"VIUSID" AS IMMUNOMODULATOR DRUG FOR THE TREATMENT OF IMMUNOLOGICAL DISTURBANCES IN PSORIATIC ARTHRITIS

Rodica PASCAL[1], Eugeniu RUSSU[2],
State Medical and Pharmaceutical University "N. Testemitanu"

1- Associate Professor
2- Junior lecturer

Abstract

There are few 'second-line' drugs available for the treatment of immunological disturbances in psoriatic arthritis (PsA) and their use is often limited by nonspecific activity and toxicity. Viusid is accepted as an effective immunomodulator drug for treating different immunodeficiency diseases, but rarely evaluated in psoriatic arthritis. An earlier open study suggested that it was well tolerated and potentially beneficial.

The present study of 17 patients has now confirmed its efficacy as immunomodulator in PsA immunological disturbances patients with active PsA recruited from Rheumatology department of Republican Clinical Hospital, they have administrated Viusid 9,0 gr per day 2 months (group 1). Eight patients with active PsA have been treated without Viusid (group 2). In both groups we have studied immunological status (cellular and humoral).

Evaluation of effect of treatment revealed significant improvements in immunological indexes in group with Viusid. By 4 wk the immunocellular indexes in that group was still showing benefit. Greater improvement occurred in those patients on active treatment by 6 wk, with more benefit being detected in immunohumoral status (normalization of Ig G, M, A and circulatory immunocomplexes) which were associated at the beginning with a high acute-phase response. No exacerbation of psoriasis was observed in first 6 months. This study is in progress now to determine the degree of efficacy of Viusid in different clinical subgroups of psoriatic arthritis.

In addition to immunological index the Viusid group improved significantly in terms of visual analogue scale, duration of morning stiffness. Viusid is effective in immunocompetent control of PsA and indicates the importance of such studies in this variable disease.

Introduction

Psoriatic arthritis is a form of arthritis that occurs in patients with psoriasis. It has the hallmarks of an "inflammatory" arthritis, including joint pain, erythema, and swelling, often with prominent stiffness, not unlike the most well-characterized form of inflammatory arthritis, rheumatoid arthritis (RA) [1,2,4]. However, in terms of clinical, genetic, histologic, and immunohistochemical patterns, PsA best fits with the spondyloarthropathies, which include ankylosing spondylitis, reactive arthritis, the arthritis associated with inflammatory bowel disease, and undifferentiated spondyloarthropathy [1,5,6]. Distinct features of PsA, shared with other spondyloarthropathies, include enthesopathy (inflammation of insertion sites of tendon, ligament, and joint capsule), dactylitis (swelling of a digit), a tendency toward asymmetric, sometimes oligoarticular joint involvement, iritis, and a greater chance for male involvement than what is seen in RA [1,2,7].

In recent years attempts have been made to identify prognostic factors that would classify the disease with respect to disease severity and progression. Clinical signs and specific HLA antigens have been suggested as such possible prognostic factors. Variable associations between PsA and HLA antigens B13, B17, B27, B38, B39, Cw6, DR 4, DR 7 and DQ 3 have been reported [3,5,7,8].

Increased understanding of the pathophysiology of PsA demonstrates the central role of inflammatory cytokines such as tumor necrosis factor TNF-á and activated T cells, which are targets of current targeted therapies. Several other cellular, cytokine, and chemokine targets have been identified, and there are numerous drug development programs in RA, PsA, and psoriasis aiming at these additional targets, which will affect future options for PsA therapeutics [6,8,9].

Several important therapeutic studies in PsA described in a review article in this journal last year, while in abstract form, have been published in 2004, and will be further detailed here. Additionally, several drug development programs in PsA as well as psoriasis have matured, thus providing further data to review. As a result of findings from these studies, rheumatologists, now quite familiar with the use of biologics for the treatment of rheumatoid arthritis (RA), are actively using these agents in PsA patients with progressive disease who have not adequately responded to nonsteroidal anti-inflammatory drug (NSAID) or traditional disease-modifying antirheumatic drug (DMARD) therapy alone. In parallel, using of these drugs have been induced different abnormalities in immune system and actually it is important to now modern medication of these disturbances by immuno-modulating drugs such us Viusid [3,4,5,6,8].

