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Succes of labor induction methods in obese women: A scoping review

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ABSTRACT

Background: Obese women require labor induction more often than normal-weight women, but induction among obese women is less often successful, and the best method has not been established. The aim of this scoping review was to examine available evidence of the success of different induction methods in obese women.

Methods: We searched PubMed, Embase and Web of Science as well as bibliographies for studies of labor induction in obese women. Search terms included “obesity”, “induction of labor”, “cesarean section”, “misoprostol”, “amniotomy” and “mechanical induction”. Studies reporting outcomes of specific methods of labor induction in obese women were included, with cesarean section as the primary outcome.

Results: The search identified 644 studies, of which 27 were included, most of these were retrospective. There was a tendency towards more doses of misoprostol needed for the obese, but no benefit of using 50µg compared to 25µg oral misoprostol. Vaginal delivery rates rose with more days of misoprostol administration. Vaginal misoprostol seemed to be more efficient in the obese compared to oral misoprostol, with shorter time to delivery and more vaginal deliveries, but it might also carry a higher risk of uterine hyperstimulation. Evidence of the efficiency of Foley or balloon catheters in the obese was insufficient. Amniotomy led to more cesarean sections if performed at less than 4 cm of cervical dilation

Conclusion: The available evidence indicates that vaginal misoprostol might be more efficient than oral in obese parturients, and that obese women might have a better chance of achieving vaginal delivery after multiple days of induction. There is a lack of randomized trials examining labor induction in the obese.

Keywords: Labor, Induced; obesity, amniotomy, misoprostol, cesarean section

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INTRODUCTION

Obesity, defined as a BMI≥30, is increasing worldwide (1). Pregnant women with a pre-pregnancy BMI≥30 have an increased risk of gestational diabetes, hypertensive disorders and post-term pregnancy (3). High BMI is associated with greater risk of fetal, perinatal and neonatal death (4), especially at later gestational ages (5). Some studies indicate that this risk is reduced with active induction of labor (6, 7). As a result, obese women undergo labor induction more often than normal-weight women. However, induction of labor is less successful in obese women (8, 9).

Common induction methods include synthetic prostaglandins such as misoprostol (PGE1-analogue) and dinoprostone (PGE2-analogue), oxytocin, balloon catheters and amniotomy. Prostaglandins seem to be more efficient than mechanical methods with similar safety profile (10, 11). Misoprostol and dinoprostone have shown comparable outcomes in time to delivery, cesarean section and uterine hyperstimulation, which has led to increased use of misoprostol, which is cheaper and easier to store (10, 12). A combination of mechanical induction and misoprostol might lead to a shorter time to delivery without increasing cesarean section rate and uterine hyperstimulation (13). These results are from studies of mainly normal-weight women with no stratification by BMI, however.

Currently, guidelines from the Danish Society of Obstetrics and Gynecology recommend induction of labor at gestational age 41 for obese women. Women with unfavorable cervix are induced with 25µg of oral misoprostol every 2 hours, up to eight doses daily for two days, with either continued misoprostol or balloon catheter on day three (14). There are no separate recommendations for obese women, and a lack of solid evidence regarding the optimal method of labor induction, both in Denmark and internationally (15). Therefore, a scoping review was conducted in order to systematically map existing evidence of the efficacy and safety of different labor induction methods specifically in obese women, and to examine whether obese women might benefit from a specific induction method, route of administration or dose compared to normal-weight women. The goal of this review was not to address a single research question, but rather to examine all evidence on the subject and provide a foundational overview.

MATERIALS AND METHODS

This review was conducted following the PRISMA extension for scoping reviews (16).

