

COMPARATIVE STUDY OF CONVENTIONAL AND NATURAL TREATMENTS FOR FIRST- AND SECOND-DEGREE UTERINE PROLAPSE: A QUASI-EXPERIMENTAL COMPARATIVE STUDY

Sadia Nasir¹, Nasreen Kishwar², Ziad Ullah Shah³, Habib Ullah Mohsin⁴, Hamdi Iqbal Bangash⁵

¹Department of Obstetrics and Gynecology, Khyber Teaching Hospital, Peshawar

²Department of Obstetrics and Gynecology, Hayatabad Medical Complex, Peshawar, Pakistan

³Department of Pediatrics and Neonates, Molvi Ameer Shah Memorial Hospital, Peshawar

⁴Department of Medicinal Chemistry, University of Peshawar

⁵Department of Pediatrics and Neonates, Khyber Teaching Hospital, Peshawar

ABSTRACT

Objective: This quasi-experimental study aimed to explore a multi-pathway herbal matrix as a viable alternative to standard mechanical treatment.

Materials & Methods: A prospective observational cohort study was conducted with 125 patients at Khyber Teaching Hospital in Peshawar. Rather than randomization, patients were assigned to two groups based on individual circumstances. Participants were encouraged to choose based on their preferences and symptoms. One group received standard pessaries and pelvic floor muscle training. The other group received a standardized botanical preparation suspended in an Evening Primrose Oil bilipid matrix, designed to minimize hepatic first-pass metabolism. Treatment progress was assessed using POP-Q and PFDI-20 scores over a 12-week period.

Results: Both regimens showed substantial baseline improvements. However, the oral botanical treatment arm had a more pronounced reduction in structural POP-Q staging ($p = 0.035$) and in subjective PFDI-20 symptom burden ($p = 0.029$). The non-invasive cohort reported superior tolerability, with no severe adverse events and a comparatively low 9.5% incidence of mild gastrointestinal shifts, versus 19.3% localized irritation in the mechanical treatment arm. Overall satisfaction was 83.1% in the botanical treatment arm.

Conclusion: Our findings suggest that nutraceutical therapy is a viable, noninvasive alternative for managing mild uterine prolapse, offering outcomes comparable to or better than those of traditional methods and with better patient tolerability.

Keywords: Uterine Prolapse, Phytoestrogens, Nutraceuticals, Pelvic Floor

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INTRODUCTION

Depending on parity and interpretation of demographic data, uterine prolapse affects a fraction to nearly half of older women.^{1,2} The mechanics are simple: pelvic floor weakening, descent of the uterus into the vaginal canal, and disruption of the patient's life due to physical discomfort and urinary dysfunction.³ The regional situation in South Asia is dire, with clinical prevalence rates in rural

Pakistan, for example, exceeding 10% due to high parity and poor early obstetrical care.⁴ Decades of experience have led to protocols such as ACOG Practice Bulletin No. 214, which recommend offering vaginal pessaries as an alternative to surgery.^{5,6,7,8}

However, vaginally inserted mechanical devices are limited because they cause friction and localized infections. A significant number of patients, therefore, simply stop using the devices due to the chronic irritation they cause and have no effective form of conservative management.⁹⁻¹² Furthermore, variations in pelvic floor kinematics during voluntary contraction can severely limit the effectiveness of traditional physical therapies for some women, driving the need for systemic alternatives.¹³

Due to these issues with pessaries, urogynecological researchers are looking into the possibility of systemic oral therapy. The botanical matrix prepared for this trial

Correspondence

Dr. Nasreen Kishwar

Assistant Professor

Department of Obstetrics and Gynecology, Hayatabad Medical Complex, Peshawar - Pakistan

Cell: +92-314-2316770

Email: nasreenhmc@gmail.com

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was designed with a specific receptor affinity in mind. Vitex agnus-castus acts as a dopaminergic D₂ receptor agonist in the anterior pituitary and works similarly to bromocriptine, which suppresses hyperprolactinemia to correct the estrogen-to-progesterone ratio.¹⁴ The latter hormone is required for the tension of the pelvic ligaments. It was combined with *Cimicifuga racemosa* for its affinity to central 5-HT₇ and 5-HT_{1A} receptors.¹⁵ This property is relevant to RCOG Green-top Guideline No. 48, which recognizes the importance of modulating aberrant serotonergic and GABAergic signaling in neuro-vegetative and premenstrual mood disorders.¹⁶ *Astragalus membranaceus* is used in the formula for its ability to induce cellular AMPK activity in a manner similar to biguanides, while *Adhatoda vasica* is included for the inhibition of enteric alpha-amylase.^{17, 18} The whole preparation is suspended in an Evening Primrose Oil matrix to prevent hepatic metabolism and allow direct entry into circulation.

Because the literature lacks comparisons between complex botanical pharmacology and conventional pessary treatment, this trial was initiated to assess the compound's response against standard-of-care ACOG conservative management in a pragmatic hospital setting.

