium concentrations during supplementation and for 36 hours after supplementation was discontinued, while hypocalcaemia after 12 hours of age occurred in none of the eight supplemented infants compared with three of eight control infants. Although both studies examined oral calcium

supplementation, the treatment regimens, comparison groups and study populations differed, and the findings cannot be considered directly equivalent.

Sann et al. (1980)^[17] investigated oral calcium supplementation at 80 mg/kg per 24 hours in 23 preterm infants compared with 23 matched controls. Serum calcium remained at the baseline concentration of 2.31 ± 0.18 mmol/L in the supplemented group, whereas the control group experienced a decrease from 2.27 ± 0.18 to 1.91 ± 0.24 mmol/L at 12–16 hours of age; four control-group measurements were below 1.75 mmol/L. These findings supported the potential role of enteral calcium supplementation in preventing early neonatal hypocalcaemia. Similarly, Romagnoli et al. (1981)^[18] studied 66 healthy low-birth-weight newborns, including 28 preterm infants and 38 small-for-gestational-age infants. They reported an overall hypocalcaemia incidence of 25.7%, with incidences of 32.1% among preterm infants and 21% among small-for-gestational-age infants. Their study also reported that oral administration of high doses of 10% calcium gluconate rapidly normalized serum calcium concentrations. These earlier studies provided supportive evidence for oral calcium supplementation, although neither directly established the comparative effectiveness of oral administration of an injectable preparation versus intravenous calcium gluconate in the present study population.

The duration of treatment and NICU stay were additional outcomes of clinical importance. In the present study, mean treatment duration was 3.4 ± 0.8 days in the oral group compared with 3.7 ± 0.9 days in the intravenous group ($p = 0.19$). Mean NICU stay was 6.2 ± 2.1 days and 6.8 ± 2.4 days, respectively ($p = 0.32$). Although these durations were numerically lower in the oral group, neither difference was statistically significant. The findings therefore did not demonstrate that oral administration reduced treatment duration or hospitalization. Differences in clinical management, feeding status, underlying neonatal characteristics and discharge practices may have influenced these outcomes, but their individual effects could not be determined from the available retrospective data.

Dhir et al. (2023)^[19] conducted a randomized study involving 60 children aged one month to five years who presented with hypocalcaemic seizures. Following initial seizure control with intravenous calcium, participants received

either intravenous 10% calcium gluconate ($n = 30$) or oral elemental calcium ($n = 30$) for 48 hours. Seizures recurred in three children (10%) in the intravenous group and four children (13.3%) in the oral group ($p = 0.278$). Serum calcium concentrations were comparable at 24 hours (7.96 ± 1.32 versus 8.23 ± 1.58 mg/dL; $p = 0.476$) and 48 hours (8.50 ± 1.01 versus 8.63 ± 1.39 mg/dL; $p = 0.681$). Although this study reported comparable biochemical values during continuation therapy, its population consisted of children with hypocalcaemic seizures rather than neonates with asymptomatic hypocalcaemia. The findings consequently offered contextual support for investigating oral calcium therapy but could not directly validate the regimen evaluated in the present study.

Regarding treatment-related outcomes, recurrence of hypocalcaemia was documented in two neonates (5.9%) in the oral group and none in the intravenous group, while feeding intolerance occurred in one neonate (2.9%) in the oral group and none in the intravenous group. No rescue calcium therapy or documented treatment-related adverse events were recorded in either group. These observations were reassuring within the limits of the available records, but the small number of events and retrospective data collection limited conclusions regarding comparative safety. Molotsky et al. (2025)^[20] retrospectively evaluated 39 infants aged zero days to 12 months who received calcium gluconate in sodium chloride alongside parenteral nutrition. Hypocalcaemia occurred in 16 of 39 infants (41%), including seven with mild, seven with moderate and two with severe hypocalcaemia. Their study addressed an alternative intravenous formulation rather than oral versus intravenous treatment, so it did not provide a direct comparison with the present findings. Overall, the present study demonstrated an increase in serum calcium concentrations with both oral administration of injectable calcium gluconate and intravenous calcium gluconate. The absence of statistically significant between-group differences in calcium improvement, treatment duration and NICU stay should be interpreted cautiously rather than as evidence of equivalent effectiveness.

CONCLUSION

The present study demonstrated that both oral administration of injectable calcium gluconate and intravenous calcium gluconate were associated with an improvement in serum

calcium concentrations over 72 hours in neonates with asymptomatic hypocalcaemia. Although the mean increase in serum calcium was numerically greater in the intravenous group than in the oral group, the difference was not statistically significant. Similarly, treatment duration and NICU stay did not differ significantly between the groups. Recurrence of hypocalcaemia and feeding intolerance were infrequently documented in the oral group, while no rescue calcium therapy or treatment-related adverse events were recorded in either group. However, the retrospective design, limited sample size and possibility of incomplete adverse-event documentation restricted definitive conclusions regarding comparative effectiveness and safety. These findings do not establish equivalence or non-inferiority of oral administration. Further large-scale prospective studies with standardized dosing, clearly defined treatment protocols and systematic safety monitoring are required to determine the role of oral administration of injectable calcium gluconate in selected clinically stable neonates with asymptomatic hypocalcaemia.

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