Eligibility criteria

Studies reporting outcomes of specific methods for cervical ripening or labor induction in obese women (BMI≥30) were included, with no restriction to publication year or language. Due to the low number of published studies for each induction agent, evidence published only as abstracts was also included. Studies using BMI cut-offs for obesity ≥30 were included, whereas studies grouping overweight and obese parturients together were excluded. Studies were excluded if they did not report outcomes separately for each induction method, or for obese women specifically. Case reports and case series were also excluded. Since dinoprostone is no longer included in Danish guidelines, and has been proven to be

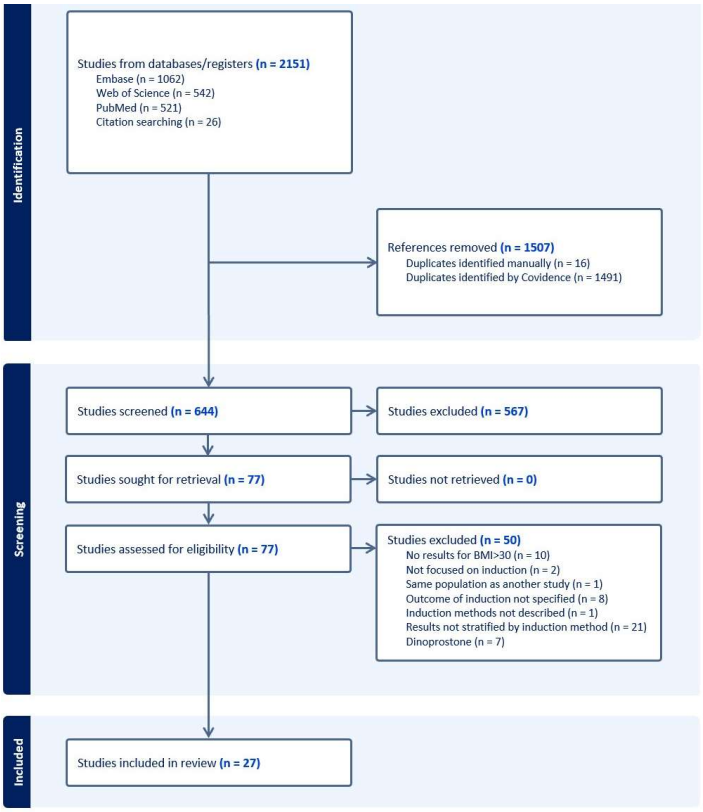

Figure 1: Flowchart of the included studies.

similar or inferior to misoprostol, studies of dinoprostone were excluded. Studies comparing various other induction methods as well as dinoprostone were kept in order to include results of other induction methods. This was done after the initial search.

Search strategy

A literature search was performed by one author in PubMed, Embase and Web of Science. The search strategy was constructed with assistance from a university librarian. Search terms related to "obesity", "induction of labor", "cesarean section" as well as other relevant outcomes and "misoprostol", "amniotomy", "mechanical induction" as well as other induction methods were combined with AND. The first search was performed the 10th of November 2024, and the search was updated the 16th of November and the 9th of December with addition of a few search terms. The final, detailed search strategy is shown in Supplementary Table S1: Search Strategy. Furthermore, reference lists of all included studies as well as relevant reviews were examined to identify relevant articles not found in the primary literature search.

Study selection and data extraction

All studies identified in the literature search were imported into the reference manager Covidence (17), where duplicates were removed automatically. One author screened title and abstract of all references for potentially eligible articles. The full texts of these were then examined, also by one author, to reach the final decision to include or exclude.

The primary outcome was cesarean section, secondary outcomes were time to delivery, vaginal delivery within 24 hours and uterine tachysystole defined as ≥5 contractions per 10 minutes. Indication for cesarean section was extracted if reported. Outcomes were reported grouped by the induction method used. Obesity was defined according to the WHO classification as BMI ≥30, while normal-weight was defined as BMI between 18.5 and 25(1). If studies did not differentiate between normal-weight and overweight women (BMI 18-25 and BMI 25-30), this group was called non-obese.

RESULTS

A total of 1335 singleton term breech deliveries were analyzed. The intended mode of delivery was vaginal (PVD) for 183 (13.7%) cases and cesarean (PCS) for 1152

The literature search yielded 644 studies after removal of duplicates. After screening of title and abstract 567 studies were excluded, and after full text evaluation, 25 studies were included (18-45) (Figure 1: Prisma flowchart). Six of these were only published as abstracts. The included studies were published from 2011 to 2024. The majority of included studies were retrospective cohort studies (n=18), followed by randomized controlled trials (RCT) (n=8). In total, the studies included 29,111 parturients, and of these, 12,680 had a BMI≥30. Study characteristics are displayed in Table 1: Characteristics of included studies.