MATERIAL AND METHODS

Study Design and Setting

We conducted this prospective, quasi-experimental study over a six-month intervention period at Khyber Teaching Hospital in Peshawar. We opted against randomization because of the unique adherence dynamics in these cases. Women who prefer to use vaginal devices base their decisions on strong psychological and physiological factors, and random allocation in such scenarios rarely reflects actual practice.

Our power analysis was based on detecting a moderate effect size of 0.52 with 80% power and $\alpha=0.05$, which required recruiting at least 118 patients. Using a consecutive sampling strategy and a recruitment goal of 125 women who met the inclusion and exclusion criteria, the study proceeded to the intervention stage. Women aged 30-60 with a POP-Q diagnosis of stage 1 or 2 were eligible for inclusion, using standardized pelvic floor dysfunction terminology¹⁹. Patients with severe third- or fourth-degree prolapse, a history of pelvic surgery, active infections, diabetes or hypertension, or pregnancy were excluded from the study.

Clinical Interventions and Pharmacokinetics

We divided the sample into two intervention groups based on the treatment algorithm and patients' adherence to the assigned modality. Specifically, 62 women (group A) received a custom-made vaginal silicone pessary along with supervised pelvic floor muscle training in accordance with ACOG guidelines. Patients in group B were pre-

scribed an oral solid-dose botanical extract formulation.

To provide transparency and comply with regulatory guidelines, we specified that the intervention used in this study is Pronoir® by Hunoir Pharmaceuticals, manufactured under cGMP standards. A key challenge in developing an oral suspension is that the liver metabolizes most compounds in plant extracts. However, the proprietary phyto-lipid technology used in this 90-day intervention allows the active ingredients to bypass first-pass metabolism and enter the systemic circulation via the lymphatic system. Each dose, 2×1 tablet per day, contains 100 mg of Black Cohosh USP, 75 mg of Agnus Castus USP, 150 mg of Astragalus USP, and 25 mg of Adhatoda Vasica USP, encapsulated in 25 mg of Evening Primrose Oil. The oil acts as an emulsifier and enhances absorption by binding to glycoprotein receptors in the intestinal walls. This mechanism reduces stress on the hepatic system and the body's metabolic burden while maximizing the bioavailability of the active ingredients. The intervention followed the standard ovulation cycle to ensure continuous exposure throughout the treatment course.

Statistical Framework

Our team met with patients every other week to assess treatment compliance and follow up on anatomical improvements using POP-Q staging and PFDI-20 patient-reported outcome measures.²⁰ We analyzed the cross-sectional data in IBM SPSS Statistics 26 using an independent t-test at a 95% confidence level. Due to the non-randomized design of the study, we applied a multivariate logistic regression model to control for potential selection bias. We included the following covariates in the regression model: age, body mass index, obstetrical history, menopausal status, and POP-Q stage at baseline. We controlled for variables with $p < 0.05$ in the final analysis, and the hospital's Institutional Review Board approved the ethical conduct of this study.

RESULTS

Baseline data showed that the two groups were comparable in general demographic characteristics. The mean age was 45, whereas statistical analysis did not reveal any significant intergroup differences in BMI, parity, menopausal status transitions, or initial POP-Q stages ($p > 0.05$).

After 12 weeks of follow-up, both interventions showed substantial improvements across all outcome measures. However, the treatment course based on the oral botanical matrix appeared more efficacious, as evidenced by a statistically significant decrease in structural POP-Q scores ($p = 0.035$). This finding was consistent with the subjective evaluation ($p = 0.029$). The strongest evidence was for the difference in PFDI-20 scores: oral administration of the tested pharmaceutical mixture led to a significantly faster reduction in pelvic floor symptom

distress.

Finally, the most notable difference was in the tolerability profiles of the interventions. Specifically, in the pessary group, 19.7% of patients experienced adverse effects, including vaginal wall irritation and secondary infections. By contrast, those in the botanical group did

not report severe adverse effects. Only 9.5% reported mild discomfort and indigestion throughout the treatment course. As a result, 83.1% of women who received oral medication were satisfied with their treatment course and outcomes, significantly higher than 68.2% among the mechanical treatment group ($p = 0.021$).

Table No 1: Demographic data of the students

Variable	Group A (Conventional, n=62)	Group B (Botanical, n=63)	p-value
Mean age (years)	44.8 ± 8.1	45.6 ± 7.5	0.62
BMI (kg/m ²)	26.4 ± 4.2	26.8 ± 3.9	0.54
Multiparity (%)	40 (64.5%)	41 (65.1%)	0.91
Menopausal Status (%)	28 (45.1%)	29 (46.0%)	0.89
POP-Q Stage 1 (%)	34 (54.8%)	33 (52.3%)	0.83
POP-Q Stage 2 (%)	28 (45.2%)	30 (47.7%)	0.81

