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RESEARCH ARTICLE

Adverse Obstetric and Neonatal Outcomes in Maternal Diabetes: Prediction by Glucose-to-Potassium Ratio

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Abstract

Introductıon: The aim of this study is to investigate whether the glucose-to-potassium ratio (GPR) can predict adverse obstetric and neonatal outcomes in pregnant women diagnosed with diabetes.

Methods: This retrospective observational study included 80 pregnant women diagnosed with pregestational or gestational diabetes, as well as 120 healthy pregnant women, between 2023 and 2025. GPR was calculated by dividing the glucose level by the potassium level in the venous blood sample taken at the time of delivery. Receiver Operating Characteristic curves were constructed to evaluate the predictive value of GPR for adverse obstetric and neonatal outcomes.

Results: In maternal diabetes, multiparity and comorbid conditions were found to be higher. The gestational age at delivery was similar in both groups; however, the birth weight of neonates born to diabetic mothers was statistically higher. The NICU admission and adverse obstetric outcomes were higher in the case group. The median GPR level was 23.4 in the diabetes group and 20.3 in the control group ($p < 0.001$). When all participants were analysed, the optimal cut-off value of GPR for predicting NICU admission was found to be 21.7 (AUC 0.583, Sensitivity 55.3%, Specificity 55.1%, 95% CI 0.505–0.667, $p = 0.043$). Glucose levels were found to be statistically significant in predicting NICU admission and adverse obstetric outcomes ($p = 0.017$ and $p = 0.005$, respectively). However, these markers did not show predictive value within the diabetic group.

Conclusion: GPR and hyperglycemia may be associated with adverse obstetric outcomes.

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Introduction

Maternal diabetes is a serious metabolic disease with increasing prevalence and is associated with significant obstetric and neonatal complications. The majority of diabetes observed during pregnancy is gestational diabetes, but pregestational diabetes, defined as Type 1 and Type 2 diabetes, also negatively affects the health of both the mother and the fetus.[1] Due to factors such as a hyperglycemic environment, accompanying lipid abnormalities, chronic inflammation, and epigenetic differences, diabetes is associated with many complications in the newborn, including respiratory distress, hypoglycemia, the need for neonatal intensive care, neurodevelopmental disorders, and cardiac dysfunction.[2,3]

Potassium, the other determinant of the glucose-to-potassium ratio, also plays a key role in cellular homeostasis.[4] Insulin facilitates not only glucose but also potassium uptake into cells, and disturbances in this balance may further contribute to metabolic instability in diabetic pregnancies.

The glucose-to-potassium ratio has been calculated to provide prognostic information regarding various adverse medical conditions such as hypoxia, ischemia, intensive care unit admission, and cerebrovascular events. Since this ratio is derived from basic blood parameters, it provides ease of use in predicting mortality and morbidity.

It is known that diabetes disrupts the balance of oxygen by impairing its delivery due to microvascular damage caused by hyperglycaemia.[5] In this study, we aimed to investigate whether the glucose-to-potassium ratio (GPR), which is associated with ischemia and hypoxia, can predict adverse obstetric and neonatal outcomes in pregnant women diagnosed with diabetes.

Material and Methods

This study is a retrospective observational study, including a total of 80 pregnant women aged between 18 and 45 years, diagnosed with pregestational diabetes (PGD) and gestational diabetes (GDM), whose pregnancies were followed and deliveries occurred in the hospital between 2023 and 2025, and 120 healthy pregnant women as a control group. In the study group, 68 women (85%) were diagnosed with GDM, 4 patients (5%) with Type 1 diabetes (T1DM), and 8 patients (10%) with Type 2 diabetes (T2DM). Thus, the proportion of pregestational diabetes cases was 15%, of which 33% were type 1 and 67% were type 2 diabetes.

The study was approved by the Clinical Research Ethics Committee of Uşak University (Ethics Number: 732-732-05, Date: 23/06/2025). The study complies with the Declaration of Helsinki. Since the data were anonymized and collected retrospectively, written informed consent was waived. Exclusion criteria included poor glycemic control, multiple pregnancies, smoking, any inflammatory condition, a history of cancer, and fetal chromosomal or structural anomalies.

All patients were followed up in the endocrinology department, and information regarding glycemic control (fasting glucose and HbA1c values during follow-up) was available in hospital records. However, these data could not be comprehensively included in the analysis due to incomplete documentation in some cases.

More than 4.000 deliveries took place in our hospital within two years, and all patients diagnosed with diabetes and with good glycemic control by the endocrinology department were included in the study group through retrospective screening using the hospital archive and operating system. The control group consisted of randomly selected healthy pregnant women who were matched with each study patient based on the date of delivery and had random glucose or oral glucose tolerance test results within normal limits.

The diagnoses of T1DM, T2DM, and GDM were made according to the criteria accepted by the American Diabetes Association.[6] All patients were followed up in the endocrinology department. The demographic characteristics of the participants, as well as the treatment methods (diet or insulin) of the pregnant women diagnosed with diabetes, were recorded. GPR was calculated by dividing the glucose level by the potassium level in the venous blood sample taken at the time of delivery. Adverse obstetric outcomes were defined as hypertensive disorders of pregnancy, fetal growth restriction, preterm birth, birth weight over 4000 g (macrosomia), and amniotic fluid abnormalities. In addition, the need for emergency cesarean section and admission to the neonatal intensive care unit (NICU) was recorded.

Statistical analysis was performed using IBM SPSS Statistics 26.0. The normality of the variables was tested using both the Shapiro-Wilk and Kolmogorov-Smirnov tests. Non-normally distributed data were evaluated using the Mann-Whitney U test and

presented as median, minimum–maximum (min–max), number (n), and percentage (%). A p-value of < 0.05 was considered statistically significant.

To evaluate the predictive value of adverse obstetric and neonatal outcomes, Receiver Operating Characteristic (ROC) curves were generated and the Area Under the Curve (AUC) values were calculated using standard methods. The data were presented as AUC ROC (95% CI). Appropriate cut-off values for inflammatory indices were determined using the Youden index. In a similar study, for sample size estimation, a minimum of 35 patients per group was required with a 5% margin of error and 80% power with G-power .[7]

Results

Table 1 presents the demographic and obstetric baseline characteristics of both groups. The median age of patients in the diabetes group was found to be higher compared to the healthy group. A larger proportion of the pregnant women with maternal diabetes were multiparous, and the comorbidities were also found to be higher in the diabetes group. In the diabetes group, 47 patients (58.7%) were followed with diet therapy and 33 patients (41.2%) with insulin therapy. Regarding comorbidities, four patients in the diabetes group had chronic hypertension, four had hypothyroidism, and one patient each had a diagnosis of epilepsy and asthma. Although the gestational age at delivery was similar in both groups, the birth weight of neonates born to diabetic mothers was found to be statistically higher. The NICU admission and adverse obstetric outcomes were significantly higher in the maternal diabetes ($p < 0.001$ and $p = 0.012$, respectively). The most common complications in the case group were hypertensive disorders of pregnancy (n = 3), preterm labor (n = 5), and macrosomia (n = 4), whereas in the healthy group, the most frequent complication was preterm labor (n = 15).

Table 2 presents hematological and biochemical profiles of in diabetic and healthy pregnant women. Complete blood count, platelet count, white blood cell count, and potassium levels were similar in both groups. The serum glucose level in the diabetic group was 97 mg/dL (range: 62–314), while it was 84 mg/dL (range: 60–155) in the healthy group ($p < 0.001$). The GPR level was 23.4 (range: 17.2–74.4) in the study group and 20.3 (range: 12.5–40.7) in the control group ($p < 0.001$).

Table 1: Baseline characteristics of participants

	Case group (n=80)	Control group (n=120)	P value
Maternal age (years)	30 (20 - 41)	28 (18 - 41)	**<0.001**
Nulliparity (n, %)	19 (23.7)	55 (45.8)	**0.002**
Comorbidity (n, %)	10 (8)	0 (0)	**0.003**
Male fetal gender (n, %)	44 (55.5)	63 (52.5)	0.782
Gestational age at birth (week)	38 (35- 40)	37 (32 -41)	0.974
Birth weight (gram)	3377 (2350 - 4380)	2790 (1775 - 4700)	**0.001**
Emergency cesarean section (n, %)	8 (10)	15 (12.5)	0.587
APGAR score at 1st minute	9 (1- 9)	8 (3- 9)	0.883
APGAR score at 5th minute	10 (3 - 10)	9 (6 - 9)	0.476
NICU admission (n, %)	45 (56.2)	32 (26.6)	**<0.001**
Adverse perinatal outcomes (n, %)	22 (27.5)	16 (13.3)	**0.012**

Note: Data given as median (interquartile range), number, percentile (%). P-values < 0.05 were considered statistically significant. *Mann Whitney U test BMI, body mass index; NICU, neonatal intensive care unit

Table 2. Hematological and biochemical profiles of the study population

	Case group (n=80)	Control group (n=120)	P value
Hemoglobin (g/dL)	12.6 (8.7 - 15)	11.6 (8.2 - 15.5)	0.336
Platelet (10^9 /L)	254 (122 - 494)	248 (131- 524)	0.939
WBC (10^9 /L)	9.9 (6.8 - 20.3)	10.6 (5.8 - 25.3)	0.176
Glucose (mg/dL)	97 (62 - 314)	84 (60 - 155)	**<0.001**
Potassium (mg/dL)	4.2 (3.1 - 4.8)	4.1 (3.5 – 4.8)	0.187
GPR	23.4 (17.2 – 74.4)	20.3 (12.5 – 40.7)	**<0.001**

Note: Data given as median (interquartile range), number, percentile (%). P-values < 0.05 were considered statistically significant. *Mann Whitney U test GPR: Glucose-potassium ratio

Tables 3 and 4 show ROC analysis of glucose and GPR in predicting adverse obstetric outcomes and NICU need for all participants and the diabetes group. When all participants were analyzed, the optimal cut-off value of GPR for predicting NICU admission was found to be 21.7 (AUC 0.583, Sensitivity 55.3%, Specificity 55.1%, 95% CI 0.505–0.667, $p = 0.043$). Glucose levels were found to be statistically significant in predicting NICU admission and adverse obstetric outcomes ($p = 0.017$ and $p = 0.005$, respectively) (Figure 1, Figure 2).

