Etiopathogenic, therapeutic and histopathological aspects upon the anterior vaginal wall prolapse

SABIN SORIN BADI1, MARIA-CAMELIA FOARFĂ2, NICOLAE RÎCĂ3, FLORIN GROSU4, CASIANA STĂNESCU5

1)Department of Urology, Emergency County Hospital, Craiova, Romania  
2)Department of Pathology, Emergency County Hospital, Craiova, Romania  
3)Department of Obstetrics and Gynecology, University of Medicine and Pharmacy of Craiova, Romania  
4)Department of Histology, “Victor Papilian” Faculty of Medicine, “Lucian Blaga” University of Sibiu, Romania  
5)Department of Obstetrics and Gynecology, Faculty of Medicine, “Vasile Goldiș” Western University, Arad, Romania

Abstract
The pelvine organ prolapse (POP) is a condition affecting million of women, with a major impact upon the social and professional life of the patients. According to various studies, it affects approximately 40% of the women aged over 50 years. About 10% of women with POP require a surgical procedure for POP or urinary incontinence. Our study comprised a number of 14 patients, aged between 55 and 70 years, hospitalized and treated in the Clinic of Urology within the Emergency County Hospital of Craiova, Romania, between 2011 and 2013, for second-degree cystocele. Of these, 11 (78.57%) patients had more than two natural deliveries, 10 suffered more than three abortions, and eight (57.14%) women suffered from obesity. The increase of abdominal pressure, induced by chronic coughing, constipation or hard physical work, was identified in more patients. Thus, six (42.8%) patients presented chronic bronchitis, four (28.57%) patients were smokers, eight (57.14%) patients presented chronic constipation, and 10 (71.42%) patients stated that they had performed hard physical work. The presence of effort urinary incontinence, associated to the cystocele, was found in eight (57.14%) cases. The surgical intervention consisted in the performance of a direct cystopexia with a synthetic tent, placed in a transobturator way, in a “tension free” manner (Perigee System). The post-operative evolution was a good one; the results after six months showed that 12 (85.71%) women were cured, two (14.29%) cases of cystocele relapsed, while in two patients there maintained the effort urinary incontinence. The histopathological examination of the anterior vaginal wall fragments, harvested during the surgical intervention, showed the presence of a chronic inflammatory infiltrate in the lamina propria of the uterine mucosa, which may cause the post-operative relapses. We consider that the reduction of the inflammatory process through the administration of anti-inflammatory drugs could reduce the POP onset and progress.

Keywords: pelvine organ prolapse, cystocele, direct cystopexia, vaginal atrophy, inflammatory process.

Introduction

Proplapse is a term referring to the movement or slipping of a part or a whole organ from its anatomical place, which leads to the alteration of its relation with the surrounding organs. The pelvine organ prolapse (POP) represents their descend through the vaginal channel, having as result the protrusion of the cervix and/or the vagina. Sometimes, the genital prolapse may be associated with the rectal prolapse [1]. The most frequent form of the genitall prolapse is the cystocele or the vaginal anterior wall prolapse [2].

POP is frequently associated with the effort urinary incontinence (EUI), both conditions having a major impact upon the social and professional life of the patients.

The POP incidence and prevalence varies quite a lot in various studies, according to the population categories included in the study [3]. According to some authors [2], the genital prolapse affects approximately 40% of the women aged over 50 years. Other studies state that almost 10% of women require a surgical intervention for POP, urinary incontinence, or both [4]. It is thought that, worldwide, POP affects millions of women, being a burden for the national health systems, and also a really unpleasant condition for women, seriously affecting life quality [4, 5]. The social, psychological and economical cost of POP is quite high at worldwide level [6–9]. For example, the social cost of urinary incontinence in USA, in 1995, for women aged over 65 years, was estimated at 26.3 billion dollars [8, 10, 11].

In USA, about 11% of women undergo a surgical intervention for POP or urinary incontinence, and 30% of the operated women require at least one repetition of the surgery [12, 13]. The trans-vaginal remake of the cystocele through anterior colporrhaphy is associated with a high rate of failure, which may reach 40% or even more [14, 15]. All these data underline the POP severity and motivate the efforts of the researchers and clinicians for the elaboration of new medical and surgical techniques, in order to reduce the condition incidence, and especially post-operatory relapses.