Viusid is a nutritional preparation specially designed for the increase of the immunological defences in all those processes that cause immunodeficiency.

The activation of the components of Viusid increases to a great extent the power of the biological function of all of them, without modifying or changing the molecular structure. All the compounds that make up the Viusid formulation are present in the human organism in a natural way, and for this reason, there have not been detected either side effects or any toxicity after the use of the product. The antioxidant substances of this preparation eliminate the negative effects of the free radicals that appear in all the infectious processes. Hence the high effectiveness of Viusid [7,8,9,10,11,14].

On the other hand, the deficiencies of certain vitamins have been related to anemic processes. Viusid provides the vitaminic elements necessary to avoid these deficiencies and their consequences. Moreover, the essential amino acids contained in Viusid make possible the nutritional development appropriate for the increase of the immunological defences [12,13,15].

Materials and Methods

In this cross-sectional study at the rheumatology clinic, Republican Clinical Hospital, Republic of Moldova, 17 patients (5 females, 12 males) with psoriasis or a history of psoriasis and inflammatory arthropathy, defined as peripheral arthritis of more than 6 weeks' duration and/or radiologically assessed axial involvement, were consecutively examined. All patients were assessed at a follow-up by a standardised protocol at one time point. Their previous disease history from disease onset was collected both from the patients and from their hospital records at the department of rheumatology and dermatology. Laboratory and radiological examinations were performed concurrently with the actual clinical examination. All patients were diagnosed by a dermatologist as having psoriasis, except one whom had pustulosis palmoplantaris. All patients had been on DMARD treatment for 6 months or longer (sulphasalazine, antimalarials, methotrexate, azathioprine). Eight were on treatment with oral corticosteroids for their joint disease.

Diagnostic Criteria and Radiographic Examination

Peripheral arthritis was diagnosed, by a rheumatologist, when there was a swollen and tender joint with duration of more than 6 weeks, located outside the spinal column and/or sacroiliac joints. These patients were further classified as having oligoarthritis when fewer than five joints were affected and with polyarthritis when five or more joints were affected. Aggressive joint manifestations were defined as radiological erosions and/or irreversible deformities (e.g. ankylosis, subluxation and/or loss of function or reduced mobility) of peripheral joints. All patients with peripheral arthritis were examined radiologically in the affected joints at the time of the study, or those with previous arthritis during the disease course.

These radiographs were evaluated for erosions (5 grade 2) according to Larsen´s grading system. Ten patients were unwilling to undergo radiographic examination for this study. The diagnosis of axial disease was based on radiological findings in the sacroiliac joints according to the New York criteria (5 2) and/or syndesmophytes, ligamentous ossification, vertebral squaring and shining corners of the spine. The spinal column and/or sacroiliac joints were examined radiologically in 12 patients with an actual or previous history of back pain and/or decreased movements of the spine diagnosed in at least two directions as described in ESSG criteria and/or according to Schober.

The classification of the disease pattern, both at onset and during the disease course, was based on actual and/ or previous findings of peripheral/axial engagement, diagnosed by a rheumatologist and as reported in the hospital records.

Laboratory Tests and Tissue Typing

Erythrocyte sedimentation rate (ESR mm/h, Westergren) and blood levels of C-reactive protein (CRP, mg/l) were determined. Also we have studied immunocellular (T- and B-lymphocytes with subgroups) and immunohumoral status (Ig G, M, A and circulatory immunocomplexes) at the beginning of the study and after 4 and 6 wk. This study is in progress now to determine the degree of efficacy of Viusid in different clinical subgroups of psoriatic arthritis by longer time of examination.