Misoprostol

A total of 21 studies looked at the efficacy and safety of misoprostol for induction of labor in obese parturients, either alone or compared to other induction agents.

Saucedo et al (39) compared 25µg and 50µg vaginal misoprostol every 4 hours (up to 6 doses) in obese women. Cesarean rates (24/88 (27%) vs 25/91 (28%)) and 24-hour delivery rates (54/88 (61%) vs 65/91 (71%), P=0.16) were similar, with a trend towards shorter time to delivery with 50µg (21.59 h vs 18.56 h, P=0.065). However, the 50µg group had a higher rate of tachysystole (20 (22%) vs 9 (10%)). Lassiter et al (35) found that women with a higher BMI required significantly more 25µg doses to achieve favorable cervix: 1.59 doses for BMI<30, 2.05 for BMI 30-40 and 2.32 for BMI>40), P=0.003. This remained significant when excluding women who did not achieve vaginal delivery. In a study comparing 42 obese and 49 non-obese women (40), the authors found that the obese required more doses of misoprostol (25µg) compared to the non-obese women (6 vs 5 doses). Further, the obese had a higher rate of cesarean section (8/42 (25%) vs 2/49 (4%)) and failed induction, defined as no onset of labor after eight doses of misoprostol, (10/42 (24%) vs 2/49 (4%)).

Helmig et al (31) studied 198 women induced with 25µg oral misoprostol and found higher cesarean risk in obese vs normal-weight women (66/282