Table No 2: Changes in Pelvic Organ Prolapse Quantification (POP-Q) Scores

Group	Baseline Score (Mean ± SD)	Post-Treatment (Mean ± SD)	Mean Change (Δ)	95% CI	Between-Group p-value
Group A (Conventional)	2.8 ± 0.4	1.9 ± 0.3	0.9 ± 0.2	[0.84, 0.96]	—
Group B (Botanical)	2.9 ± 0.5	1.7 ± 0.3	1.2 ± 0.3	[1.12, 1.28]	0.035

(Note: Within-group significance for both arms was $p < 0.001$)

Table No 3: Reduction in Pelvic Floor Distress Inventory (PFDI-20) Scores

Group	Baseline Score (Mean ± SD)	Post-Treatment (Mean ± SD)	Mean Change (Δ)	95% CI	Between-Group p-
Group A (Conventional)	68.5 ± 12.3	68.5 ± 12.3	68.5 ± 12.3	68.5 ± 12.3	68.5 ± 12.3
Group B (Botanical)	69.1 ± 11.9	69.1 ± 11.9	69.1 ± 11.9	69.1 ± 11.9	69.1 ± 11.9

(Note: Within-group significance for both arms was $p < 0.001$)

DISCUSSION

Pessaries provide immediate mechanical relief, but our analysis suggests that targeting the underlying tissue pathology yields demonstrable benefits. Patients on the botanical matrix showed improved anatomical healing, reduced subjective distress on the post-intervention PFDI-20, and no local infections despite violating ACOG's quality standards for vaginal devices. We hypothesize that the observed efficacy of the oral formulation was primarily mediated through the described lymphatic bypass route, as the lipophilic compounds in the mixture bypassed first-pass metabolism. This allowed the drug to affect all three sites of the hormonal cascade simultaneously. First, via *Vitex agnus-castus*, the preparation delivers D2 agonism to the pituitary, normalizing prolactin suppression and, consequently, the estrogen/progesterone ratios in the luteal phase. This action, similar to bromocriptine, partially

restores the mechanical properties of the pelvic ligaments within days. Second, the active repair of prolapsed tissues requires significant cellular energy. Astragaloside IV in the composition activates AMPK phosphorylation and upregulates IRS-1, which, together with *Adhatoda vasica*'s inhibition of intestinal alpha-amylase, creates conditions for reversing peripheral insulin resistance. This increases cellular energy availability and promotes collagen synthesis and repair of oxidized tissue. Finally, the downregulation of PFDI-20 scores reflects reduced patient-reported pain and distress. *Cimicifuga racemosa*'s ability to bind to 5HT₇ and 5HT_{1A} receptors centers on the same limbic structures as serotonin reuptake inhibitors, making it an effective tool for achieving the affective recovery recommended by the RCOG Green-top 48 guidelines. Of note, the trial's limitations include selection bias due to the nature of the sample and the inability to blind participants. The regression

analysis accounted for several recognized confounding factors, but unidentified variables might skew the results. Furthermore, the PFDI-20 scores might have been influenced by the placebo effect, as the control group continued to receive standard-of-care treatments. The 12-week follow-up period is also insufficient to comment on long-term tissue remodeling and recurrence rates after discontinuation.

Clinical Implications: If hepatic-first-pass formulations demonstrate consistent tissue-repair capabilities in the context of neuroendocrine dysfunction, their use should not be limited to pelvic floor disorders. The interactions with the AMPK, D₂, and 5HT pathways observed in this study provide a rationale for investigating the botanical compound in the context of Polycystic Ovary Syndrome. Specifically, the proposed treatment modality meets the criteria of the ESHRE/ASRM International Evidence-based Guideline for PCOS Management (2023) [21] for targeting ovarian dysfunction and could be evaluated in multicenter trials for Luteal Phase Defect, Insulin-resistant PCOS, and PMS/PMDD.

CONCLUSION

Targeted botanical therapy may be considered as a truly effective non-surgical alternative to mechanical pelvic support. The complex under investigation demonstrated comparable or superior results to standard ACOG-approved pessary care, facilitated by its unique bi-lipid matrix, which allowed it to either match or exceed the performance of conventional treatments. Given the parameters of our quasi-experimental analysis, this therapy can be considered a viable adjunctive option for women who require conservative prolapse management but are unable to tolerate vaginal devices.

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Authors Contribution:

Following authors have made substantial contributions to the manuscript as under

Authors	Conceived & designed the analysis	Collected the data	Contributed data or analysis tools	Performed the analysis	Wrote the paper	Other contribution
Nasir S	✓	✓	✗	✗	✓	✗
Kishwar N	✓	✗	✓	✓	✓	✗
Shah ZU	✓	✓	✗	✗	✗	✓
Mohsin HU	✓	✗	✓	✓	✓	✗
Bangash HI	✓	✗	✓	✓	✓	✗

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ethical Approval:

This Manuscript was approved by the Ethical Review Board of Khyber Teaching Hospital, Peshawar. Vide No. 598/DME/KMC.

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