In our study, we clinically and histopathologically evaluated a number of 14 patients diagnosed with 2nd degree cystocele, hospitalized and treated in the Clinic of Urology within the Emergency County Hospital of Craiova, Romania, in order to establish the importance of certain etiological factors in the POP onset and progress.

Patients and Methods

Our study included 14 patients, aged between 55 and 70 years, hospitalized and treated for 2nd degree cystocele
in the Clinic of Urology within the Emergency County Hospital of Craiova, between 2011 and 2013. We mention that the patients were aged between 55 and 60 years, while nine patients were aged between 61 and 70 years. For every patient included in the study, there was previously obtained the “informed consent”, explaining to the patients that their identification data or other confidential data will not be made public, the study performed by us having only a purely scientific characteristic. Also, there was obtained the Accord of the Ethics Board of the Emergency County Hospital of Craiova.

The data obtained from every patient were very minutely introduced in the clinical observation sheet. During the clinical examination, there were followed: number of deliveries, way of delivery, number of abortions, lifestyle, physical activity, practicing of any sports, presence of associated diseases (diabetes mellitus, obesity, dyslipidemia), urinary or genital infections, surgical interventions of the perineum, anus or vagina. For the present condition, we were interested in the onset and progress of the cystocele, previously performed (surgical) treatments, hormone or birth control pills administration, association with urinary incontinence or presence of defecation problems.

The clinical examination included the general clinical examination, followed by a thorough examination of the abdomen, for highlighting some possible abdominal hernias, and for evaluating a possible hidden urinary incontinence. The local examination included the external genital organs, the perineum, the anal orifice and the vagina. The vagina examination was performed both manually, and by using a vaginal speculum. Also, for evaluating the POP stage, there was performed the Valsalva maneuver, using the genital prolapse quantification system POP-Q (Pelvic Organ Prolapse Quantification system).

After establishing the diagnosis of 2nd degree cystocele, there were prepared the patients for the cystocele treatment, during which there were harvested small fragments of the anterior wall of the vagina, of the formed lesion, which have been subsequently fixed in 10% formalin solution, and sent to the laboratory of anatomical pathology, where they were included in paraffin and stained with Hematoxylin–Eosin.

Results

The study on our group showed that 11 (78.57%), out of 14 women, had more than one natural delivery, situations when there could have been produced important changes of the perineum, followed by a cystocele. Also, the physical examination highlighted that 10 (71.42%) women had more than three abortions. Being known the fact that body weight increase may favor the prolapse of the pelvic organs, we evaluated the weight of every patient and observed that eight (57.14%) women suffered from obesity.

The abdominal pressure increase induced by chronic coughing, constipation or hard physical work, represents another favoring factor for POP. In our study, six (42.8%) patients presented chronic bronchitis, four (28.57%) patients were heavy smokers, eight (57.14%) patients presented chronic constipation, while 10 (71.42%) patients declared that they performed hard physical work.

The presence of effort urinary incontinence, cystocele associated, was present in eight (57.14%) cases.

The clinical symptoms presented by the patients were quite diverse. They can be classified into three types of symptoms:

- local symptoms: diffuse pain of the perineum, intra-vaginal sensation of a foreign body, pelvic discomfort, pressure in the anterior perineum region;
- urinary symptoms: dysuria, polakiuria, imperious feeling of mictioning, small effort mictioning, two-steps mictioning;
- genital symptoms: genital discomfort, vagina dryness, lack of sexual satisfaction.

The clinical examination represents the fundamental element of a positive and differential diagnosis. That is why we looked for this to be as complex and thorough as possible, in order to establish the presence of genital prolapse, of its degree and of the treatment imposed in order to rebuild the region anatomy and to suppress the symptoms.

The clinical diagnosis was that of 2nd degree cystocele, the most protuberant part of the prolapse being situated at 1 cm, or less, proximal or distal on the hymen line, but no more than 2 cm across the vagina length.

All the patients accepted the surgical treatment, whose objectives were to rebuild and consolidate the means of support for the pelvic organs, placing them in a natural anatomical position, to reduce the symptoms up to zero, to maintain and improve the urinary, sexual and digestive function, and to prevent other anatomical defects. The surgical treatment for the whole group was a minimally invasive procedure, namely one of direct cystopexia with a synthetic tent, placed in a transfibrotary way, in a “tension free” manner (Perigee System) (Figure 1).

The immediate post-operative evolution was a favorable one; still, in a single case, dysuria was maintained, and a patient presented persistent hematuria.