Clinical Assessment of Articular Involvement

Patients were asked about the duration of morning stiffness. Clinical assessment included examination of the joints: number of tender, swollen and deformed joints defined as ankylosis; subluxation or decreased range of motion attributable to joint damage rather than active inflammation; dactylitis and plantar fasciitis or tendo-Achilles tendinitis. Clinical lumbar spondylitis was defined as the presence of clinical features of sacroiliac involvement found by testing for sacroiliac stress pain, using at least three techniques, and/ or inflammatory spinal pain defined as low back pain and stiffness, not relieved by rest or limited lumbar flexion on modified (10 cm) Schober's test, with points of measurement 5 cm above and below the posterior superior iliac spine, and limited lumbar flexion defined as < 5 cm excursion between these points at maximal lumbar flexion. Cervical involvement was diagnosed if inflammatory symptoms attributed to the cervical spine were present, with evidence of tenderness and/ or limitation on physical examination.

Based on the clinical features, patients were classified into one of the following patterns: oligoarthritis, defined as d"4 joints; polyarthritis, defined as e"5 joints; clinical axial involvement.

Clinical Assessment of Skin Disease

Psoriasis was classified by an experienced dermatologist as plaque (psoriasis vulgaris, guttate, erythrodermic or pustular). The distribution was recorded – scalp, trunk, upper limbs and lower limbs – and the current severity was graded according to the Psoriasis Area Severity Index (PASI) (max. score = 72). This score takes into account the grade of severity on a scale from 0 to 4 of different parameters such as erythema, infiltration and scaling, and the percentages of involved skin in each area, i.e. head, trunk, upper limbs and lower limbs.

Nail involvement was defined as the presence of 10 or more pits and/or onycholysis, dystrophy, subungual hyperkeratosis, discoloration, loss of nails or postulation.

Relationship between Skin and Joint Diseases

Patients were asked about synchronous flares of skin and joint diseases. Correlations were sought between PASI score,

scalp, trunk, upper limb, lower limb and nail score on the one hand, and parameters of joint disease such as morning stiffness, number of tender and swollen joints, deformed joints, presence of dactylitis, DIP involvement, presence of inflammatory neck and back pain and Schober's test on the other. These correlations were studied in the whole group of 17 patients and in according to the time of onset of joint and skin disease, family history of psoriasis, articular patterns of PsA and history of simultaneous onset of skin and joint disease.

Statistics

Student's t-test was used to test for differences for continuous data and the w2 test was used to test categorical data between groups. Spearman's correlation was used to test for correlations between variables in small samples. A corrected P value was calculated for multiple comparisons. For multivariate analysis, logistic regression was performed with backward and forward elimination methods, with all variables included and with aggressive disease as an independent variable. The two different methods yielded identical results. All P values refer to two-tailed tests and $P < 0.05$ was considered statistically significant.

Results

Patients Demographic and Clinical Characteristics

Demographic data for the 17 patients (5 females/12 males) with PsA at the time of the study are presented in Table 1.

Table 1

Demographic data for patients with psoriatic arthritis at the time of the study

All patients n= 17	
Mean age at inclusion, years ± SD	47.0 ±11.1
Mean age at onset of skin disease, years ±SD	22.3 ±12.0
Mean age at onset of joint disease, years ±SD	37.1 ±14.0
Skin onset before joints (%)	62
Joint onset before skin (%)	14
Patients with nail lesions (%)	31

Skin disease was mild, with only a few small lesions in more than half of the patients (60%), and in 14 of them (82%) it started before the age of 40. All patients had peripheral arthritis, of whom 5 females and 7 males also had axial disease. All patients had active arthritis at examination with a mean number (±SE) of 3.0 ± 0.5 of active arthritis. The number of active arthritis correlated with ESR (rs = 0.275, P = 0.011) and CRP (rs = 0.444, P < 0.0001). The disease manifestations at onset and manifestations accumulated during the disease course are presented in Table 2.