Table 3: The ROC curve analysis for the performance of serum markers in predicting advers obstetric outcomes and NICU admission in all participants

	Cut-off	AUC	p value	95% CI	Sensitivity	Specificity
NICU						
Glucose (mg/dL)	90.5	0.601	**0.017**	0.522-0.680	%58.4	%59.3
GPR	21.7	0.586	**0.043**	0.505 - 0.667	%55.3	%55.1
Advers obstetric outcome						
Glucose (mg/dL)	93.5	0.647	**0.005**	0.551-0.742	%60.5	%63
GPR	21.7	0.585	0.101	0.485 - 0.685	%55.3	%52.6

Note: P-values < 0.05 were considered statistically significant.
AUC, area under the curve; NICU, neonatal intensive care unit ; GPR: Glucose-potassium ratio

Table 4: The ROC curve analysis for the performance of serum markers in predicting advers obstetric outcomes and NICU admission in maternal diabetes

	Cut-off	AUC	p value	95% CI	Sensitivity	Specificity
NICU						
Glucose (mg/dL)	97.5	0.442	**0.372**	0.310-0.537	%51.1	%48.6
GPR	24.7	0.417	**0.065**	0.289 - 0.545	%42.2	%45.5
Advers obstetric outcome						
Glucose (mg/dL)	98.5	0.519	**0.792**	0.381-0.657	%54.5	%53.4
GPR	23.3	0.422	0.071	0.282 - 0.562	%45.5	%46.4

Note: P-values < 0.05 were considered statistically significant.
AUC, area under the curve; NICU, neonatal intensive care unit ; GPR: Glucose-potassium ratio

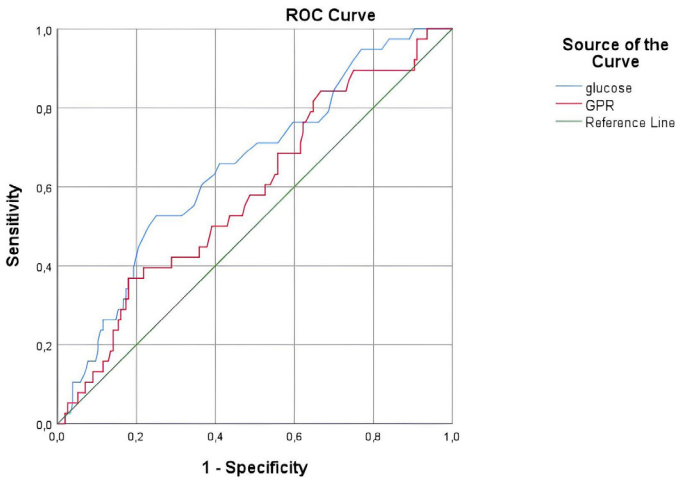

Figure 1: The ROC curve analysis for the performance of glucose and GPR in predicting advers obstetric outcomes in all participants

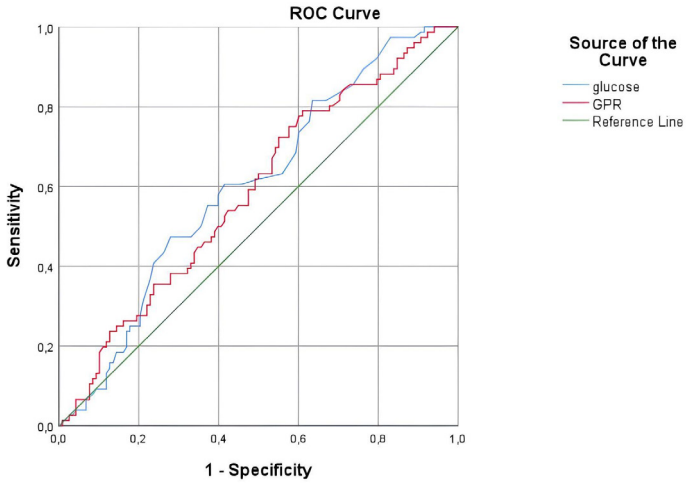

Figure 2: The ROC curve analysis for the performance of glucose and GPR in predicting NICU admission in all participants

Discussion

According to the World Health Organization, the prevalence of diabetes has increased fourfold over the past thirty years and continues to be a serious public health problem affecting more than 800 million people.[8] Advanced maternal age, family history of diabetes, obesity, ethnicity, comorbid metabolic diseases, and physical inactivity are among the risk factors for diabetes.[9] For gestational diabetes, additional factors such as a history of adverse obstetric outcomes in previous pregnancies, history of delivering large-for-gestational-age infants, excessive weight gain during pregnancy, and multiparity should also be considered. These risk factors are consistent with the baseline characteristics of the diabetes group in our study. In our study, diabetic pregnancies were associated with significantly higher NICU admission rates and adverse obstetric outcomes compared to controls. Although glucose levels and GPR were higher in pregnant women diagnosed with diabetes compared to the healthy group, they did not maintain statistical significance in predicting adverse obstetric and neonatal outcomes. Additionally, glucose and GPR were found to be statistically significant in predicting NICU admission among all participants.

Glucose metabolism functions optimally in the human body through hormones such as insulin and glucagon, which are secreted by the islets of Langerhans and specialized cells located in the pancreas. Although the exact mechanism has not been clearly elucidated, T1DM occurs as a result of the autoimmune destruction of specialized pancreatic cells, rendering them unable to produce insulin.[10] T2DM

is associated with a reduction in glucose sensitivity of pancreatic beta cells and an inadequate response of insulin-sensitive tissues to insulin.[11] GDM is a serious and common obstetric complication characterized by hyperglycemia, insulin resistance, and pancreatic dysfunction, and it is considered an indicator of the potential development of diabetes in later life.[12] The diagnosis of GDM is established between the 24th and 28th weeks of gestation using either a one-step 75 g oral glucose tolerance test or a two-step 50 g oral glucose challenge test. Since GDM is associated with adverse pregnancy outcomes such as preterm birth, preeclampsia, shoulder dystocia, increased cesarean section rates, neonatal hypoglycemia, and increased NICU admission, early diagnosis and glucose regulation through insulin or dietary modifications are of great importance.[13] In our study, the most common complications observed in the diabetic group were preterm labor and preeclampsia. Additionally, diabetes may affect microvascular structures through molecular mechanisms such as endothelial dysfunction and increased reactive oxygen species, leading to complications such as retinopathy, nephropathy, cerebrovascular events, and heart disease.[14] Interestingly, adverse outcomes such as macrosomia and preterm birth have also been observed in pregnant women with hyperglycemia despite normal OGTT results.[15,16]

Potassium is the most abundant cation in intracellular fluid. Insulin facilitates not only the uptake of glucose but also of potassium into the cell. Stimulation by insulin and other catecholamines activates the Na^+/K^+-ATPase pump in the cell membrane, thereby promoting the entry of potassium into cells and maintaining intracellular balance.[17] A previous study showed that potassium concentrations increased in patients with poorly controlled type 2 diabetes.[18] Our study revealed no significant difference in potassium levels between the diabetic and healthy groups. This may be because we included pregnant women with good glycemic control in the study.

GPR is a ratio that is easy to calculate as a predictor, especially in ischemic conditions. In subarachnoid hemorrhages accompanied by cerebral vasospasm, GPR has shown a significant correlation with the degree of vasospasm and infarction.[19] Similarly, in acute intracerebral hemorrhage, GPR levels have been found to be significant in predicting hematoma volume after bleeding and poor outcomes three months after the event.[20] In previous studies, high GPR has been associated with postoperative mortality in patients with aortic dissection and those admitted to the coronary care unit for any reason.[21,22] In studies conducted in Turkey on GPR, it has been found to be valuable in assessing morbidity, mortality, and prognosis in patients with blunt abdominal or thoracic injuries and carbon monoxide poisoning.[23-25]

To the best of our knowledge, our study is the first to investigate the predictive value of GPR levels for adverse obstetric and neonatal outcomes in pregnant women with maternal diabetes. Several studies have examined the link between blood parameter ratios and obstetric complications in women with maternal diabetes. These investigations have shown that high neutrophil-to-lymphocyte ratios and systemic inflammation markers are statistically significant predictors of poor obstetric outcomes.[26,27] In our study, GPR did not reach statistical significance in predicting adverse obstetric outcomes and NICU admission. However, the findings suggest a clinically meaningful trend, indicating the need for studies with larger sample sizes. When all participants were evaluated, GPR reached statistical significance in predicting NICU admission. Additionally, elevated glucose levels were successful in predicting poor outcomes. In diabetic mothers, not only hyperglycemia but also other contributing factors may be involved in the development of adverse outcomes.

Limitations

This study has several limitations. First, patients with GDM and pregestational diabetes mellitus were analyzed together. Although both conditions share hyperglycemia as a common pathway, their pathophysiology and risk profiles differ, which may have influenced the results. Second, data on longitudinal glycemic control (HbA1c, fasting glucose trends) could not be fully included due to missing records. Third, the ROC analysis of GPR in the diabetic subgroup was statistically insignificant with very low AUC values, limiting the predictive validity of the marker. Future multicenter studies with larger cohorts and subgroup analyses are warranted.

Conclusion

GPR and hyperglycemia may be associated with adverse obstetric outcomes.

Availability of Data and Materials

The data supporting the findings of this study are available from the corresponding author upon reasonable request. The data are not publicly available due to privacy or ethical restrictions.

Conflicts of Interest

The authors declare no conflicts of interest.

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Authors' Contributions

B.A.A.: Writing, data curation, original draft.
E.B.: Data curation, writing – review and editing.

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RESEARCH ARTICLE

Clinical Outcomes of Intravaginal Misoprostol Use in Cases with Therapeutic Abortion Indications

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Abstract

Introductıon: This study aimed to evaluate the clinical outcomes of intravaginal misoprostol for therapeutic abortion indications and to determine whether this regimen represents a safe and effective option in routine practice.

Methods: This prospective observational study included 36 patients (mean age 27.5 ± 6.8 years; mean gestational age 16.3 ± 8.5 weeks) admitted with therapeutic abortion indications. Following baseline ultrasound and pelvic examination with modified Bishop scoring, intravaginal misoprostol was administered every 6 hours: 200 µg for pregnancies ≤20 weeks and 100 µg for >20 weeks, until expulsion. Patients were monitored with 2-hourly vital signs and post-expulsion uterine revision when indicated. Outcomes analyzed included success rates, adverse events, and induction-to-delivery intervals.

Results: The mean age of patients was 27.5 ± 6.8 years, with gestational ages ranging from 7–40 weeks. Most cases (80.6%) occurred at ≤20 weeks. The overall successful abortion rate was 97.2%. Mean induction-to-delivery intervals was significantly shorter at ≤20 weeks (583 ± 437 min) compared to >20 weeks (1183 ± 933 min; $p < 0.001$). Dose escalation beyond the initial dose occurred in over half of patients in both gestational groups (51.7% at ≤20 weeks and 57.2% at >20 weeks). Only one patient experienced transient diarrhea; no severe complications occurred.

Conclusion: Intravaginal misoprostol demonstrates high efficacy and safety for therapeutic abortion across all gestational ages, with appropriate adjustments in dosing. Initial higher doses at ≤20 weeks and cautious dosing escalation beyond 20 weeks appear effective and safe.