The late post-operative results were good. Still, in two patients, there persisted the effort urinary incontinence, but with a lower frequency, a patient continued to have dysuria, and in two cases, the cystocele relapsed.
The histopathological examination of the anterior vaginal wall fragments, at prolapse level, showed significant changes, both in the epithelium and the conjunctive tissue of the vaginal mucosa. Most often, the epithelium presented normal or obsolete areas (Figure 2). In some cases, the epithelium appeared thickened, with the increase of the cell number in the intermediary and superficial layer, taking an aspect of simple hyperplasia, leukoplasia and even acanthosis (Figure 3).

Also, in the lamina propria, in some patients, there were highlighted the presence of a chronic inflammatory infiltrate, with a nodular or diffuse disposal, made up of numerous lymphocytes, macrophages and rare granulocytes (Figures 4 and 5). Some lymphocytes were localized intraepithelially. In lamina propria, too, there were frequently highlighted a moderate vascular congestion, angiogenesis vessels, with a diffuse erythrodiapedesis.

**Discussion**

POP is a multifactorial disease that may affect all ages, but is more frequent in women over 60-year-old. In young, healthy women, the pelvic organs are maintained in an anatomical position through the complex interaction between the rising anal muscles, vagina and perineal conjunctive tissue, which maintain the urogenital hiatus closed [16]. The decrease of the anal rising muscle tonus or the change of collagen fibers leads to the creation of low resistance areas, thus favoring POP [17, 18].

The main cause of the POP onset is multiple pregnancies with natural delivery, situations when the anal rising muscles are prolonged by 3.3 times [16] or even partially damaged [19]. The destruction of the perineal diaphragm appears more marked when the fetuses have high birth weight and episiotomy is required [20]. In our study, 78.57% of the women had multiple pregnancies, with natural deliveries. We consider that the pregnancy itself, through the created abdominal hyper-pressure, labor and natural delivery, determine damages of the pelvic conjunctive tissue, of the muscles and the platform, thus
favouring the POP onset. The higher the number of pregnancies and vaginal deliveries, the more highlighted the morphological changes of the pelvic platform will be. In comparison to nulliparous women, the women who delivered vaginally a single baby have four times higher a risk to develop POP, while women who delivered vaginally two babies have an 8.4 higher risk to develop POP [21, 22]. Other studies showed that more advanced is the age of the first pregnancy and vaginal delivery, the higher the risk for developing POP [23].

Neuromuscular lesions also seem to be an important etiopathogenic factor for POP. These appear through direct compressions and elongations of the nerves and muscles, phenomena that occur during labor and vaginal delivery [21, 24].

Advanced age constitutes an important etiological factor for POP, by at least two ways [25–27]:

• decrease of the estrogen level subsequent to menopause onset, with its determined metabolism changes in the support conjunctive tissue, with the reduction of the elastic fiber quality of the vaginal wall;

• biological depletion of the tissues.

According to some studies, the estrogen administration would reduce the need for a surgical intervention in women over 60-year-old [28], which confirms the theory according to which the decrease of estrogen quantity represents a risk factor for POP.

In our study, all patients were aged over 55 years: five (35.71%) of these were aged between 55 and 60 years, while nine (64.29%) patients were aged between 61 and 70 years. Apart from the advanced age, our patients also presented, in association, other risk factors: obesity (57.14%), chronic bronchitis (28.57%), chronic constipation (57.14%) or performed intense physical activity (71.42%). All these risk factors acted synergistically in the POP development.

The data obtained by us are in accordance with other studies that have identified similar risk factors [12, 29, 30].

Lately, there was given a special attention to obesity as a risk factor in developing POP. According to some authors [31, 32], the increase of body mass, and especially obesity, play a major part in the POP etiopathogeny, while weight loss does not seem to be significantly associated to the POP reduction, thus suggesting that the pelvic platform damaging due to body mass increase might be irreversible.

The clinical symptoms presented by the patients in our group is quite diverse (genital, urinary, anal), denoting that the cystocele is a major expression of POP, but during the clinical evaluation and the applied treatment, there should be taken into account all the symptoms presented by the patients.