Table 1: Characteristics of included studies

Author, year	Study design	Population size	Population characteristics	Induction method studied	Primary outcome
Battarbee et al, 2020(18)	Retrospective cohort	Total: 15,525 BMI≥30: 6605	Uncomplicated, GA ≥37, cervix <4 cm	Amniotomy	Cesarean section
Battarbee et al, 2020(19)	Retrospective cohort	Total: 2,081	Uncomplicated	Amniotomy	Cesarean section
Beckwith et al, 2017(20)	Retrospective cohort	Total: 1502 BMI≥30: 280	Uncomplicated	Misoprostol, 25µg vs Foley catheter + Pitocin	Cesarean section performed at <5 cm dilation
Bender et al, 2024(21)	Randomized trial, unblinded	Total: 108 BMI≥30: 29	GA≥36, PROM, Bishop score <8, cervix ≤2 cm	IV oxytocin only (2-40 mU/min) vs oral misoprostol, 50µg	Time to delivery from initiation of IOL
Brewton et al, 2024(22)	Retrospective (abstract only)	Total: 104	BMI≥30, nulliparous	Foley catheter plus amniotomy	Total induction time
Croll et al, 2024(23)	RCT, secondary analysis	Total: 517 Foley: 254 PGE1: 176 PGE2: 87	BMI≥30, GA ≥37, Bishop score <6, intact membranes	Foley catheter vs vaginal PGE2-gel or oral misoprostol	Cesarean section, postpartum blood loss >1000 mL
Durie et al, 2011(24)	Retrospective – two physician groups (abstract only)	Total: 498	Term	Oxytocin 1 mU/min increase every 45 min vs oxytocin 2 mU/min increase every 30 min	Vaginal delivery
Estrade et al, 2023(25)	RCT, secondary analysis of two studies	Total: 336	GA ≥41, BMI≥30, Bishop score ≤5	Dinoprostone slow-release pessary vs vaginal misoprostol, 25µg vs double balloon catheter	Cesarean section
Ferrazzi et al, 2021(26)	Retrospective cohort	Total: 409 BMI≥30: n unspecified	Late-term or PROM with unfavorable cervix	Misoprostol vaginal insert (200µg, up to 24 h)	Time to delivery from IOL, cesarean section
Gomez et al, 2024(28)	RCT, secondary analysis	Total: 215 BMI≥30: 160	Singleton, gestation ≥37, Bishop score ≤6, cervix ≤2 cm	Vaginal vs buccal misoprostol, 25µg	Time to delivery from IOL
Guerby et al, 2024(29)	RCT (abstract only)	Total: 379	BMI≥30, nulliparous, GA≥36, Bishop score <6	Oral misoprostol, 25µg alone or plus a Foley catheter	Cesarean section
Handal-Orefice et al, 2019(30)	Retrospective cohort before/after	Total: 276 BMI≥30: 173	GA ≥34, cervix ≤1 cm	Vaginal misoprostol, 25µg vs oral misoprostol, 50µg	Cesarean section
Helmig et al, 2021(31)	Retrospective cohort, secondary analysis	Total: 1637 BMI≥30: 282	Singleton, GA ≥37	Misoprostol, oral, 25µg	Cumulative misoprostol dose, mode of delivery
Hermesch et al, 2019(32)	Retrospective cohort (abstract only)	Total: 1443	Term, nulliparous, unfavorable cervix	Oxytocin	Oxy_{max} necessary to achieve 75% vaginal delivery
Hill et al, 2015(33)	Retrospective cohort	Total: 54 BMI>40: 27	BMI>40 / BMI<28, vaginal delivery	Oxytocin, 2-20 mU/min	Oxytocin dose
Kehl et al, 2019(34)	Retrospective cohort	Total: 400	BMI>35, term	Oral misoprostol alone vs double balloon catheter and oral misoprostol, 50-100µg	Cesarean section
Lassiter et al, 2016(35)	Retrospective cohort	Total: 329 BMI>30: 226	GA ≥37, Bishop score <5	Vaginal misoprostol, 25µg	Time to delivery from IOL
Minor et al, 2019(37)	Retrospective, secondary analysis (abstract only)	Total: 286	BMI≥30, term	Amniotomy	Mode of delivery
Pasko et al, 2018(38)	Retrospective, secondary analysis	Total: 285	BMI≥40, GA 37-41+6	Foley + oxytocin + Amniotomy	Cesarean section
Saucedo et al, 2014(39)	RCT	Total: 179	BMI≥30, GA ≥36, cervix ≤3 cm	Vaginal misoprostol, 25 vs 50µg	Time to delivery from IOL
Sfregola et al, 2023(40)	Prospective, secondary analysis	Total: 91 BMI≥30: 42	GA ≥37, Bishop score ≤6, PROM	Oral misoprostol, 25µg	Time to active labor from IOL
Soni et al, 2019(41)	Retrospective cohort	Total: 1280	BMI≥30, GA 37-42, intact membranes, Bishop score ≤7, cervix <2 cm	Vaginal misoprostol, 25µg vs oral misoprostol, 20-60µg	Time to 3cm dilation from IOL
Suidan et al, 2014(42)	Retrospective	Total: 564	BMI≥30, intact membranes	Oral / vaginal misoprostol vs dinoprostone vaginal insert	Successful ripening (cervix >4cm and contractions), cesarean section
Viteri et al, 2021(44)	RCT	Total: 236	BMI≥30, nulliparous, Bishop score ≤6, GA ≥32, intact membranes	Vaginal misoprostol alone, 25µg vs vaginal misoprostol + Foley catheter	Cesarean section
Wei et al, 2022(45)	RCT	Total: 140 - BMI≥30: 70	GA ≥37, reassuring fetal heart rate	Oxytocin, start at 2 mU/min vs 6 mU/min	Time to delivery from IOL
Williams et al, 2016(46)	Retrospective (abstract only)	Total: 124	BMI≥30, GA ≥34	Vaginal, 25µg vs oral misoprostol, 50 µg	Vaginal delivery within 24 h

Abbreviations: AROM = artificial rupture of membranes, BMI = body mass index, GA = gestational age, IOL = induction of labor, PGE = prostaglandin E, PROM = premature rupture of membranes, RCT = randomized controlled trial

(23%) vs 132/900 (15%)). The study also found that only 32-42% of obese parturients gave birth vaginally within 24 hours, but this increased to 77% with up to 72 hours of induction. Ferrazzi et al (26) investigated vaginal misoprostol inserts in 409 pregnant women and found similar rates of cesarean section and time to delivery between the obese and non-obese. Notably, BMI ≥30 was associated with lower odds of tachysystole (OR = 0.92, 95%CI (0.86-0.99)).