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Introduction

Although abortions are increasingly being performed earlier in gestation worldwide, about 10–15% still occur at relatively later stages.[1] Second-trimester terminations often arise from serious fetal anomalies or intrauterine fetal demise and pose greater clinical challenges compared to first-trimester procedures. Second-trimester terminations can be done surgically (e.g., dilation and evacuation) or via medical induction, the latter being more common in settings without surgical expertise.[2] However, there remains no universal consensus on the optimal method for terminating second-trimester pregnancies indicated by fetal anomalies or fetal death,[3] underscoring the need for evidence-based approaches in this context.

One pharmacologic agent central to mid-trimester abortion care is misoprostol, a prostaglandin E_1 analog. It is widely used for second-trimester termination because of its high effectiveness, low cost, ease of use (multiple routes of administration), and generally mild adverse effects.[4] International guidelines support misoprostol as a safe and effective option: for example, the World Health Organization recommends a misoprostol-only regimen (approximately 400 μg administered vaginally or sublingually every 3–6 hours) for induced abortions beyond the first trimester, including in cases of fetal demise between 14–28 weeks.[5] A meta-analysis of second and third trimester pregnancy losses reported that both vaginal and oral misoprostol regimens resulted in 100% expulsion of the fetus within 48 hours in those trials.[6] Importantly, misoprostol also has a generally favorable safety profile when used for second-trimester induction. Serious complications, such as uterine rupture, are rare.[7] However, caution and close monitoring are recommended, particularly in patients with multiple uterine scars.[8,9] Ongoing research continues to refine the optimal misoprostol protocol for mid-trimester termination, examining the ideal dose, route, and dosing interval for various gestational ages and indications.[10,11]

Despite the widespread use of misoprostol for second-trimester pregnancy termination, the literature is relatively limited and heterogeneous regarding its use as a single agent in therapeutic abortion cases. Many studies focus on specific regimens or subpopulations, and further data are needed to establish the most effective and safe protocol for varying indications. Therefore, this study aimed to evaluate the clinical efficacy and outcomes of intravaginal misoprostol for terminating pregnancies indicated for therapeutic abortion.

Material and Methods

This was a single-center prospective study conducted in an Obstetrics and Gynecology Clinic during the period from March 1995 to November 1995. The study adhered to internationally recognized ethical standards, including those outlined in the Declaration of Helsinki.

During the study period, 36 patients admitted to the hospital with indications for therapeutic abortion were included in the study. Patients who had a Bishop score >3, ultrasound-detected dilation of the cervical internal os, or cervical canal length <30 mm were excluded from the study. Based on ultrasonographically determined gestational age, patients were grouped into ≤20 weeks and >20 weeks categories.

Pre-procedure assessment

All patients underwent ultrasonography (US) using a Hitachi EUB-310 system (Hitachi, Tokyo, Japan) equipped with 3.5- and 5-MHz convex transducers. The US examination assessed fetal biometry, fetal structural anomalies, placental location, internal cervical os patency, cervical canal length, and fetal cardiac activity (FCA). A pelvic examination was then performed and cervical favorability was graded with a modified Bishop score, incorporating station, cervical consistency, position, effacement, and dilatation.[12] Following US and pelvic examination, baseline laboratory tests were obtained, including a complete blood count and bleeding/clotting times; serum fibrinogen was measured when clinically indicated. Patients were subsequently admitted for induction. Laminare and balloon methods were not used.

Indications for therapeutic abortion were classified into two groups: those related to maternal health (cardiovascular diseases, cases where heart surgery is not possible, causes leading to heart disease, lung diseases, kidney diseases, severe skeletal deformities and diseases, dermatological diseases, endocrine diseases, malignant tumors, birth-related diseases, psychiatric diseases) and those related to child health (severe hereditary diseases, viral diseases, ionizing radiation, maternal teratogenic drug use).

Intravaginal misoprostol protocol

To facilitate dissolution of the tablets, a vaginal lavage with 10 mL of normal saline was performed prior to placement. Misoprostol tablets were moistened with normal saline and placed into the posterior vaginal fornix at 6-hour intervals until abortion or delivery occurred. Dosing was based on ultrasound-estimated gestational age: patients ≤20 weeks

received 200 µg (1 tablet) per dose, and patients >20 weeks received 100 µg (½ tablet) per dose. No further doses were given to patients who developed effective uterine contractions. Patients remained on bedrest for 2 hours after each dose.

Monitoring and outcome measurements

Patients were monitored every 2 hours until abortion or delivery. At 2-hour intervals the following were recorded: arterial blood pressure, pulse rate (beats per minute), and axillary temperature. The time from the administration of the first misoprostol dose to the onset of abortion (incomplete abortion) or to delivery was recorded for each patient. Any adverse events potentially related to the medication were recorded.

Post-Expulsion Management

For all patients ≤20 weeks' gestation, uterine evacuation was accompanied by an infusion of 20 IU oxytocin (Syntocinon) added to 1000 mL 0.9% saline; uterine evacuation was performed concomitantly. For patients >20 weeks, uterine evacuation was performed selectively based on ultrasound assessment of the uterine cavity following expulsion. After evacuation, a control complete blood count was obtained and patients were evaluated for any drug-related side effects; findings were recorded.

Statistical analysis

All data were analyzed using SPSS version 6.0 for Windows software (SPSS Inc., Chicago, IL, ABD). Numerical data are given as mean ±standard deviation (SD) values, while categorical variables are given as numbers and percentages.

Results

The patients comprised 36 patients with a mean age of 27.5 ± 6.8 years (range, 17–42 years) and a mean gestational age of 16.3 ± 8.5 weeks (range, 7–40 weeks). Terminations predominantly occurred at ≤20 weeks (80.6%), with the remainder beyond 20 weeks (19.4%). The predominant indication was in utero fetal demise (IUFD) (72.2%), followed by premature rupture of membranes (PROM) (8.3%) and inadequate fetal visualization on ultrasound (8.3%). Less frequent indications included fetal anomaly (2/36; 5.6%), hydrops fetalis (1/36; 2.8%), and anembryonic pregnancy (1/36; 2.8%). Patient demographic data are detailed in Table 1.

Table 1. Demographic and clinical findings.

Variable	All population n = 36
Age, years	27.5 ± 6.8
Gestational age, weeks	16.3 ± 8.5
≤20 weeks, n (%)	29 (80.6)
>20 weeks, n (%)	7 (19.4)
Indication, n (%)	
Maximum dose of misoprostol, n (%)	26 (72.2)
Premature rupture of membranes	3 (8.3)
Fetus not clearly visualized	3 (8.3)
Fetal anomaly	2 (5.6)
Hydrops fetalis	1 (2.8)
Anembryonic pregnancy	1 (2.8)
Maximum dose of misoprostol, n (%)	
100 µg	3 (8.3)
200 µg	16 (44.4)
400 µg	10 (27.8)
>400 µg	7 (19.4)
Successful evacuation, n (%)	35 (97.2)
Adverse event, n (%)	
Diarrhea	1 (2.8)
Serious complication, n (%)	0
Revision curettage, n (%)	30 (83.3)
≤20 weeks (n=29)	29 (100)
>20 weeks (n=7)	1 (14.3)

Data were were shown as number (percentages) or mean ± SD.

Misoprostol resulted in successful uterine evacuation in 35 patients (97.2%), with one case of failure (Table 1). In this unsuccessful case, abortion was not achieved approximately 36 hours after administration of 1200 µg misoprostol. However, cervical ripening occurred, with the Bishop score rising from an initial 0 to 5. Vaginal mycosis was detected, and repeated attempts revealed insufficient tablet dissolution. The decision to use alternative methods was made with consideration of the patient's request. Extra-amniotic rivanol instillation (150 cc) was performed first, followed by administration of 1000 cc of serum containing 40 units of Syntophin after 6 hours. As abortion did not occur within 24 hours, serum with a higher concentration (50 units of Syntophin in 500 cc) was infused, ultimately achieving abortion. The case was classified as a failure, resulting in a 97.2% overall success rate.

Only one patient experienced transient watery diarrhea (5–6 times per day); no other adverse effects or complications were observed. Revision curettage was performed after abortion in all cases at ≤20 weeks gestation, and in 14.3% of cases beyond 20 weeks

due to suspected retained intrauterine tissue (Table 1). For pregnancies ≤20 weeks gestation, the mean induction-to-delivery intervals was 583 ± 437 min (range: 120–2040 min), compared to 1183 ± 933 min (range: 210–2400 min) in those >20 weeks (Table 2).

Multiparity was more frequently observed in pregnancies ≤20 weeks, whereas nulliparity was more common in pregnancies >20 weeks (Table 2). Mean induction-to-delivery intervals was longer in the >20-week group than in the ≤20-week group (1183 ± 933 vs. 583 ± 437 min; $p < 0.001$). Within parity strata, nulliparous patients showed the same pattern. For primiparous and multiparous patients at >20 weeks, only one case was available in each category (times 1770 and 210 min, respectively), precluding meaningful intergroup comparisons (Table 2).

Table 2. Parity distribution and time to expulsion according to gestational age group.

Variables	≤20 weeks n = 29	>20 weeks n = 7	p
Maximum dose of misoprostol, n (%)			
100 µg	-	3 (42.8)	<0.001*
200 µg	14 (48.3)	2 (28.6)	
400 µg	10 (34.5)	-	
>400 µg	5 (17.2)	2 (28.6)	
Parity, n (%)			
Nulliparous	9 (31.0)	5 (71.4)	<0.001*
Primiparous	8 (27.6)	1 (14.3)	
Multiparous	12 (41.4)	1 (14.3)	
Induction-to-delivery intervals, min	583 ± 437	1183 ± 933	<0.001*
Nulliparous	443 ± 150	1260 ± 988	0.027*
Primiparous†	565 ± 377	1770	-
Multiparous†	698 ± 588	210	-

Data were were shown as number (percentages) or mean ± SD. * P-value <0.05 shows statistical significance. † Due to having only one patient each in primiparous and multiparous categories for pregnancies over 20 weeks, intergroup comparisons could not be performed.