Table 2

Disease manifestations at onset and accumulated manifestations during disease course in 88 patients with psoriatic arthritis

	Onset n (%)	During disease course n (%)
Monoarthritis	2 (11.8)	0 (0)
Oligoarthritis	4 (23.6)	1 (5.9)
Polyarthritis	11 (64.7)	3 (17.6)
Inflammatory back pain	14 (82)	7 (41)
Dactylitis	5 (29)	2 (11.8)

In 5 patients (29%) the disease first occurred in the small joints, mostly the fingers or toes, and in another – the knee and sacroiliacs were the first affected joints. At onset as polyarthritis the small joints were involved in 88% of patients, whereas onset as monoarthritis more often affected the large joints (70% of patients, data not shown); these associations were statistically significant (w2 = 21.18, P < 0.0001). In almost two-thirds of the patients with onset in the large joints the disease became polyarticular.

In patients with first-degree relatives affected by psoriasis (n=9) the onset was more frequent in large joints than in small (w2 = 7.88, P = 0.005). Patients with a family history of psoriasis had an earlier onset of skin disease (P = 0.031) but there were no significant differences in deformities or severity of disease.

Characteristics of the Skin Involvement

Psoriasis vulgaris was by far the most prevalent skin manifestation, present in 7 out of 17 patients. Only four presented with psoriasis guttata and a single patient had erythroderma. The mean PASI of the entire group was 7.8 ± 9.6. The distribution of the skin lesions was as follows: scalp, 89% of patients; trunk, 66%; upper and lower limbs 73% and 64%, respectively. Sixty three per cent of the patients presented typical nail changes.

Characteristics of Joint Involvement

Morning stiffness of more than 1 hour's duration was experienced by 17 patients (100%). The mean number ± standard deviation of swollen and tender joints was 2 ± 2 and 5 ± 4, respectively. Dactylitis was present in 3 of the patients. Deformed joints were found at all the patients: monoarthritis – 2, oligoarthritis – at 4 and polyarthritis – at 11 patients. Cervical or lower spinal involvement, characterized by inflammatory pain, was present in 14 (82%) of the patients, 7(41%) presented with limitation of neck movement.

Interrelationships between Skin and Joint Diseases Onset and Course

The onset of skin disease preceded the arthritis in 6 patients (group 1) (mean 6.3 years), occurred within the same year in 5 (group 2), and in others – arthritis preceded the skin manifestations (mean 3.5 years).

Distribution and Extent Whole Group. No significant correlation was found between PASI, scalp, trunk, upper limbs and lower limb score and the number of tender or swollen joints. On the other hand, a significant correlation was found between the degree of skin involvement, expressed by the PASI score, and Schober test ($P = 0.02$): higher PASI scores correlated with limited Schober tests. Deformed joints were associated with a high PASI score ($P = 0.04$). The scalp score was found to correlate positively with the number of swollen joints ($P = 002$). Similarly, an association was found between nail involvement and deformed joints: 7 out of 10 patients with nail involvement had more than one deformed joint, whereas 1 out of 7 patients without nail involvement had deformed joints. Nail involvement was correlated with the number of tender and swollen joints: patients without nail involvement had a mean ± standard deviation of 1.0 ± 1.1 swollen joints and 4.1 ± 3.7 tender joints, whereas patients with nail involvement had 2.4 ± 2.1 swollen joints and 6.9 ± 3.7 tender joints ($P = 0.05$ and $P = 0.02$, respectively).

Interrelationships between immune system of PsA patients and Viusid administration al 6 wk

The study of immunocellular and immunohumoral status have determined a deep modification in group 1 beginning 4 wk, but more statistic important at 6 wk.

