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Recommended Citation

Published quarterly by Midwest-based health system Advocate Aurora Health and indexed in PubMed Central, the Journal of Patient-Centered Research and Reviews (JPCRR) is an open access, peer-reviewed medical journal focused on disseminating scholarly works devoted to improving patient-centered care practices, health outcomes, and the patient experience.
Calcium Carbonate as a Potential Intervention to Prevent Labor Dystocia: Narrative Review of the Literature

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Abstract
Anecdotally, there are attestations from clinicians of calcium carbonate being used successfully for laboring people experiencing labor dystocia. The goal of this narrative review was to provide a synopsis of pertinent literature on calcium use in obstetrics to explore the potential benefit of calcium carbonate as a simple and low-cost intervention for prevention or treatment of labor dystocia. To answer how calcium and carbonate physiologically contribute to myometrium contractility, we conducted a literature search of English-language peer-reviewed articles, with no year limitation, consisting of the keywords “calcium,” “calcium carbonate,” “calcium gluconate,” “pregnancy,” “hemorrhage,” and variations of “smooth muscle contractility” and “uterine contractions.” Though no overt evidence on calcium carbonate’s ability to prevent labor dystocia was identified; relevant information was found regarding smooth muscle contractility, calcium’s influence on uterine muscle contractility, and carbonate’s potential impact on reducing amniotic fluid lactate levels to restore uterine contractility during labor. Studies reporting the potential effectiveness of calcium gluconate and sodium bicarbonate in preventing labor dystocia offer background, safety information, and rationale for a future randomized control trial to evaluate the ability of calcium carbonate to prevent labor dystocia and reduce rates of cesarean section. (J Patient Cent Res Rev. 2023;10:128-135.)

Keywords
calcium carbonate; pregnancy; labor dystocia; Tums; obstetrics; cesarean
is commonly discussed among group members. In some cases, oral calcium carbonate is given in combination with a 1-hour "pit break" or turning off IV oxytocin; in other cases, it is used with maternal position changes. The aforementioned social media group contains many attestations dating from November 2019 — the date of the first comment — to December 2022. Within this timeline, a total of 92 posts had been made by labor and delivery nurses and midwives in the United States on calcium carbonate as a potential solution to correct labor dystocia and prevent a cesarean section.

Calcium carbonate is sold as an over-the-counter antacid used to decrease heartburn and treat indigestion. When taken as directed, it has little to no reported risk of harm during pregnancy. However, there is not any specific guidance regarding use of calcium carbonate in labor. This led us to seek evidence and risk versus benefit information about the potential of calcium carbonate as an intervention to prevent labor dystocia and increase spontaneous vaginal deliveries. Due to a lack of applicable data reported on calcium carbonate, this narrative review evaluates the physiological effects of calcium and carbonate, independently, on uterine muscle in an effort to understand how calcium carbonate may function in obstetrics, specifically as a factor in the prevention of labor dystocia.

**Literature Search Strategy, Outcomes**

A senior medical librarian (R.M.) customized and conducted the search strategy for all published articles on calcium carbonate, calcium gluconate, or general calcium increasing contractions and improving uterine contractility or reducing hemorrhage. Also included were articles about calcium and muscle contractility. The electronic databases OVID Medline, EBSCO CINAHL, EBSCO Health Business Elite, EBSCO Psychology & Behavioral Sciences, Clinical Key, Cochrane Library, and PubMed were searched using PICO-based inquiries, controlled vocabulary, and keywords. Central concepts were identified as calcium, calcium gluconate, calcium carbonate, reduce hemorrhage, improve uterine contractility, muscle contractility, and smooth muscle contractility. To determine the appropriate search criteria for each database, controlled vocabulary, keywords, and variants were identified (Figure 1). Results were limited to English language only.

This search strategy yielded 1638 articles. The librarian (R.M.) screened all titles and abstracts for potential eligibility, and the other 3 authors (an obstetrician, a nurse midwife, and a medical student) read the full texts of those remaining to determine relevance of the final selected articles. Overall, 21 articles were included based on authors’ discretion, and are hereinafter described as literature reviews, laboratory studies, or randomized controlled trials.