Misoprostol, oral versus vaginal

A few studies compared oral misoprostol with vaginal misoprostol. Generally, vaginal administration was associated with a shorter time to delivery and/or fewer cesarean sections (28, 30, 41, 45).

In a study by Williams et al (45), the authors found that 25µg vaginal misoprostol was associated with shorter time to delivery compared to 50µg oral misoprostol among 124 obese women (16.3±9.5 hours vs 19.5±7.3 hours, P=0.02), with similar 24-hour vaginal delivery and cesarean rates. Handal-Orefice et al (30) studied 276 women receiving either vaginal or oral misoprostol and found a slightly lower cesarean section rate with vaginal misoprostol. Particularly cesarean section for failed induction, defined as failure to progress, was less likely in the group receiving vaginal misoprostol (21/84 (25%) with vaginal misoprostol vs 28/89 (31%) with oral for the obese). Especially cesarean section for failed induction, defined as failure to progress, was significantly less frequent in parturients receiving vaginal misoprostol, regardless of BMI group. Notably, vaginal misoprostol was associated with tachysystole across all BMI categories (20% vs 11%, P=0.04). Supporting these findings, a larger study by Soni et al(41) including 1280 obese women also reported a lower cesarean section rate with vaginal vs oral misoprostol (77/314 (25%) vs 301/966 (31%), P=0.03), and shorter time to delivery (17.4±10.1 h vs 24.8±12.2 h, P<0.0001) with vaginal misoprostol, as well as a larger proportion of vaginal deliveries within 24 hours (186 /314 (59%) vs 409/966 (42%), P<0.0001). Suidan et al (42) studied 564 pregnant women primarily to compare a vaginal dinoprostone insert with either oral or vaginal misoprostol and found similar rates of cesarean section and failed induction, defined as cervix ≤4 cm or no contractions, when comparing oral and vaginal misoprostol.

Gomez et al (28) reported significantly shorter induction-to-delivery time with vaginal compared to buccal misoprostol (21.3 h vs 25.2 h, P=0.006) in 215 parturients, in both groups combined with a Foley catheter. Cesarean rates did not differ, but the indication varied. In the group receiving vaginal misoprostol, non-reassuring fetal heart rate was more common, while failed induction (undefined) was more common with buccal administration.

Misoprostol versus mechanical induction

Two studies compared vaginal misoprostol to mechanical induction. Beckwith et al (20) found similar cesarean section rates in obese parturients induced with either 25µg vaginal misoprostol or a Foley catheter supplemented with Pitocin (75/216 (35%) vs 20/64 (31%), respectively). In contrast, in a study of 336 pregnant women, Estrade et al (25) reported the highest rate of spontaneous vaginal delivery in obese pregnant women receiving vaginal misoprostol 66/94 (70%) compared to a double balloon catheter 23/89 (26%) or a slow-release dinoprostone-pessary 89/153 (58%), with similar cesarean rates (6 (6%) and 2 (2%), respectively).

Three studies compared combined misoprostol and mechanical induction vs only misoprostol. Viteri et al (43) observed no significant differences in outcomes between vaginal misoprostol plus a double balloon catheter and misoprostol alone in 236 pregnant women. Similarly, in a study of 400 women, Kehl et al (34) reported similar time to delivery (~30 h) and failed induction rates, defined as no vaginal delivery within 72 h (8%), but significantly fewer cesareans with oral misoprostol plus a balloon catheter (59/216 (28%) vs 69/184 (38%)). In contrast, in an RCT of 379 women, Guerby et al(29) found a higher cesarean rates with oral misoprostol plus Foley catheter compared to oral misoprostol alone (90/191 (47%) vs 79/188 (42%)), particularly due to non-reassuring fetal heart rate, as well as a greater risk of postpartum hemorrhage >1L. Due to these findings, the study was stopped after the interim analysis to avoid further adverse outcomes in the intervention group.