Discussion

Our findings indicate that both misoprostol regimens were highly effective for inducing uterine evacuation, with no significant difference in the overall success rates or induction-to-delivery intervals between the lower-dose and higher-dose protocols. Nearly all patients in both groups achieved complete expulsion within 24 hours, which is consistent with the high efficacy of misoprostol reported in the literature for first-, second-, and third-trimester pregnancy termination and stillbirth management.[6,13-16] The average induction time observed in our study is comparable to that in prior studies using misoprostol regimens, underscoring that misoprostol can reliably induce delivery within a day in the majority of case.[17]

The choice of initial misoprostol dose, the total dose administered, and the interval between doses are all key factors influencing the success and speed of abortion. Numerous studies suggest that gestational age plays a crucial role in determining optimal dosing, with higher doses generally required as pregnancy progresses. A trial in very early gestation (≤8 weeks) observed a 91% overall success rate (96% efficacy in <6-week pregnancies) using repeated 800-µg vaginal misoprostol doses.[18] In one study, women were administered 800 µg of vaginal misoprostol every 24 hours, with a maximum of three doses. The study reported a complete abortion rate of 87%. Notably, 73% achieved complete abortion after a single dose, while an additional 9% required two doses and 5% needed all three doses to complete the process.[19]

However, increased uterine sensitivity with advancing gestational age underscores the importance of cautious dose adjustment. In a randomized trial of second-trimester abortion, an initial 200 µg misoprostol dose achieved a significantly higher success rate than a 100 µg dose (92% vs. 74% complete abortion within 36 hours).[20] This aligns with existing evidence that misoprostol is a safe option in the second trimester even in patients with a prior cesarean (under carefully controlled doses), as studies have reported no increase in adverse outcomes when using moderate dosages in women with uterine scars.[21,22] Overall, our results confirm that misoprostol is an efficient and safe agent for midtrimester labor induction, achieving high success rates within 24–48 hours as noted in international studies.[23,24] Nevertheless, starting with too low of a dose may lead to protracted inductions or the need for multiple dosing rounds. Likewise, a recent cohort study of late second-trimester intrauterine fetal demise found that low-dose protocols (≤200 µg in 6 hours) were associated with a substantially prolonged induction, whereas higher-dose regimens accelerated the time to expulsion; women in the low-dose group were almost twice as likely to still be undelivered after 12 hours compared to those receiving higher cumulative doses.[25] Using only 100–200 µg as an initial

vaginal dose in mid-pregnancy often yields slower uterine activation; one comparative study noted significantly lower efficacy with a 200 µg regimen than with 400 µg.[14]

While a dose-response plateau at approximately 400 µg is considered optimal,5 exceeding this dose does not significantly enhance effectiveness and could increase the likelihood of side effects. In our cohort, we opted for a lower starting dose in more advanced pregnancies to mitigate the risk of uterine hyperstimulation or rupture. Approximately half of the patients in each gestational age group required some dose escalation beyond the initial dose (with about 17% of ≤20 week cases and 29% of >20 week cases needing a cumulative dose above 400 µg), yet only one patient experienced any notable side effect. A comprehensive review has suggested that 400 µg vaginal misoprostol every 3–6 hours is an optimal regimen for second-trimester abortion, whereas exceeding about 800 µg in total dosage may lead to increased side effects (particularly diarrhea).[26] A pivotal dose-optimization study by Dickinson and Evans compared vaginal misoprostol administered as 200 µg every 6 hours, 400 µg every 6 hours, or a 600 µg loading dose followed by 200 µg every 6 hours. The 400 µg and the 600/200 µg regimens significantly shortened the median time to delivery compared to the 200 µg regimen, though the 600/200 µg regimen was associated with higher side effects.[27] Reported side effects of misoprostol include maternal fever, chills, nausea, vomiting, diarrhea, and gastrointestinal symptoms such as abdominal pain.[21] Although no serious complications were observed in our study, the occurrence of diarrhea in one patient was consistent with the existing literature.

This study is limited by its small sample size (36 cases) and single-center design. Second, we did not have a comparison group using an alternative method or a different misoprostol regimen (such as a mifepristone–misoprostol group or a different dosing schedule). Third, the number of patients beyond 20 weeks' gestation was low, which limits the strength of conclusions regarding outcomes in later second trimester or in nulliparous vs. multiparous subgroups. Finally, the study focused on intravaginal administration exclusively – while this route is well-supported by evidence, we cannot comment on outcomes with oral or sublingual use of misoprostol from our data. Future studies with larger samples, randomized designs, and broader inclusion criteria would be valuable to confirm and expand upon our findings.

Conclusion

Our study provides meaningful insights into the design of clinically translatable 3D cartilage grafts. The regimen achieved high success rates in first- and second-trimester abortions and proved capable of inducing third-trimester labor in cases of fetal anomaly or demise. Using a higher initial dose in earlier gestations (200 µg ≤20 weeks) appeared to facilitate faster expulsion, while a lower starting dose beyond 20 weeks balanced efficacy with safety considerations for the more sensitive, late-pregnancy uterus. Importantly, most failures responded to repeated or escalated dosing, underscoring the utility of continuing misoprostol until expulsion occurs.

Ethical Declarations

This article is extracted from my master thesis/doctorate dissertation entitled "Clinical Outcomes of Intravaginal Misoprostol Use in 36 Cases with Therapeutic Abortion Indications", supervised by Taksim Hospital, İstanbul, 1993).

Ethical Standards: The study adhered to internationally recognized ethical standards, including those outlined in the Declaration of Helsinki.

Conflict of Interest Statement: The authors declare they have no conflicts of interest.

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RESEARCH ARTICLE

Efficacy of Intralesional Purified Protein Derivative (PPD) in Refractory Warts: A Randomized Placebo-Controlled Study

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Abstract

Introductıon: This study aimed to evaluate the efficacy and safety of intralesional Purified Protein Derivative (PPD) in patients with recalcitrant warts in a randomized, double-blind, placebo-controlled setting.

Methods: A total of 55 patients with treatment-resistant warts were enrolled between July 2003 and February 2005. Participants were randomized into two groups: one received intralesional PPD injections, and the other received placebo (saline) at two-week intervals for a total of four sessions. Only one target lesion per patient was injected. Baseline and post-treatment wart dimensions were recorded, and patients were followed for two months after treatment completion. Clinical response was categorized as complete, partial, minimal, stable, or progressive. Adverse effects were monitored throughout the study.

Results: Forty-five patients completed the treatment and follow-up period. Both groups showed statistically significant reductions in target wart size (PPD: from 34.86 ± 30.58 mm² to 13.55 ± 21.71 mm², $p<0.001$; Placebo: from 48.65 ± 62.08 mm² to 23.96 ± 21.45 mm², $p<0.05$). Complete or ≥50% regression was observed in 68.2% of the PPD group and 50.8% of the placebo group; however, the difference between groups was not statistically significant ($p>0.05$). No serious adverse effects were reported, and minor local reactions occurred in only two patients in the PPD group.

Conclusion: Intralesional PPD is a safe and potentially effective therapeutic option for recalcitrant warts. Although clinical improvements were observed, its efficacy did not significantly differ from placebo in this trial.

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Introduction

Warts (verrucae) are common dermatological conditions caused by human papillomavirus (HPV) infections, which are transmitted through direct or indirect contact.[1,2] HPV can infect both keratinized and non-keratinized stratified squamous epithelium and may affect almost any region of the body.[3] However, lesions most commonly appear on acral areas.[4] Although warts are most frequently observed between the ages of 12 and 16, they can occur at any age and often present as chronic and recurrent lesions.[5]

Warts are a frequent concern in dermatological practice due to their persistence and resistance to treatment.[6] Patients often seek medical care for cosmetic, functional, or social reasons. The therapeutic approach is influenced by various factors including the patient's age, immune status, duration and extent of lesions, and willingness to undergo treatment.[7, 8] While spontaneous regression is possible and mediated by both humoral and cellular immune responses, it is often unpredictable and may take months or years.

Several treatment modalities are available for warts, including keratolytics, caustic and cytotoxic topical agents, cryotherapy, electrosurgery, surgical excision, and immunotherapy.[9-11] However, none of these options has proven to be entirely safe and consistently effective. An ideal treatment for HPV infection should not only eliminate visible lesions but also eradicate the virus and prevent recurrence.[12, 13] In addition, such a treatment should be safe, easily applicable, time-efficient, and cost-effective. To date, no single therapy fulfills all these criteria.

In recent years, the intralesional administration of antigens such as Candida albicans and mumps has shown promise, with studies reporting wart clearance rates of up to 70% through the induction of a cellular immune response.[14, 15] Given the high rate of tuberculin positivity in the Turkish population, intralesional injection of Purified Protein Derivative (PPD) has also been explored as an immunotherapeutic option. In an open-label study conducted in our clinic involving patients with warts resistant to conventional treatments, approximately 60% showed clinical improvement following intralesional PPD administration. These results are comparable to the success rates reported with traditional therapeutic approaches.

Based on these observations, the present study aims to evaluate the efficacy of intralesional PPD in the treatment of recalcitrant warts through a prospective, randomized, double-blind, placebo-controlled clinical trial.

Material and Methods

Study Design and Ethical Approval

A prospective, randomized, double-blind, placebo-controlled clinical trial was designed to evaluate the efficacy of intralesional PPD in the treatment of recalcitrant warts. The study protocol was approved by the Marmara University School of Medicine Research Ethics Committee (approval date: May 2, 2003; approval number: Mar-YÇ-2003-0050). All patients were informed about the study, and written informed consent was obtained from both the patients and the investigators.

Patient Selection

Participants were recruited from the dermatology outpatient clinic of Marmara University. Eligible patients were aged 12 years or older, had at least one wart resistant to a prior conventional therapy, had not received any wart-directed treatment in the past month, and demonstrated a PPD induration of ≥5 mm following intradermal testing. Patients were excluded if they had active tuberculosis infection, were pregnant or breastfeeding, had received topical or systemic wart treatments within the previous four weeks, had a history of immunosuppression or autoimmune disease, were using immunomodulatory drugs, were receiving additional wart treatments concurrently, had lesions located exclusively on the face, or showed a PPD induration <5 mm or >15 mm in the presence of BCG vaccination, or <5 mm without BCG vaccination.

Between July 2003 and February 2005, a total of 55 patients were enrolled in the study, with 24 patients assigned to the PPD group and 31 patients to the placebo group. All participants had previously failed to respond to at least one conventional treatment, including topical 5-fluorouracil (5-FU), topical acids, cauterization, cryotherapy, or surgical excision. Of these patients, 10 discontinued follow-up voluntarily. In the PPD group, 2 patients dropped out after the first injection, 4 after the second, and 2 after the third. In the placebo group, 2 patients discontinued after the second injection. All dropouts were contacted by telephone, and it was determined that the primary reason for withdrawal was the inability to attend follow-up visits at the required intervals due to personal or logistical constraints. No patient discontinued tre-

atment due to adverse effects. A total of 45 patients successfully completed the 2-month treatment period and the 2-month follow-up and were included in the final statistical analysis.