At 6 wk we have found accelerating of number of T-lymphocytes from the beginning 39,8±2,39% to 51,87±2,85% ($p<0,01$) at 6 wk and in absolute number from 654,92±62,3 to 955,67±95,1x10^6/l ($p<0,02$), at the same time we have determined growing activity to T-suppressor's number from 19,0±0,83 to 23,82±0,83 % ($p<0,001$), in absolute number from 193,18±15,0 to 249,09±14,9x10^6/l ($p<0,02$) and by the 6 wk we have found an accelerating activity of T-helper, which initially was depressed from 14,69±0,71 to 21,29±0,77% ($p<0,001$), from 119,58±6,8 to 179,3±14,7x10^6/l. A positive modification was confirmed by reduce of pre-T-lymphocytes with inactive status from 74,83±1,43 to 61,33±2,74% ($p<0,002$), from 614,28±29,2 to 490,07±36,36x10^6/l ($p<0,05$), which probably have been induced by accelerating of T-suppressors. The comparisons of these indexes between first and second group found statistics differences in normalization of T-suppressor ($p<0.05$), in elevating of T-helper ($p<0.001$) with better control of immune response. In the rest there are no statistics evidences between group 1 and group 2 in immunocellular regulating, but indexes of comparisons are at the border which indicate a possible differences by the results which would have achieved in future at longer time of Viusid administration.

In first group under the treatment by the 6 wk we observed modification of immunohumoral indexes and in particular have been reduced at normalization the number of B-lymphocytes from 74,83±1,43 to 61,93±2,74% ($p<0,02$) in absolute number from 614,28±29,2 to 490,07±36,3x10^6/l ($p<0,05$), which have been accompanied by normalization of IgA (from 2,21±0,12 to 1,95±0,11 gr/l; $p<0,01$), IgG (from 11,72±0,38 to 10,93±0,41 gr/l; $p<0,01$) and circulatory immunocomplexes (from 0,14±0,02 to 0,10±0,01 UN; $p<0,01$). In immunohumoral status there are no statistics differences between first and second group and these data have demonstrated activity of Viusid for 6 wk predominantly at immunocellular status when it was associated with specific treatment of PsA (traditional disease-modifying antirheumatic drug therapy).

Discussion

The relationship between the severity of skin lesions and joint disease in PsA and immunological status is a matter of controversy. It has been suggested that those with more severe psoriasis tend to develop arthritis with autoimmune components. It has shown a 20 % frequency of arthritis in a group of patients with severe psoriasis, in contrast to 2 % in patients with mild skin disease. Others have reported a higher frequency of arthritis among hospital inpatients with psoriasis and severe immune disturbances. However, in larger studies of patients with PsA, as well as in the present series, a proportion of patients have developed arthritis before the skin lesions, suggesting that the arthritis is not uniformly related to the overt presence of skin lesions, but induced by autoimmune process. Moreover, simultaneous flares of skin and joint disease have been reported in only 35 % of patients. We have studied the relationship between joint disease, immune system status and skin and nail involvement in a cohort of 17 patients with PsA: they could find no association between the type and distribution of the skin involvement and the arthritis subgroups, nor was there any relationship between the activity of psoriasis and the severity, activity and functional status of the arthritis. Cohen et al. studied 221 patients with PsA and found that baseline relationships between psoriasis and PsA tend to be weak, except for nail involvement. Jones et al. prospectively evaluated a small group of 24 patients with PsA and found that only a minority of patients with PsA had simultaneous flares of peripheral, skin and nail disease, independently of the time of onset of joint disease in relation to skin disease.

In the present study the most striking finding was the clear correlation between skin, autoimmune processes and joint disease in the subgroup of patients in whom disease onset was synchronous. This group of patients reported a history of frequent simultaneous flares, compared to the group in which skin disease preceded joint involvement. Likewise, clinical evaluation of these patients disclosed a highly significant correlation between their parameters of skin severity and most of the clinical parameters of both their peripheral and their spinal disease. A similar observation was suggested by Baker et al., who reported synchronous exacerbations and remissions of skin and joint disease in eight patients in whom skin and joint disease occurred simultaneously. Other studies which have assessed the relationship between skin and joint disease have not addressed this issue.