Oxytocin

Five studies examined oxytocin for induction. Hill et al (33) studied 54 pregnant women and found that women with BMI>40 received significantly higher rates of oxytocin during the first stage of labor (from regular contractions until full cervical dilatation) (11.6±4.8 mU/min vs 8.6±4.1 mU/min, P=0.02) compared to women with BMI<28. Spontaneous vaginal delivery rates were similar (23/27 (85%) vs 25/27 (93%), non-significant). Wei et al (44) observed no difference in cesarean section rates or time to delivery between low and high dose oxytocin (2 vs 6 mU/min starting dose) in 70 obese women. Durie et al(24) also compared non-obese and obese parturients (n=498 women) receiving two different dosing regimens (1 vs 2 mU/min starting dose). In the low-dose group, obese women had significantly lower hazard ratio (HR) for vaginal birth (HR 0.63, 95%CI 0.44-0.96), whereas the hazard ratios were similar for obese and non-obese receiving the higher dose (obese HR 0.9, 95%CI 0.69-1.18). A larger study by Hermesch et al (32) involving 1443 pregnant women aimed to determine the maximum oxytocin dose required to achieve vaginal delivery in 75% depending on BMI group. While only normal-weight and overweight women achieved this threshold, the authors calculated a theoretical maximum oxytocin dose needed for all BMI groups: 20mU/min for BMI<30, rising to 24 mU/min for BMI 30-35, 28 mU/min in BMI 35-40 and 36 mU/min in BMI>40. None of these studies specified the timing of initiation of oxytocin.

Bender et al (21) compared oxytocin to oral misoprostol in a study of 108 pregnant women, reporting a shorter time to delivery in the oxytocin group for both obese and non-obese parturients (16.6 hours vs 21.8 hours, P=0.04 for the obese). Cesarean rates were not reported specifically for obese women but did not differ in the overall cohort.

Amniotomy

The studies investigating amniotomy as induction method in obese parturients primarily focused on the timing in relation to cervical dilation. A large retrospective study by Battarbee et al including more than 15,000 pregnant women (18) found that early amniotomy (<4 cm dilation) significantly increased cesarean risk in obese women (adjusted OR 1.27, 95% CI 1.1–1.47 for BMI=30, increasing with BMI), but not in non-obese (OR 1.13, 95% CI 0.93–1.28). Another retrospective study by Battarbee et al (19) found that delayed amniotomy (after >8 hours of oxytocin infusion, regardless of cervical dilation) also raised cesarean odds, more strongly in obese (OR 2.06, 95% CI 1.65–2.59 vs OR 1.47, 95% CI 1.06–2.04 for BMI=20). Time to delivery did not differ significantly. A retrospective study of 286 obese women by Minor et al (37) found a trend towards higher cesarean section rate in obese parturients with amniotomy at ≤4cm dilation (21% vs 13%, P=0.075, numbers not specified). There were similar time to delivery and 24-hour vaginal birth rates. Consistent findings were found in a retrospective study of 285 pregnant women by Pasko et al (38). The authors found an increased rate of cesarean section with early amniotomy in BMI≥40 (54/107 (51%) vs 57/187 (30%)), mainly due to failed induction, defined as failure to enter active labor within 48 hours. When stratifying by parity, the results only remained significant among nulliparous. Brewton et al (22) divided 104 parturients into quartiles by timing of amniotomy, and found no significant difference in cesarean section rate or time to delivery.

DISCUSSION

This scoping review identified 25 primary studies of labor induction in obese women, primarily retrospective cohort studies. Few RCT's focused primarily on obesity. The interventions and outcomes, as well as the results, were quite heterogenous. While two earlier reviews addressed this topic (8, 9), our review included more recent publications. Their conclusion was that misoprostol was preferable to dinoprostone, which has not been studied in this review.