Treatment Protocol

Participants who met the inclusion criteria were randomly assigned to either the treatment (PPD) group or the placebo group using a random number table by a physician who was not a researcher in the study and had no knowledge of the treatment protocol. The study results were also recorded in the file by the same healthcare professional. All patients (Those who have not previously received the BCG vaccine) received a standardized intradermal PPD injection into the volar forearm using a 26-gauge insulin syringe, and the PPD induration was measured after 48 hours. Only those with an induration diameter ≥5 mm were included in the treatment phase. The PPD solution used in this study (PPD Test Tuberculin Tween 80, BB-NCIPD Ltd, Sofia, Bulgaria) was supplied by the Istanbul Provincial Health Directorate and stored at +4°C.

In each patient, the size and location of all warts were documented. A single target wart was selected for treatment, and intralesional injection was administered only to this lesion using a 26-gauge insulin syringe. This approach was based on the hypothesis that immune stimulation from a single lesion could affect distant warts as well. Patients in the treatment group received intralesional PPD, while those in the placebo group received normal saline. Injections were performed by physicians not involved in the evaluation of treatment response, in order to maintain blinding. The injection volume was determined according to the size of the lesion, with 0.1 mL administered for every 0.5 cm^2 of wart surface area.

To minimize pain during the procedure, EMLA cream was applied before each injection. For lesions on the hands and feet where EMLA was insufficient, cold anesthesia was used. All patients received a total of four injections at two-week intervals. Clinical photographs were obtained at baseline and after completion of therapy. If complete clearance of the target lesion was observed and maintained, treatment was discontinued. Patients were re-evaluated two days after each injection for local and systemic side effects. Those experiencing pain or swelling were treated with paracetamol. Patients who missed two consecutive treatment sessions or experienced a grade 3 or higher adverse event were withdrawn from the study. Following completion of the treatment protocol, patients were monitored with monthly follow-up visits for two additional months. Patients who did not respond to treatment were offered alternative therapies.

Clinical Evaluation and Follow-up

Clinical efficacy was assessed by measuring the size of the target wart and other lesions at baseline, during each treatment visit, and two months after treatment completion. Treatment response was categorized as follows: complete response was defined as 100% resolution of the target wart; partial response as ≥50% reduction in size; minimal response as <50% reduction; stable disease as no change in wart size; and disease progression as an increase in target lesion size or the appearance of new warts. In addition, clearance of distant, non-treated lesions was also recorded.

Adverse effects were evaluated two days after each injection. Patients were specifically asked about the presence of pain, swelling, vesicle formation, itching, or necrosis at the injection site. Each symptom was scored on a 0–3 scale (0 = none, 1 = mild, 2 = moderate, 3 = severe), and the cumulative score was recorded as the overall adverse effect severity.

Statistical Analysis

Statistical analyses were performed using SPSS software. The distribution of gender and the number of warts between the two groups were compared using the chi-square test. Independent samples t-tests were used to assess differences in mean age, disease duration, PPD induration size, and the number of BCG scars between groups. Within-group comparisons of the mean target wart size at baseline, post-treatment, and post-follow-up were performed using paired samples t-tests. In the PPD group, the relationship between the percentage change in target wart size and PPD induration was evaluated using ANOVA and t-tests. The percentage change in wart size from baseline to post-treatment and from baseline to follow-up was also compared between the two groups using independent samples t-tests. Additionally, the number of patients in each response category was compared between groups using the chi-square test. Correlation analyses were used to assess the relationship between treatment response and variables such as PPD induration, number of BCG scars, patient age, and disease duration. A p-value of less than 0.05 was considered statistically significant.

Results

Baseline Characteristics

When comparing baseline characteristics between the two groups, no statistically significant differences were observed regarding sex distribution, age, duration of disease, number of BCG scars, number of warts, or PPD induration ($p > 0.05$). In the PPD group, 4 patients were under 18 years of age, while this number was 6 in the placebo group. The majority of patients completing the study presented with common warts located on the hands or feet, including some with subungual or periungual involvement. Additionally, four patients had filiform warts in the head and neck region, and one patient had a flat wart on the face (Table 1).

Table 1. Baseline characteristics and wart burden of patients.

Variables	PPD n = 22	Placebo n = 23	*p*
Age, years (mean [min–max])	23.0 ± 9.7	28.1 ± 13.0	0.144
Gender, n (%)			0.550
Female	14 (63.6)	12 (52.2)	
Male	8 (36.4)	11 (47.8)	
Disease duration, years (mean)	3.01 ± 2.9	3.7 ± 3.2	0.516
PPD induration, mm (mean)	12.6 ± 4.8	11.9 ± 5.4	0.354
Number of BCG scars (mean)	1.6 ± 1.0	1.5 ± 1.0	0.786
Total number of warts, n			0.450
Single wart (target wart)	4 (18.2)	2 (8.7)	
2–10 warts	15 (68.2)	15 (65.2)	
>10 warts	3 (13.6)	6 (26.1)	

Abbreviations: PPD, purified protein derivative; BCG, Bacillus Calmette–Guérin.

Clinical Outcomes

In the treatment group, therapy was discontinued for 6 patients after complete resolution of the target wart following the second or third injection, and these patients entered the follow-up phase. In the placebo group, 2 patients experienced complete clearance of all lesions, including the target wart, after the second injection and were similarly transitioned to follow-up.

In the PPD group, the mean size of the target wart decreased significantly from 34.86 ± 30.58 mm^2 at baseline to 13.55 ± 21.71 mm^2 at the end of treatment ($p < 0.001$). At the two-month post-treatment follow-up, a slight increase to 15.86 ± 28.28 mm^2 was observed. In the placebo group, the mean target wart size decreased from 48.65 ± 62.08 mm^2 to 23.96 ± 21.45 mm^2 ($p < 0.05$) at the end of treatment, and further to 22.57 ± 25.68 mm^2 at the two-month follow-up. These reductions were statistically significant within both groups, indicating that both PPD and placebo were associated with a measurable decrease in wart size.

However, no statistically significant correlation was found between treatment response (defined as the percentage change in target wart size) and PPD induration, BCG scar count, disease duration, or patient age in either group ($p > 0.05$). In the PPD group, the mean percentage reduction in wart size did not significantly differ among patients with <50% response, ≥50% response, or complete clearance ($p > 0.05$). Patients with PPD induration of 5–9 mm (n=3) had a mean response of 78.5 ± 30.34%, while those with induration of 10–15 mm (n=19) had a mean response of 68.39 ± 35.08%, again with no statistically significant difference ($p > 0.05$).

The mean percentage reduction in wart size after two months of treatment was 61.15 ± 34.00% in the PPD group and 50.76 ± 56.54% in the placebo group. At the end of the two-month follow-up, these values were 54.50 ± 49.60% and 53.62 ± 58.86%, respectively. The between-group differences at both time points were not statistically significant ($p > 0.05$).

When patients were categorized based on percentage change in wart size, chi-square analysis revealed no significant difference between the two groups ($p > 0.05$). A complete response or ≥50% reduction in target wart size was observed in 68.2% of the PPD group and 47.8% of the placebo group; however, this difference was not statistically significant ($p > 0.05$) (Table 2).

Table 2. Distribution of percentage change in wart size at the end of follow-up in the PPD and placebo groups.

Percentage change in wart size	PPD n = 22	Placebo n = 23	*p*
<50% reduction	7 (31.8)	12 (52.2)	
≥50% reduction	9 (40.9)	10 (43.5)	0.085
100% clearance	6 (27.3)	1 (4.3)	

PPD, purified protein derivative.

Response in Non-Target (Distant) Warts

Treatment responses of non-target, distant warts are presented in Tables 3 and 4. Among patients with multiple warts, regression of distant warts was observed in 2 of 18 patients (11.1%) in the PPD group, compared to 7 of 20 patients (35.0%) in the placebo group.

Table 3. Total number of warts in the PPD group at baseline, end of treatment, and end of follow-up.

Patients no	Baseline warts	End of treatment		End of follow-up warts
		warts	Notes	
1	3	3	—	3
7	5	4	Target wart cleared after the 3rd injection.	4
8	4	3	Target wart and 2 additional warts cleared; however, a new wart developed.	3
16	9	9	—	9
17	11	11	Target wart cleared after the 3rd injection; a new wart developed.	11
20	9	10	—	11
21	3	3	Target wart cleared by end of follow-up.	2
22	6	7	Target wart cleared after the 3rd injection; 2 new warts developed after the 1st injection.	6
30	2	3	—	0
32	1	1	—	1
33	2	2	Target wart cleared by end of follow-up.	1
37	1	0	Target wart cleared after the 3rd injection.	1
38	10	10	—	10
41	7	7	—	7
42	1	1	—	0
44	18	23	—	6
45	7	7	—	8
48	1	1	—	1
50	6	6	Target wart cleared after the 3rd injection; a new wart developed.	7
51	5	5	—	5
53	13	12	Target wart cleared after the 2nd injection.	13
54	2	1	Target wart cleared after the 2nd injection.	1
Total (n=22)	126	129		110

Table 4. Total number of warts in the placebo group at baseline, end of treatment, and end of follow-up.

Patients no	Baseline warts	End of treatment		End of follow-up warts
		warts	Notes	
4	2	0	Both warts cleared after the 2nd injection.	0
9	8	8	—	8
10	10	10	—	10
11	12	1	All warts except the target wart cleared after the 2nd injection.	1
14	7	7	—	7
18	17	21	One non-target wart cleared.	21
19	22	0	All warts cleared after the 2nd injection.	0
25	6	6	—	5
27	9	10	A new wart developed after the 3rd injection.	10
28	11	10	—	10
29	1	2	A new wart developed after the 2nd injection.	1
31	2	2	—	2
34	5	5	—	7
35	4	5	—	5
36	7	7	—	7
39	5	3	—	0
40	2	2	—	2
43	20	20	—	20
46	2	2	—	2
47	11	8	Two new warts developed after the 2nd injection; five warts cleared after the 3rd injection.	0
49	4	4	—	4
52	1	1	—	1
55	1	1	—	1
Total (n=23)	169	135		124

When the relationship between the total number of warts and percentage response in the target wart was analyzed, it was observed that patients with a ≥50% response in the PPD group were mostly those with 2–10 warts at baseline (Table 5). In the placebo group, patients with <50% response were also predominantly those with 2–10 warts at baseline (Table 5).

Table 5. Relationship between baseline total wart count and treatment response of the target wart at the end of follow-up in the PPD and placebo groups.

Baseline total number of warts	PPD			Placebo		
	100% clearance	≥50% reduction	<50% reduction	100% clearance	≥50% reduction	<50% reduction
Single wart, n (%)	1 (25.0)	-	3 (75.0)	-	3 (100.0)	-
2–10 warts, n (%)	4 (26.7)	7 (46.7)	4 (26.7)	1 (7.1)	4 (28.6)	9 (64.3)
>10 warts, n (%)	1 (33.3)	2 (66.7)	-	-	3 (50.0)	3 (50.0)

Data are presented as n (%); percentages are calculated within each baseline wart-count category for each treatment group. Abbreviations: PPD, purified protein derivative.