**Uterine Muscle Contractility and Versatility**

The uterine muscle has a second messenger signaling system that opens intracellular channels to release the calcium into the cell and cause contraction. The second messenger signaling system includes oxytocin receptors, which are G protein-coupled receptors (GPCR) on the cell membrane where the uterotonic (oxytocin) bind. This activates a cascade of events, ultimately releasing calcium intracellularly to initiate muscle contractility as outlined in Figure 2. The intrinsic ionic change also opens L-type calcium channels causing an influx of additional calcium, resulting in stronger uterine contractions.

Calcium release promotes contractility in myometrium, the uterine muscle. In 2015, Hanley et al determined L-type calcium channels to be the major route of entry of calcium ions (Ca\(^{2+}\)) into uterine muscle. Understanding that calcium promotes contractility in smooth muscle leads us to further investigate how it might be used to promote contractility in the uterine myometrium to prevent labor dystocia. Research by Pehlivanoglu and colleagues showed that calcium release from the sarcoplasmic reticulum is more transient and rapidly depleted compared to the extracellular calcium from L-type calcium channels. A research model of this mechanism explored by Loftus and colleagues demonstrated that calcium influx is a major contributor to the rhythmic depolarization of pacemaker areas within the uterine myocyte and plays an integral role in facilitating myometrial contraction and coordination. The study identified additional calcium channels expressed in the myometrium of birthing people at the time of labor and an increased number of gap junction development, which facilitates the carriage of these electrical impulses supported by calcium.

The human myometrium also contains Ca\(^{2+}\)-activated chloride (Cl\(^{-}\)) channels, also known as CaCCs. CaCCs are activated by increased intracellular calcium levels and maintain cell depolarization by increasing extracellular Cl\(^{-}\) concentration, which depolarizes the myometrial membrane and activates L-type calcium channels. CaCC expression has been identified in myometrium of humans and rodents. In 2004, Jones and colleagues isolated myometrial cells from pregnant rat myometrium and discovered that CaCC current was evident in 101 of 320 (30%) freshly isolated rat myocytes. Blocking these channels with niflumic acid, a Cl\(^{-}\) channel blocker, significantly decreased the frequency of contraction in oxytocin-stimulated and spontaneously
**A.**

Calcium carbonate, calcium gluconate, and general calcium to reduce hemorrhage or increase contractions and role in muscle contractility

- Calcium carbonate
- Calcium gluconate
- Calcium
- Calcium signaling

Pregnancy, hemorrhage

- Pregnancy
- Hemorrhage

Muscle contractility, contractions, smooth muscle

- Muscle, smooth
- Muscle contractions
- Muscle contract*
- Myometrium
- Uterine contractions

**B.**

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**Figure 1.** A: Schematic showing the identification of concepts, keywords, and controlled vocabulary used in the search strategy of this literature review. *Indicates wild card truncation when at the end of a word. B: Medical Subject Headings (MeSH) used in database search (<1946 to December 02, 2022>).
Uterine muscle contraction caused by calcium release from L-type calcium channels and inositol 1,4,5-trisphosphate (IP3) receptors via G protein-coupled receptor (GPCR) activation.
contracted strips of myometrium. The increase in uterine contractility from calcium via various pathways provides physiological rationale to use calcium as a supplement to improve uterine contractions and prevent labor dystocia.

Oxytocin and Uterine Contractility
The synthetic version of oxytocin (trade names: Pitocin®, Syntocinon®) is frequently used to induce or augment labor. Pregnant people have different responses to IV oxytocin use. McAlpine and colleagues determined that exposure to synthetic oxytocin may contribute to oxytocin receptor desensitization, resulting in reduced endogenous oxytocin secretion and therefore decreased uterine contractions. Based on physiological myometrium literature studies and obstetric investigation, uterine activity and reactivity are amplified by ionized calcium uterine activity. When there is decreased uterine activity along with reduced sensitivity to synthetic oxytocin, it may be due to relative calcium insufficiency. Understanding oxytocin’s synergetic relationship with calcium to increase effective uterine contractility offers a potential rationale for using this method to prevent labor dystocia.