Overall, obese women required more misoprostol doses and higher oxytocin infusion rates to achieve vaginal delivery, yet still faced increased cesarean section rates. However, higher misoprostol dose (50µg vs 25µg) did not improve vaginal delivery rates in one study (39) but only increased the rate of tachysystole. When continuing administration of misoprostol for 72 hours, the rate of vaginal delivery increased

markedly compared to induction with misoprostol for only 24 hours. Obese women also needed higher rates of oxytocin infusion to achieve vaginal delivery rates comparable to the non-obese. When comparing 2 mU/min infusion rates with 6 mU/min, there was no difference in cesarean section rate or other outcomes, while the obese achieved less vaginal deliveries with 1 mU/min compared to 2 mU/min in another study. However, the sample size in the study of 2 vs 6 mU/min was very small, with only 35 women in each group, and this might conceal any potential differences in outcome. Another study attempted to calculate the theoretical maximum dose of oxytocin necessary to achieve vaginal delivery in 75%, and this increased in a dose response relationship to BMI, but adverse outcomes at increasing doses were not assessed. It has previously been hypothesized that obese women would benefit from a larger dose of either misoprostol or oxytocin for induction, primarily due to their larger distribution volume (20, 33). A study on the pharmacokinetics in 22 obese and 18 non-obese parturients found no difference in the peak concentration, time to peak or total exposure to misoprostol after administration of 25µg of vaginal misoprostol (27). However, women experiencing failed induction, of whom 80% were obese, had reduced maximum misoprostol concentration. The authors propose that obese women might benefit from a higher loading dose to achieve the same maximum concentration, without changing the maintenance dose. Currently, no clinical studies have investigated the effect of a higher loading dose.

Three studies (30, 41, 45) comparing vaginal and oral misoprostol found that vaginal misoprostol seemed to lead to a shorter time from induction to delivery in the obese. Two studies found a lower cesarean section rate in the obese parturients receiving vaginal misoprostol. Vaginal misoprostol led to fewer cesarean sections due to failed induction, but more due to fetal distress. All three studies were retrospective, but the study by Handal-Orefice et al compared women giving birth before and after a guideline change from vaginal to oral misoprostol and found a lower cesarean section rate with vaginal misoprostol, especially a reduction in cesarean sections due to failed induction. This study design might introduce less bias by indication, as all women in a specific time period received the same treatment. There might have been other changes in clinical practice, however, which introduces other biases. The other two studies were both retrospective cohort studies. A large retrospective study including 1280 women by Soni et al found that vaginal misoprostol was associated with a lower cesarean section rate, whereas the findings were not supported by Williams et al including 124 obese women.

The current literature recommends 25-50µg oral misoprostol every 2 to 4 hours regardless of BMI to women with no previous cesarean section. A Cochrane review of 6417 women found that oral and vaginal misoprostol were comparable in terms of vaginal birth within 24 hours, uterine hyperstimulation with fetal heart rate changes and cesarean section, but with a lower Apgar score at five minutes when using vaginal misoprostol (12). A review by Alfirevic et al found the lowest probability of cesarean section with oral misoprostol <50µg, while vaginal misoprostol ≥50µg had the highest probability of achieving vaginal delivery within 24 hours (46). The final recommendation was to use oral misoprostol out of safety concerns. None of these reviews focused on obesity, however. Studies have shown that obese parturients have fewer contractions both before and after administration of misoprostol, and that the increase in contractions from baseline is lower (47, 48). One study found that the rate of uterine hyperstimulation after induction was significantly lower in obese women (26). This indicates that the myometrium of obese women responds less to misoprostol, leading to a lower chance of vaginal delivery, but also a lower risk of uterine hyperstimulation, possibly due to a lower misoprostol plasma concentration after administration. This could be due to a higher distribution volume or a decreased myometrial response to prostaglandins. Thus, obese parturients may benefit from a stronger stimulation of labor, which could be achieved with vaginal misoprostol. No RCT's have been conducted comparing oral and vaginal misoprostol in the obese, however.

Many of the included studies use either time from induction to delivery or delivery within 24 hours as primary outcome. However, if induced electively,

it might be less important to achieve labor within 24 hours, and more important to achieve it safely. Cesarean section increases the risk in subsequent pregnancies, and obese women have increased morbidity after cesarean section (49-51). Studies have shown that outpatient induction is safe, which makes longer inductions feasible (52, 53). Helmig et al (31) found that significantly more obese women achieved vaginal delivery after 72 hours of induction compared to 24 hours, and this corresponds to Danish guidelines, where induction is attempted for 3 days with oral misoprostol, before switching to a balloon catheter. Since obese parturients are slower at achieving labor, it might be relevant to continue induction even longer in this group. However, no trials have been conducted exploring this hypothesis, and almost none of the included studies report the duration of the induction attempt.