Adverse Events

A total of 29 adverse event evaluations were conducted across all 55 patients, two days following each injection. Overall, the treatment was well tolerated in both groups. Adverse effects were observed in only two patients (Patients 37 and 42), both of whom received PPD and had only a single lesion. These patients experienced mild erythema and edema, which resolved within a few days and occurred only after the first injection. Notably, both patients achieved complete resolution of their warts. No systemic side effects were reported in any participant during the study.

Discussion

In this randomized, double blind, placebo controlled study, we evaluated the efficacy of intralesional PPD immunotherapy for the treatment of warts resistant to conventional approaches. Despite extensive research into various therapeutic modalities, an ideal treatment that consistently yields complete and durable remission of warts has not yet been identified. Indeed, wart management remains challenging for clinicians due in part to the heterogeneous nature of the disease, the intrinsic variability in host immune responses, and the limited number of robust, well designed randomized clinical trials.

Traditional wart therapies such as cryotherapy, electrosurgery, laser ablation, topical acids, and surgical excision are widely used and have demonstrated varying degrees of efficacy.[9, 16, 17] However, these methods are often associated with disadvantages including pain, scarring, high cost, and variable effectiveness, particularly in recalcitrant cases. Furthermore, even when treated lesions resolve, new lesions frequently emerge, complicating long term disease control. The present study sought to address these limitations by investigating an immunotherapeutic strategy based on intralesional antigen stimulation.

Immunotherapy for cutaneous warts relies on enhancing the host's immune response to HPV.[8,18] The rationale for such strategies is supported by observations that spontaneous regression of warts is frequently associated with activation of both humoral and cellular immune mechanisms.[19] Immunotherapeutic approaches have included topical sensitizers such as dinitrochlorobenzene (DNCB), diphenylcyclopropenone (DPCP), and squaric acid dibutyl ester (SADBE), as well as systemic agents such as cimetidine.[20] Despite some promising reports, the clinical adoption of these agents has been limited due to safety concerns, logistical challenges in administration, and inconsistent evidence of efficacy. For example, DNCB has been associated with mutagenicity, while DPCP and SADBE have been linked to significant local and systemic reactions, including erythema multiforme–like responses and dyschromia.[21] Cimetidine's immunomodulatory effects observed in early non controlled studies were not consistently reproduced in placebo controlled trials, and its use is not recommended in adults.[22] Together, these limitations illustrate the need for safer, more effective, and more easily administered immunotherapeutic options.

Intralesional antigens such as Candida, mumps, and tuberculin have been investigated over the past two decades, with several studies reporting encouraging outcomes. Phillips et al. demonstrated wart clearance in approximately 72% of cases treated with intralesional Candida antigen, and other trials showed superior responses with antigen inoculation compared with cryotherapy.[23] In some reports, non targeted distant warts also resolved, suggesting a systemic immune activation following local antigen stimulation.[14] A similar open label study using intralesional tuberculin reported a 60% treatment success rate in a small cohort of patients with recalcitrant warts. These findings provided the impetus for the present, more rigorously designed trial.[24]

In our study, both the PPD and placebo groups experienced statistically significant reductions in mean target wart size at the end of treatment and at two month follow up. The average percentage reduction in wart size following PPD treatment was 61.15 ± 34.00%, with complete clearance or >50% reduction observed in 68.2% of patients. Although these outcomes were numerically higher than those in the placebo group (mean reduction 50.76 ± 56.54% and 50.8% achieving ≥50% reduction), the differences between groups did not reach statistical significance. The response observed in the placebo group may be explained by several non-specific mechanisms previously described in the literature. Intralesional injection itself can induce local tissue injury and a mechanical needling effect, leading to the formation of an inflammatory microenvironment that enhances antigen presentation and triggers cell-mediated immune responses. In addition, local cytokine release and activation of innate immune cells following injection may contribute to the clearance of HPV-infe-

cted keratinocytes. Considering the natural course of warts, spontaneous regression is a well-recognized phenomenon, particularly in the context of immune system activation. Therefore, the reduction in lesion size observed in the placebo group is more likely attributable to non-specific immune stimulation and local immune responses induced by mechanical trauma rather than a specific therapeutic effect. Nevertheless, the more robust and sustained response observed in the BCG-treated group supports the contribution of a specific immunomodulatory effect to the overall clinical outcome.

First, the high response rate in the placebo group warrants consideration. Literature reviews of multiple controlled trials encompassing traditional wart therapies report an average placebo response rate of approximately 30% (range 0–73%).[25] In the present study, the placebo group's response rate was higher than the reported pooled average, yet still within the boundaries of previously observed outcomes. The elevated placebo response may be attributable to the mode of administration; intralesional injection itself can trigger a non specific inflammatory response that may accelerate wart regression independent of antigen specificity. However, prior studies examining needle based interventions without active antigen did not consistently demonstrate such pronounced placebo responses,[26] suggesting that procedural factors alone may not fully account for these results.

Another finding of interest was the relatively modest clearance of distant, non targeted warts. While earlier studies with Candida and mumps antigens reported distant wart resolution rates as high as 78%.[15] the present trial observed distal regression in only 11.1% of PPD treated patients and 35.0% of those receiving placebo. The differential response may reflect variations in host immune priming, antigen specificity, or methodological differences such as the number, frequency, or quantity of injections.

The lack of correlation between PPD induration diameter and clinical response is also noteworthy. Although some earlier studies with tuberculin antigen suggested a possible association between stronger skin test reactivity and treatment outcome,[27] this relationship was not observed in the present cohort. Similar findings have been reported in other investigations, indicating that baseline immune reactivity as measured by induration may not reliably predict therapeutic benefit from antigen based immunotherapy.

Safety is a critical consideration in any therapeutic approach, and intralesional antigen administration in this study was generally well tolerated. Only two patients in the PPD group experienced mild erythema and edema, both of which resolved without intervention and did not necessitate discontinuation of therapy. This favorable safety profile contrasts with the relatively higher incidence of local and systemic side effects reported in some Candida and mumps antigen studies, including blistering, flu like symptoms, and treatment discontinuation in a minority of subjects.

From a clinical perspective, the findings of this study underscore the complexity of wart immunotherapy. Although PPD induced significant reductions in wart size and achieved high rates of clinical response, the absence of a statistically significant difference compared with placebo highlights the challenge of demonstrating clear superiority over non specific immune stimulation in controlled settings. It remains possible that refining antigen selection, dosing regimens, or combining immunotherapy with other modalities could enhance therapeutic efficacy.

The present study also emphasizes the importance of standardized protocols in immunotherapy trials. Variability in antigen types, injection intervals, dose determination, and lesion selection criteria across different studies complicates direct comparisons and synthesis of results. For example, while some protocols adjust antigen dosage based on lesion size or skin test induration, others employ fixed doses irrespective of individual characteristics.[28] In this trial, antigen volume was tailored to lesion surface area, which may influence outcomes relative to alternative dosing strategies.

Limitations of this study include the relatively small sample size and the short duration of follow up, which may limit the ability to detect late recurrences or differences that emerge with longer observation. Additionally, the study was conducted in a population with high baseline tuberculin reactivity, which may affect generalizability to populations with different epidemiologic backgrounds.

In conclusion, intralesional PPD immunotherapy demonstrated clinically meaningful reductions in wart size and achieved substantial response rates among patients with recalcitrant lesions. However, its outcomes were not statistically superior to placebo in this controlled setting. The safety profile was favorable,

suggesting that PPD immunotherapy remains a viable option in selected cases. Future research should focus on optimization of antigen based strategies, including combination approaches, identification of predictive biomarkers of response, and exploration of mechanisms underlying non specific immune activation observed with intralesional interventions. Such efforts may ultimately contribute to the development of more effective and targeted immunotherapeutic treatments for chronic and treatment resistant warts.

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CASE REPORT

Coexisting Complete Hydatidiform Mole and a Viable Fetus: A Rare Twin Pregnancy Case with Favorable Neonatal Outcome

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Abstract

Introductıon: The purpose of this article is to report a rare case of twin pregnancy complicated by a complete hydatidiform mole with a live fetus and to review the clinical challenges associated with its management.

Case Presentation: A 21-year-old woman in her third pregnancy with a history of one previous birth and one miscarriage was referred to our tertiary clinic at 21 weeks of gestation with a suspected molar pregnancy. Ultrasonography revealed a dichorionic twin pregnancy consisting of a normal fetus and its anterior placenta, along with a posterior placental mass with a "bunch of grapes" appearance. Laboratory findings showed markedly elevated β-hCG levels and suppressed TSH values. Amniocentesis confirmed a normal fetal karyotype, but concurrent mole tissue analysis was initially inconclusive. The pregnancy was closely monitored with weekly β-hCG and ultrasound assessments. At 33+6 weeks, an emergency cesarean section was performed due to vaginal bleeding, and a male baby weighing 1750 g was born. Postnatal histopathology confirmed a complete hydatidiform mole in one placenta and a normal placenta in the other. Postpartum β-hCG levels gradually decreased, and no evidence of gestational trophoblastic neoplasia was observed on follow-up.

Conclusion: Twin pregnancy with a complete hydatidiform mole and a coexisting fetus is an extremely rare condition associated with significant maternal and fetal risks. Careful monitoring t may allow favorable outcomes in selected cases where continuation of pregnancy is chosen.

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Introduction

Twin pregnancies carry higher risks than singletons, and rare anomalies further complicate management.[1] One such condition is the coexistence of a complete hydatidiform mole (CHM) with a viable fetus. Hydatidiform mole, the most frequent gestational trophoblastic disease, results from abnormal trophoblastic proliferation and is classified as complete or partial, each with distinct features (2–4). The occurrence of CHM alongside a normal fetus is extremely uncommon, estimated at 1 in 20,000–100,000 pregnancies.[2]

Complete hydatidiform moles arise from abnormalities in early fertilization that disrupt normal genomic imprinting and parental gene balance. Most cases develop when an ovum lacking functional maternal chromosomes is fertilized, leading to a diploid conception composed entirely of paternal genetic material. Because maternally expressed imprinted genes such as p57/CDKN1C are absent, trophoblastic tissue proliferates extensively and villous structures become markedly edematous. Less frequently, dispermic fertilization or rare heritable imprinting defects may produce similar androgenetic or biparental patterns, each ultimately resulting in the characteristic overgrowth of molar placental tissue.[3]

In these cases, one placenta sustains normal fetal growth while the other is replaced by abnormal molar tissue.[4] CHM usually causes miscarriage or trophoblastic disease, but when a twin fetus develops normally, the pregnancy poses serious risks such as hemorrhage, preterm birth, and malignant progression.[5] Even when fetuses appear structurally normal, survival rates are low.[6]

Pregnant women in whom a complete mole coexists with a normal fetus are well known for placing both the mother and the fetus at considerable risk. On the maternal side, complications frequently arise from the excessive hormonal activity of the molar tissue, leading to early or recurrent bleeding, the development of preeclampsia often with an unusually early onset, and episodes of biochemical or symptomatic hyperthyroidism.[7,8] In line with previous case-based evidence, Erol et al. documented a CHMCF pregnancy complicated by severe preeclampsia and antepartum bleeding, supporting the view that maternal complications are common and may necessitate early delivery.[9] These pregnancies also carry a greater probability of progressing to gestational trophoblastic neoplasia. From the fetal perspective, impaired placental function is a persistent concern, contributing to growth restriction, intrauterine death, and a markedly increased likelihood of preterm birth. Together, these risks explain why overall outcomes remain guarded, even when the fetus appears structurally normal.