Muscle and Lactic Acid
The carbonate component of calcium carbonate also may play a role in promoting uterine contractility when amniotic fluid lactate (AFL) levels are elevated. Myometrial fatigue occurs when the uterine muscle metabolism switches from aerobic to anaerobic metabolism, resulting in an accumulation of intramuscular lactic acid. The lactic acid in the myometrium builds up in the amniotic fluid. Increased AFL levels are associated with labor dystocia and may lead to operative intervention. In general, lactic acid can affect skeletal muscular performance in athletes due to muscle fatigue. Athletes combat increased acid levels by taking oral bicarbonate before physical activity to prevent muscle fatigue. This is a low-cost solution that improves skeletal muscle performance. In myometrium specifically, increased lactic acid inhibits GPCR function and therefore prevents calcium’s release in myometrial cells, diminishing uterine contractility. When used as an intervention, bicarbonate, a base, alkalinizes the amniotic fluid, reducing AFL levels and restoring the uterine pH for effective myometrium contractility during labor. Since the experimental data all utilize bicarbonate, it is unclear if the carbonate component of calcium carbonate would play a role in effective myometrium contractility.

Mammalian Studies
There is extensive research in mammal species on the progression of labor after administration of calcium versus only administration of exogenous oxytocin. Labor dystocia occurs in approximately 5% of all parturient bitches (pregnant dogs) and 3.3%–5.8% of parturient queens (pregnant cats). A literature review of calcium therapy in bitches and queens showed that calcium therapy corrected labor dystocia in cases where bitches had failed to respond with oxytocin; this protocol is standard of care for dogs and is deemed to be a helpful therapy in the medical management of labor dystocia. Calcium therapy for queens is used less frequently and is controversial because of the very strong uterine contractions that occur after calcium administration.

A 2006 prospective randomized controlled trial consisted of 27 bitches with primary inertia (labor dystocia) randomly assigned to treatment groups I and II. Group I was treated with both intravenous calcium and oxytocin, while group II was treated with oxytocin only. Blood samples were collected before and after treatment. Since some bitches started to deliver after an injection of oxytocin, researchers determined low oxytocin concentration impaired uterine contractility. They determined 30% of the dogs did not respond to the oxytocin treatment alone; however, they did respond to the oxytocin and intravenous calcium. Bergstrom and colleagues determined there may be mechanisms in which calcium functions independently to facilitate uterine contractility during labor among bitches. Low plasma oxytocin levels are a cause of labor dystocia in bitches with normal serum calcium concentrations. While not statistically significant, it is noteworthy to recognize that bitches with hypocalcemia had more instances of labor dystocia. Hanley et al found that increased lactate levels resulted in decreased calcium influx into the myometrial cells via the L-type calcium channel, the main route of calcium entry into the myometrium. This markedly decreased uterine contractility and caused labor dystocia. The effect of lactate on intracellular calcium signaling was investigated using Indo-1, a calcium indicator, on myometrial strips of uteruses from pregnant rats and found that lactate abolished calcium transients and contractional force. The calcium transients did reappear when lactate was removed, and this was reflected by increased force and amplitude in contractions that returned to previous control levels.

Human Studies
An in vitro trial in Canada compared contractile responses to oxytocin of an oxytocin-pretreated human myometrium with a non-oxytocin-pretreated human myometrium in the setting of hypocalcemia, normocalcemia, and hypercalcemia. The study included 36 nonlaboring term pregnant people undergoing elective cesarean. From
the cesarean sections, 174 slivers of myometrium were divided into 6 groups. The myometrium tissue strips were pretreated with synthetic oxytocin 10-5 M (oxytocin-pretreated group) for 2 hours or bathed in physiological salt solution for 2 hours (control group). The myometrium strips were then exposed to physiological salt solution with modified calcium concentrations of 1.25 mM (hypocalcemia), 2.5 mM (normocalcemia), or 3.75 mM (hypercalcemia), providing a total of 6 study groups. In oxytocin-naïve myometrium, normocalcemia was found to have superior uterine contractility when compared to hypocalcemia and hypercalcemia. In the oxytocin-pretreated groups, the confidence levels were too wide to draw conclusions and further research is required.