More than half of the patients in our group presented effort urinary incontinence. Of the anamnestic data, there was recorded that the patients lost urine in small quantities when performing heavy work, when sneezing or coughing. If, at first, the urine losses were low, in time the lost urine quantity increased, thus creating an important discomfort for the patients. We consider that urinary incontinence was a clear sign of POP, a consequence of the pelvic platform structure damaging. Numerous studies showed that POP is frequently associated with urinary incontinence [33, 34], presenting some common physiopathological mechanisms. Urinary incontinence has negative effects upon life quality, as it alters the ability for physical effort, social relationships and the emotional state of the woman [35–37].

The histopathological study we performed highlighted important changes of the vaginal mucosa. Unfortunately, there could not be harvested fragments from the entire vaginal wall thickness, but we think that the inflammatory changes of the vaginal mucosa lamina propria were extended in all the smooth tissues of the vaginal anterior wall. The presence of a chronic inflammatory process in the smooth parts of the vaginal wall may explain the cystocele development, but also its postoperative relapses, as lymphocytes, granulocytes and macrophages, through its synthesized and secreted enzymes, contribute to the smooth tissue remodeling. It is well-known the fact that the vaginal anterior wall and the endopelvic fascia contain high quantities of type I, alpha-1 collagen, which can be degraded by matrix metalloproteinase-1 (MMP-1), also known as interstitial collagenase, produced by the leukocytes during the inflammatory process [27]. Other enzymes involved in the conjunctive tissue remodeling are matrix metalloproteinase-3 (MMP-3), also known as stromelysin-1 that degrades a high number of the extracellular matrix components, including collagen-3 and elastin [38], and matrix metalloproteinase-9 (MMP-9) (collagenase type 4) that degrades type IV and V collagen. Some studies found a high activity of MMP-9 in the soft tissue of the pelvic platform in the POP women [39].

The pelvic platform and especially the vaginal wall, undergo physiological changes mediated by hormones, during pregnancy and delivery. Still, the biomechanic stress that becomes highest during delivery has certain limits, on which the pelvic platform changes become pathological ones [40, 41]. We consider that, after delivery, in the pelvic platform, and especially in the vaginal wall, there were physiologically interferences with a process of tissue remodeling, where there are involved various types of leukocytes secreting collagenase, but at the same time, also provide the antibacterial protection of the genital tract. A difficult or prolonged labor may overcome the “stress” limits of the smooth tissue, thus causing a dysbalance in the reparatory and degrading processes, leading to a high secretion of collagenases that degrade collagen and elastin [42–44].

According to some authors, the increase of the collagenase activity is linearly correlated to the magnitude of the mechanic force that appears during delivery [45].

The surgical interventions of the perineum performed during labor highly increase the local inflammatory reaction and the risk for POP development. That is why we believe that administering certain anti-inflammatory drugs to women in a prolonged labor or episiotomy might prevent the alteration of the pelvic platform tissues, and would reduce the risk for POP.

The fact that not all women with a difficult and prolonged labor or with episiotomy develop POP lead to some studies approach of the genetic aspects of POP. Thus, there was observed that women with POP and effort urinary incontinence have a genetic predisposition.
regarding the abnormal remodeling of the extracellular matrix of the perineal conjunctive tissue after delivery [27].

Regarding the postoperative clinical results of the surgical intervention performed by us, we believe that these may be compared to the ones found in other studies [46–49]. Still, in two patients, there was maintained the effort urinary incontinence, and in two cases, the cystocele relapsed, which denotes that no operatory method is relapse free.

Conclusions

In the POP development, we may incriminate advanced age, hormonal dysfunction, obstetrical past, lifestyle, obesity and the presence of a chronic inflammatory process in the pelvic platform. These determine a damaging of the pelvic platform tissue that increases with age. Effort urinary incontinence is frequently associated with POP, which imposes the diagnosed evaluation of both clinical entities and the simultaneous surgical treatment. The minimum invasive procedure of cystocele correction (direct cystopexia with synthetic tent, inserted by a transobturatory way) is extremely effective; it requires reduced hospitalization, with good late results. We consider that the reduction of the inflammatory process through anti-inflammatory drugs administration might reduce the POP onset and progress.

Conflict of interests

The authors declare that they have no conflict of interests.

References


**Corresponding author**

Florin Grosu, MD, PhD, Department of Histology, “Victor Papilian” Faculty of Medicine, “Lucian Blaga” University of Sibiu, 10 Victoriei Street, 550024 Sibiu, Romania; Phone +40746–097 966, e-mail: drfloringrosu@gmail.com

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