Managing these pregnancies is rarely straightforward. Clinicians are forced to balance maternal safety with the hope of continuing the pregnancy long enough to benefit the unaffected fetus, and this often means very close follow-up and decisions that are adjusted from week to week. In reality, many of these pregnancies are lost early or end because of maternal complications, although there are occasional reports of families choosing to continue and achieving a favorable result under strict monitoring[10]

The information available in the literature also shows that the outcomes in such cases are far from uniform. One of the earlier large-scale reports, a Japanese nationwide study, found that a notable proportion of women eventually developed persistent trophoblastic disease, particularly when the molar tissue was confirmed to be androgenetic.[11] Later publications presented a somewhat different picture. For example, a multicenter cohort from the Americas, which included more than seventy pregnancies, showed that a number of women who continued their pregnancies did reach live birth; however, the risk of post-molar neoplasia remained considerable and did not appear to be reduced in those who opted for termination.[12] More recent institutional series have echoed these findings, reporting frequent antenatal complications and a substantial incidence of GTN even in carefully monitored cases. A contemporary meta-analysis further emphasized how widely outcomes vary across studies, reinforcing that management strategies cannot rely on a single uniform recommendation but must be tailored to each patient's clinical situation.[13]

This report describes a twin pregnancy complicated by CHM and a surviving preterm infant, and reviews available literature to underline the clinical challenges and outcomes of this rare entity.

Case

A 21-year-old woman, gravida 3, parity 1, who had previously given birth vaginally once and had a complete miscarriage in the first trimester, with no chronic medical illnesses and a pre-pregnancy BMI of 24.1 kg/m² was referred to our tertiary health center in her 21st week of pregnancy with a preliminary diagnosis of molar pregnancy. This was a spon-

taneous conception. Ultrasound imaging revealed a dichorionic twin pregnancy with a viable fetus measuring below the 3rd percentile according to Hadlock reference curves with an anterior and normal placenta corresponding to 19 weeks' gestation and a posterior placental mass showing a 'bunch of grapes' appearance (89*34 mm) in the uterine cavity with multiple anechoic spaces, identified as a hydatidiform mole, with some of the placental tissue (figure1).

Initial laboratory tests showed markedly elevated β-hCG (222,771 mIU/mL), suppressed TSH

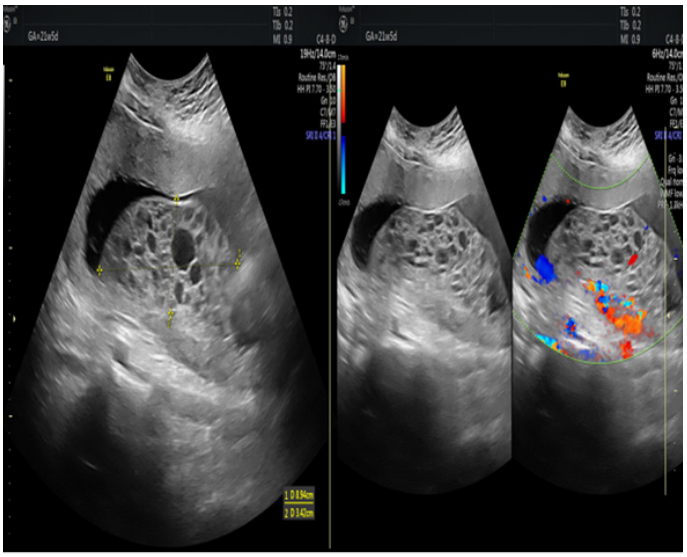

Figure1: A sonographic image of a molar placenta

(0.0647 µIU/mL) with slightly increased free T4, anemia (hemoglobin 10.5 g/dL), and normal tumor markers (CA-125, CA 19-9, CA 15-3).A 6×5 cm cystic mass, highly suggestive of a theca-lutein cyst secondary to excessive β-hCG was noted in the right adnexa. Iron and multivitamin supplementation was initiated. A sample of molar posterior placental tissue was taken using a chorionic villus sampling (CVS) needle for pathological and genetic analysis . Additionally, amniocentesis was performed on the viable fetus for genetic testing. Genetic analysis of the fetus was reported as normal, while pathology and genetic analysis of the molar tissue were did not provide sufficient viable material for molecular testing; therefore, genotyping methods such as SNP array, STR analysis, or PCR-based assays could not be completed, and assessment for paternal uniparental disomy was not feasible during pregnancy. Following delivery, the complete placental specimen became available for full evaluation, and histopathological examination confirmed the diagnosis of complete hydatidiform mole.

The patient and her family were informed about the maternal and fetal risks, including the option of termination. They chose to continue the pregnancy. Weekly β-hCG measurements and ultrasound examinations were performed, showing persistently elevated hormone levels and fetal growth restriction, but stable Doppler findings and amniotic fluid.

At 33+6 weeks of gestation, the patient presented with abdominal pain. Vital signs were stable (blood pressure: 110/70 mmHg, pulse rate :102 bpm). Ultrasound showed a live fetus with 30-week biometry (<1st percentile), normal Doppler flow, and adequate amniotic fluid. In anticipation of potential preterm delivery, Betamethasone (Celestone) was administered intramuscularly at a dose of 12 mg twice, 24 hours apart, for fetal lung maturation. The chest radiograph results were normal and the patient had no symptoms of preeclampsia. During follow-up, active vaginal bleeding was observed on examination, and an emergency cesarean section was performed.

A 1750 g male infant was delivered with a 1-minute Apgar score of 5 and was transferred to the neonatal intensive care unit. The molar placenta and the anterior normal placenta were both removed and sent for pathology

Postoperative β-hCG levels were:

- Day 1: 40.589 mIU/mL
- Day 2: 20.672 mIU/mL
- Day 9: 1.370 mIU/mL
- Day 16: 245 mIU/mL

The final pathology of the placenta was reported as:

Microscopic examination of placental tissues revealed small-diameter chorionic villi without trophoblastic proliferation in the anterior placenta (figure 2A, 2B). Immunohistochemical study showed no loss of immune reaction in the stromal cells of the villi with p57 (figure 2C). In the posterior placenta, chorionic villi showing marked hydropic changes and surrounded by proliferating trophoblastic cells were seen (figure 2D, 2E). Loss of immune expression with p57 was observed in the villous stromal cells and in most of the surrounding trophoblasts (figure 2F).

The baby was admitted to the neonatal unit due to being premature but was discharged 15 days later in good health, weighing 2250 grams. After delivery the patient was followed up closely. Serial β-hCG monitorization was performed weekly for three months, Then β-hCG levels were checked monthly and approximately five months later β-hCG

was negative. Chest imaging performed one month after birth revealed no abnormalities. Due to the ongoing risk of gestational trophoblastic disease in future pregnancies, she was counseled to seek evaluation at a specialized prenatal and gynecologic oncology center if she conceived again.

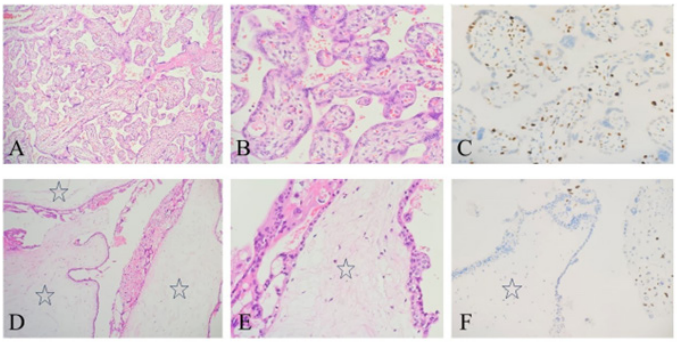

Figure2: Microscopic images of placental tissues are observed. A, B, and C belong to the first placenta; D, E, and F belong to the second placenta. In the first placenta, the trophoblastic cell arrangement and the dimensions of the chorionic villi are of normal histological appearance, and when the villi are examined stromally and seen as trophoblastic, p57 is positive. In the second placenta, trophoblastic cell proliferations are observed around the chorionic villi (stars) showing hydropic expansions, and while intermediate trophoblastic is recorded as positive with p57, there is a loss of reaction in the stromal and trophoblastic involvement in the villi (A, B, D, E: Hematoxylin/Eosin; C, F: Immunohistochemical p57 staining). A, D: 100x; B, C, E: 400x; F: 200x magnification).

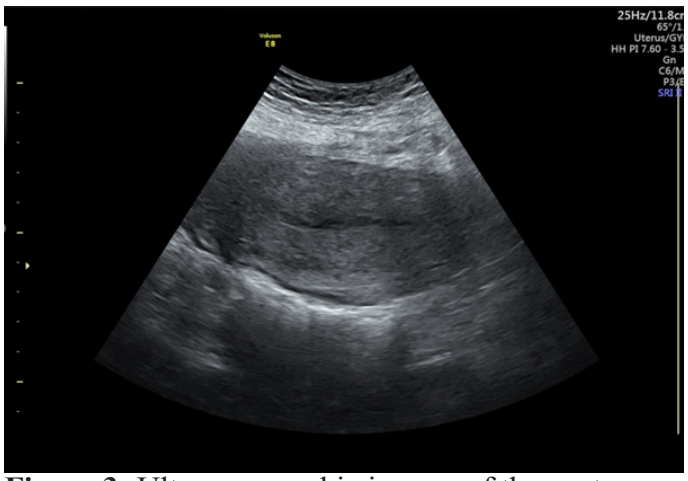

Figure 3: Ultrasonographic images of the postoperative endometrial cavity

Discussion

Twin pregnancies complicated by complete hydatidiform mole with a coexisting fetus (CHMCF) represent an extremely rare and high-risk condition. Complete moles are premalignant lesions characterized by androgenetic diploidy, markedly elevated β-hCG, and higher risks of complications such as hemorrhage, hyperthyroidism, and gestational trophoblastic neoplasia (GTN).[3,14,15] Pregnancies complicated by a complete mole with a coexisting fetus carry a considerably higher risk of developing gestational trophoblastic neoplasia (GTN). The incidence in the main cohorts is generally between 25% and 50%, reflecting variability in diagnostic treatments and follow-up protocols.[12,16]

Placental mesenchymal dysplasia (PMD) is an important differential diagnosis because it can mimic a molar pregnancy on ultrasound and often presents with extensive cystic changes and placental enlargement resembling a “grape-like” pattern.[17] However, PMD typically lacks trophoblastic proliferation and retains normal p57 expression, distinguishing it histologically from complete hydatidiform mole, in which loss of maternally expressed imprinted genes and peripheral trophoblastic hyperplasia are characteristic findings.[18] Furthermore, PMD is usually associated with a chromosomally normal fetus and is not accompanied by markedly elevated β-hCG levels or an increased risk of gestational trophoblastic neoplasia. These features help prevent misclassification when both a cystic placental mass and a viable fetus are present.[19]

The decision to continue or terminate such pregnancies remains controversial. Some reports, particularly from Asia, describe higher rates of GTN in CHMCF and advise termination.[11] Conversely, other series suggest that up to 60% of managed cases can result in live births and that termination does not necessarily reduce the risk of GTN.[12] These findings support an individualized approach, balancing maternal risks against the possibility of favorable neonatal outcomes.