In 2000–2001, a cohort study measured calcium levels of 3 groups of pregnant people: one was measured during labor at 2–3 cm dilation, 5–6 cm dilation, and at the time of delivery; one group was measured at the time of scheduled cesarean; and one group was measured at 38 weeks gestation without labor signs. Previous research has shown higher levels of serum calcium in pregnant people who delivered vaginally versus those who underwent a scheduled cesarean delivery at 38 weeks gestation. The serum calcium levels were compared for those who had scheduled cesarean sections before surgery and after delivery. Calcium levels in the neonatal umbilical vein were also measured for all groups. Serum calcium levels from the scheduled cesarean section compared to those who had spontaneous labor were significantly different (P<0.001). Furthermore, the calcium levels in the umbilical vein of the newborns born after a spontaneous labor were higher compared to the calcium levels of the newborns who were born after a cesarean section (P<0.001). The level of calcium in the serum contributes to changes in the myometrium as it causes an influx of calcium into myometrial cells, contributing to more effective contractions during labor. Reduced serum calcium levels provide a diminished reserve of extracellular calcium for uterine contractility and may result in weakened contractions during labor. Therefore, some researchers hypothesize that an increase in serum calcium by calcium carbonate ingestion during labor may promote calcium influx and more effective contractions.

**Calcium Administered During Labor**

Two dated but significant studies verified labor enhancement through calcium therapy. In 1947, Grier conducted a historically controlled study with 129 birthing people undergoing elective induction of labor who were given IV calcium gluconate. Of the 129 participants, 36 began labor after the administration of calcium gluconate alone and 93 were given intramuscular (IM) oxytocin at 30–60-minute intervals to stimulate labor. The results demonstrated that primiparous and multiparous birthing people given calcium gluconate along with IM oxytocin experienced shorter labors compared to the average labor time (statistics not reported).

In 1954, Whyte also conducted a historically controlled study consisting of 36 primigravida and 166 multigravida pregnant people. He found calcium gluconate followed by IM oxytocin was a safe and effective intervention for those undergoing an induction. The 200 participants given IM oxytocin and calcium gluconate had successful labors and delivered vaginally without any indications of labor dystocia. This pair of mid-20th century studies demonstrated how calcium’s physiological role can be portrayed in clinic-based human studies, although the era of the studies and limited statistical reporting limit their generalizability and results should be interpreted with caution.

**Studies of Bicarbonate Administered During Labor**

A randomized controlled trial conducted by Wiberg-Itzel et al randomized 200 laboring people into “sodium bicarbonate” and “non-sodium bicarbonate” groups. IV oxytocin was administered to both groups. When labor dystocia was diagnosed, AFL levels were collected. The bicarbonate group was given 2 packages of Samarin (totaling 4.26 g of sodium bicarbonate), an over-the-counter European brand name oral bicarbonate solution, with oxytocin started 1 hour afterward. New sampling of AFL was performed after 1 hour in both groups. Bicarbonate decreased AFL levels (P<0.001), and the spontaneous vaginal delivery rate after treatment with bicarbonate was increased (P=0.007). No laboring person reported stomach pain or gastrointestinal issues, and there were no differences in neonatal outcomes.

Another more recent randomized controlled trial by Seyedi and colleagues found that patients given sodium bicarbonate and oxytocin had increased rates of spontaneous delivery for those experiencing labor dystocia. The study included 142 primiparous birthing people with gestational ages between 39 and 42 weeks. The intervention group was given 4.26 g of sodium bicarbonate dissolved in 200 mL of water orally as well as IV oxytocin, while the control group received only IV oxytocin. The increase in AFL levels directly correlated with increased labor dystocia. The authors found the mean duration of the first and second stage of labor in the intervention group was shorter than the control group (P<0.001 for first stage, P>0.001 for second stage). Furthermore, in the intervention group, the rate of spontaneous delivery compared to operative vaginal birth was significantly higher (65 cases) compared with the control group (56 cases); P=0.003.
group had fewer cesarean births, but this was not statistically significant. Results showed that sodium bicarbonate reduced the level of AFL, restoring calcium-mediated contractions, increasing the rate of spontaneous delivery, and decreasing labor dystocia, although there was no significant effect on rate of cesarean delivery.