Mechanical induction has been hypothesized to be beneficial in obese women, as these methods may not depend as much on pharmacokinetics (25), or that induction outcomes could be improved by combining misoprostol and mechanical induction (43). Contrary to this, a Cochrane review found moderate quality evidence that both vaginal and oral misoprostol are slightly more efficient than a balloon catheter, but that the balloon catheter might have a better safety profile (11). In the present review, one study favored Foley catheter plus Pitocin over vaginal misoprostol (20), while another study favored vaginal misoprostol over double balloon catheter (25). One RCT found an increase in non-reassuring fetal heart rate and cesarean section when combining Foley catheter and oral misoprostol compared to only misoprostol (29), while a retrospective study found no difference (34). Another RCT found no difference between vaginal misoprostol alone and vaginal misoprostol plus double balloon catheter (43). All in all, the evidence is limited, but none of the included studies indicate that it might be beneficial to combine misoprostol and mechanical induction in the obese.

Amniotomy is the recommended induction method in women with a Bishop score ≥6 in Denmark (55). Three studies included in this review found an increased risk of cesarean section when performing amniotomy at less than 4cm cervical dilation for the obese. For the non-obese, there was no difference in cesarean section rates with amniotomy before and after 4cm cervical dilation. This is in line with evidence that the membranes play an important role in natural cervical ripening, and should not be ruptured too early (54). A Cochrane review of amniotomy for shortening labor found a near-significant increased risk of cesarean section in women who had an amniotomy, while the risk of low Apgar score seemed to be lower in women receiving amniotomy. The review suggested that amniotomy might reduce cesarean sections due to failure to progress, which combined with the results from the present review suggest that amniotomy could be beneficial in obese parturients if performed after 4 cm of cervical dilation. However, all the studies of amniotomy were retrospective, and it is possible that the women who underwent early amniotomy were progressing more slowly, leading to an earlier intervention as well as an increased cesarean section rate.

One of the strengths of this scoping review was the extensive literature search. The references of all included articles as well as relevant systematic reviews were scrutinized for studies not identified in the initial search. Only studies reporting on cesarean section were included. The biggest limitation was the small amount of randomized controlled trials, meaning that many of the findings are based on retrospective data. Therefore, the results may be subject to confounding by indication. Important maternal factors, such as parity, BMI, Bishop score and gestational age may also be unequally distributed. Notably, the indication for induction of labor varied between studies. Most studies included labor induction with various indications, including fetal distress, IUGR, oligohydramnios, hypertensive disorders, PROM, and post-term pregnancy. Induction of labor may be more readily achievable for certain indications, and if clinicians preferentially selected specific induction methods based on the indication, this could substantially influence the results of observational studies. Many of the included studies had very few participants, which may mask differences in both desired and adverse outcomes between the

groups. Furthermore, there were considerable differences between the studies regarding obesity classification, timing of BMI measurement and induction protocol. Definitions of important outcomes, such as failed induction, also varied between studies. Finally, the study was conducted as a scoping review and not a systematic review, which notably reduces the ability to make final conclusions. The literature screening was initially performed by one author only, which is a major limitation. This was due to time limitations. However, both authors read all included articles before inclusion to ensure that they met the prespecified inclusion criteria.

CONCLUSION

This review highlights the lack of high-quality evidence on the best labor induction methods in obese women, and evidence remains insufficient to recommend any one regimen. The included studies suggest that vaginal misoprostol might be better for achieving vaginal delivery in the obese, and that obese women might benefit from multiple days of misoprostol. The evidence was very limited, however, so this should be explored further, preferably in a randomized trial. Similar to evidence of labor induction in normal-weight women, misoprostol seems to be the most safe and effective method. Whether mechanical induction is beneficial in the obese cannot be determined based on the available evidence, which is conflicting and based on few studies. The two small RCT's studying misoprostol plus mechanical induction disagreed whether the combination was safe, but neither of them found it to be more efficient. Future research should focus on the optimal dosing, duration and route of administration of misoprostol.

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