Adverse perinatal outcomes are common, with fetal growth restriction (FGR), preterm delivery, and placental dysfunction frequently reported.[20] In our patient, progressive FGR led to preterm cesarean delivery, consistent with previous observations that molar tissue may compromise placental function. Diagnosis relies mainly on ultrasound, though its accuracy is limited; molecular and pathological evaluation may be required for confirmation.[21,22]

Postpartum surveillance is crucial, as the risk of GTN is higher in CHMCF compared with singleton moles, though most cases respond well to methotrexate-based therapy.[23]

This case emphasizes the need for vigilant antenatal surveillance, multidisciplinary care, and strict postpartum follow-up in achieving favorable outcomes in this rare entity.

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CASE REPORT

A Rare Complication Related to Fully Covered Stent in the Treatment of Perforation in Laparoscopic Sleeve Gastrectomy: Early Stricture and Polyp Development

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Abstract

Complications such as stricture and polyps may develop in the long term due to the fully covered stent used for the treatment of upper gastrointestinal tract perforations. However, the early presentation of these complications is rare. In the present report, our objective was to present a case of stricture development and polyp formation in the upper and lower ends of the stent in a 47-year-old woman who developed perforation during laparoscopic sleeve gastrectomy. The stent remained in place for a short period, and the lesions progressed rapidly. We aim to highlight that these complications can arise within a short period.

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Introduction

Definition

Early and late complications may occur during laparoscopic sleeve gastrectomy, which is one of the most commonly used methods in bariatric surgery. These complications include bleeding, leakage, abscess development, and stricture in the later period. Leakage occurs most commonly at the stapler site, and early reoperation is often necessary. In less common instances, leakage may develop as a result of organ damage due to the instruments used in surgery. This complication is usually present intraoperatively or in the first few days after surgery.

Aim

In the present report, we present a case of perforation caused by thermal injury due to harmonic use during LSG. The patient was initially treated with conservative methods in the postoperative period. When this approach proved unsuccessful, the patient was successfully treated with a fully covered stent. However, stricture and polyp development occurred early after stenting. The objective of this report is to raise awareness of these rare early stent complications and to contribute to the existing literature on this subject.

Case Report

A 47-year-old female patient was admitted to our clinic with a primary diagnosis of obesity. The patient exhibited no comorbidities and had no history of prior surgical procedures. The patient's body mass index (BMI) was 41. The patient was informed of all treatment options and indicated a preference for surgical intervention.

Laparoscopic sleeve gastrectomy was performed. During the operation, a perforation with a diameter of approximately 2 millimeters developed in the posterior part of the stomach approximately 3 centimeters from the duodenum as a result of thermal damage due to harmonic use. The surgical intervention was performed to address the observed defect, employing primary suturing techniques during the operation. Postoperative evaluation using methylene blue staining revealed no evidence of leakage.

On the second postoperative day, the patient underwent a second surgical procedure after the presence of bile was observed in the drain. The initial surgical intervention was repeated, yet two days following the second procedure, the patient underwent an endoscopic implantation of a fully covered stent extending from the esophagus to the bulbus, owing to the observation of recurrent bile drainage. The stent used was a fully covered nitinol alloy stent with tip diameters of 30 mm, a mid-diameter of 24 mm, and a length of 220 mm. Subsequent to a 15-day observation period, the stent was removed, and no leakage was detected. However, 15 days after the stent was removed, the patient presented with a complaint of difficulty in swallowing solid foods. Conventional imaging techniques, including ultrasonography and computed tomography, did not reveal any signs of leakage. A meticulous examination of the patient's gastrointestinal tract using a specialized endoscope (i.e., a gastroscopy) revealed the presence of a stricture in the region corresponding to the upper end of the stent. This structural abnormality was found to be the causative factor for the obstruction that precluded the successful passage of the endoscope. Upon the stricture's passage via balloon dilatation (35 mm diameter achalasia balloon), a polyp was observed to have developed in the region corresponding to the lower end of the stent (Image 1). The histopathological examination of the biopsy taken from the polyp reported a granulomatous reaction secondary to inflammation.

Gastroscopic balloon dilatation was performed once more in the subsequent month. No observable growth of the polyp was identified, and the patient was subsequently monitored. It has been six months since the most recent gastroscopy, and the patient is currently free of active complaints.

Figure 1. Endoscopic image of a polyp at the site of the lower end of the stent

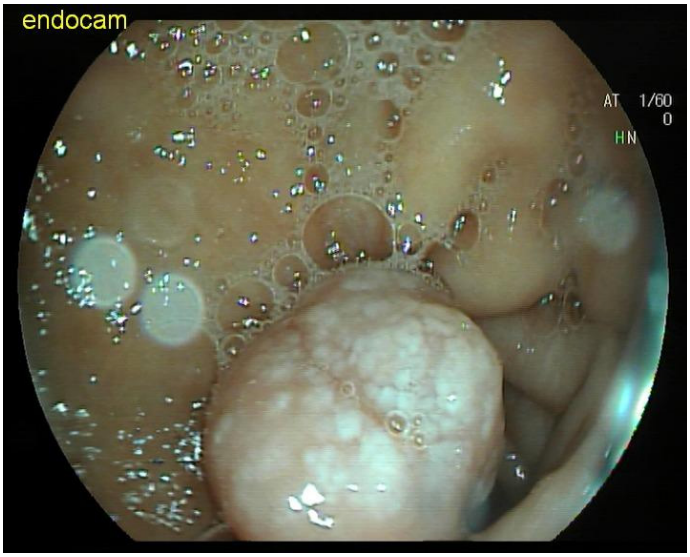

Figure 1

Discussion

Sleeve gastrectomy is a procedure that is frequently utilized in the field of bariatric surgery. This surgical procedure can be performed laparoscopically with a high degree of safety and efficacy. However, it is important to note that significant complications may develop, although they are not common. The most common complications that occur in the initial postoperative period are hemorrhage, leakage at the stapler site, and abscess development.[1] Complications may be observed in the period following one month, including the development of stenosis, reflux, nutrient deficiency, and mediastinal pouch development.[1]

A large series of 2,834 laparoscopic sleeve gastrectomy (LSG) cases revealed that 1.5% of patients developed an operation-related leak.[2] The International Sleeve Gastrectomy Expert Panel Consensus Statement documented this rate as 1.06%.[3] In the same series, leakage due to harmonic use was observed in one of 44 leak cases.[2] Early diagnosis and appropriate management have been shown to reduce morbidity. Treatment options include primary surgical repair, percutaneous drainage, and endoscopic stenting.[4] In the present case, leakage due to harmonic use developed, which was recognized at the time of operation and intervened with primary suture.

Endoscopic stent placement is a minimally invasive and effective treatment option that is widely preferred in the management of leaks after sleeve gastrectomy. In instances where conventional methods prove ineffective in sealing the leak, the utilization of fully covered stents emerges as a pivotal strategy. These stents are designed to prevent the leakage of gastric contents and to facilitate the healing process of the tissue. According to the extant literature, the success rate of stenting has been documented to exceed 90%.[5] In the present case, recurrent leakage despite primary suturing twice was successfully treated with endoscopic full-coated stent placement.

The most common post-stent complications include, but are not limited to, stent migration, dislocation, ulceration, granulation tissue formation, stricture, bleeding, and, in rare cases, pseudo-polypoid formations.[6] The term pseudo-polyp is used to describe reactive polypoid granulomatous reactions. Post-stent stricture is a complication believed to result from mucosal ischemia and inflammation due to prolonged mechanical compression. In some cases, endoscopic dilatation may be necessary to address strictures that reach a level that requires surgical revision. In the case presented, a patient who exhibited difficulty in the ingestion of solid foods following stent removal developed a stricture at the proximal end of the stent, thereby impeding the passage of the endoscope and necessitating balloon dilatation as a treatment modality.

In rare instances, polypoid mucosal proliferations may also develop subsequent to stenting. A limitation of the current literature is the lack of sufficient data regarding the histopathologic features of these lesions. Subsequent to the removal of the stent, the formation of "pseudo-polyp" formations has been observed, particularly at the distal end. These formations are believed to be associated with the granulation and healing process.[7] Post-stent strictures and pseudo-polypoid lesions have been sporadically documented in the extant literature, with these formations predominantly characterized in the late phase.

However, the occurrence of such pathologies only a few weeks after stent removal is extremely rare. In our case, although the stent was in place for a total duration of 15 days, stenosis at the upper end and polyps at the lower end were detected in the second week after removal. This finding suggests that the complications described are not confined to prolonged stent retention, and that in some patients, severe mucosal changes can occur even with short-term deployment. This may be explained by multifactorial factors, such as individual tissue response, stent characteristics, and concomitant inflammatory response. However, it should be noted that these lesions may recur. The results of a short six-month follow-up period are shared in our case, but it is essential to conduct long-term follow-ups of 12-24 months in such cases.

Our case represents a rare example of early stricture and polyp formation following short-term stenting after sleeve gastrectomy. It is noteworthy that the stent remained in place for only a short period, and the lesions developed very shortly thereafter. Given the prevalence of similar lesions in the late period in the literature, this case underscores the potential for earlier triggering of underlying pathophysiologic processes. Consequently, clinicians must pay closer attention to this possibility. Consequently, this case highlights complications that are rarely documented in the literature but may be overlooked in clinical practice. It contributes to the development of a preventive approach (early endoscopy, short-term follow-up, etc.) in this context.

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