Clinical Implications
This narrative review evaluated available English-language evidence on the role of calcium or carbonate on uterine contractility, with a focus on understanding the role of calcium in cases of labor dystocia. Methodological flaws were evident in several of the 20th century human studies, as they did not include control groups and were ethically flawed, particularly given that synthetic oxytocin and calcium gluconate were administered with minimal awareness of safe dosage and lacked scientific understanding of oxytocic physiological function. Given the role of calcium in muscle contractility, we speculate that calcium carbonate may play a role in decreasing labor dystocia for pregnant people undergoing induction of labor by increasing the sensitivity of the uterus to oxytocin. Physiologically, calcium and carbonate both enhance myometrium contractility. While there have been historically controlled studies on calcium gluconate and randomized controlled trials using sodium bicarbonate, there have not been any trials of calcium carbonate. It is important to investigate the effects of calcium carbonate, as both components play a critical role in promoting uterine contractility, preventing labor dystocia, and potentially surgical intervention.

The presented mammalian studies, as well as the 20th and 21st century human studies, provide insight into a clinical solution for labor dystocia for birthing people. A physiological understanding of calcium and carbonate provides a foundation and rationale for a future clinical trial. Calcium carbonate is a simple, low-cost treatment that could yield a potential means of increasing rates of spontaneous vaginal birth by preventing labor dystocia, thereby preventing cesarean birth and by extension improving maternal morbidity. This review supports calcium’s potential role in preventing labor dystocia physiologically and clinically. Since calcium carbonate contains calcium and carbonate, both of which are physiologically supported by research to prevent labor dystocia and increase spontaneous delivery rates, it presents as a promising treatment for further study.

Limitations
The structured assessment of methodological quality, comprehensive search, and inclusion of published evidence-based literature and research studies are strengths of this narrative review. Still, our review was limited to English language only. Furthermore, the inclusion criteria did not include additional uterotonicics that may impact labor dystocia. Our focus was solely on calcium carbonate and its ability to prevent labor dystocia by increasing the effectiveness of uterine contractions. Early research conducted by Grier and Whyte did not use a control group and was thus methodologically flawed. Randomized controlled trials conducted by Wiberg-Itzel and Seyedi et al. had small sample sizes and did not study the influence of calcium carbonate but rather sodium bicarbonate.

Summary
Synthetic oxytocin is among the most obstetrically important and useful medications available, yet the use of synthetic oxytocin does not always correct or prevent labor dystocia. We recommend well-conducted randomized controlled trials with sufficient sample size to evaluate calcium carbonate administration as an intervention to decrease labor dystocia caused by weak or ineffective myometrial contractions, evaluate maternal and neonatal outcomes, and identify risks, benefits, and any rare or unexpected outcomes. By exploring the physiological mechanisms of action of calcium in relation to muscle contractility and carbonate’s influence on amniotic fluid lactate, this narrative review indirectly examined the potential benefit of calcium carbonate in labor to prevent dystocia. Given that labor dystocia is the most common indication for unplanned cesarean section in the United States, we theorize that calcium carbonate may be a low-risk and promising preventive measure that may decrease the rate of cesarean section.

Patient-Friendly Recap
- Pregnant people experiencing slow or prolonged labor (aka dystocia) sometimes have an unplanned cesarean delivery.
- Authors reviewed the literature to learn whether one means of preventing cesarean and increasing the rate of vaginal birth might be use of oral calcium carbonate (Tums) to prevent labor dystocia.
- No results from evaluating the effect of calcium carbonate during labor were found. However, studies reporting the effect of calcium on muscle contractility and carbonate’s influence on amniotic fluid lactate were reviewed and analyzed.
- Based on the physiological effects demonstrated by each ingredient, authors concluded that oral calcium carbonate’s potential to prevent labor dystocia should be evaluated in sufficiently powered randomized controlled trials.
Author Contributions
Study design: Forgie, Malloy. Data acquisition or analysis: all authors. Manuscript drafting: Raees, Forgie, Malloy. Critical revision: all authors.

Conflicts of Interest
None.

References

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Review