Another emerging finding of our work concerns scalp involvement and its relationship to joint disease. Involvement of the scalp was the most frequent location (89%) in our PsA patients, whereas it has been reported in 50 % of patients with psoriasis only. In the whole group of patients the extent of scalp involvement was the only parameter of skin disease that correlated statistically with all different parameters of peripheral joint disease, such as swollen and tender joints, deformed joints, dactylitis. The significance of psoriatic lesions in the scalp of patients with PsA has not been emphasised except by Wright et al., who reported a higher frequency of scalp involvement in patients with distal joint disease.

With regard to nail involvement in PsA, it has been suggested that nail lesions are the only clinical features that identify patients with psoriasis who are destined to develop arthritis. Nail lesions were found in about 63%–83% of patients, nearly always with arthritis. Our study confirms these findings. We have shown a significant correlation between nail involvement and the number of tender, swollen and deformed joints, this correlation being again more striking in the subgroup of patients with simultaneous onset of skin and joints disease. Our results are concordant with those of Baker et al., who found that patients with more severe disease have a greater incidence of nail disease, although others could not confirm this observation.

It is currently accepted that psoriatic patients with a family history of psoriasis have extended skin involvement and a

higher frequency of arthritis. We could not confirm this trend in our patients. Concerning the articular subtypes of PsA, we could find no association between the severity or distribution of skin involvement and specific articular subgroups. There was a trend for a more severe skin disease in patients with spinal involvement and in those with polyarthritis: similar findings have been reported by Stern. Our present clinical study, which did not include radiological evaluation, may have underestimated the rate of spondylitis. Our results, however, are consistent with previous reports.

Conclusion

In 17 patients with PsA we have shown that an association between the degree of skin involvement, autoimmune process and the extent of severity of joint disease does exist. Scalp involvement was by far the most frequent skin manifestation and its score correlated with most of the joint manifestations and immune disturbances. These associations were more pronounced in patients with a close temporal association between their skin and joint disease presentations.

The comparisons of immune indexes between patients with only traditional disease-modifying antirheumatic drug therapy and association of DMARD and Viusid as immunomodulating drug have achieved us statistics differences in normalization of T-suppressor ($p<0.05$), in elevating of T-helper ($p<0.001$) with better control of immune response. In the rest there are no statistics evidences between these groups of patients in immunocellular regulating, but indexes of comparisons are at the border which indicate a possible differences by the results which would have achieved in future at longer time of Viusid administration.

In immunohumoral status there are no statistics differences between groups and these data have demonstrated activity of Viusid for 6 wk predominantly at immunocellular status when it was associated with specific treatment of PsA (traditional disease-modifying antirheumatic drug therapy).

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STANDARDE DE DIAGNOSTIC ŞI TRATAMENT

APENDICITA ACUTĂ
(Ghid practic bazat pe evidenţa clinică)

ACUTE APPENDICITIS
(Evidence based clinical practice guideline)

Grupul clinic consultativ
Eugen MALOMAN, Nicolae GLADUN,
Sergiu UNGUREANU, Cornel LEPADATU

Destinat chirurgilor, rezidenţilor-chirurgi şi studenţilor

Introducere

Caracterizare. În ţările europene şi în Statele Unite ale Americii apendicita acută este cea mai frecventă urgenţă chirurgicală (sau cauză de abdomen acut). Apendicele are o lungime de 6-9 cm, variaţiile posibile fiind de la 1 la 30 cm, şi un lumen îngust, iar în submucoasă există un bogat conţinut de ţesut limfoid. Un timp îndelungat apendicele era considerat ca un organ vestigial cu funcţie necunoscută. Astăzi se ştie că apendicele este un organ imunologic, care participă la secreţia imunoglobulinelor, în special IgA. Dar funcţia sa nu este esenţială, deci nu este un organ indispensabil, a căruia înlăturare ar predispune la sepsis sau la alte tulburări imunologice. În acelaşi timp fiind inflamat apendicele poate deveni periculos[1,2].

Scurt istoric. Deşi cunoscute din cele mai vechi timpuri, inflamaţiile acute supurative în fosa iliacă dreaptă purtau denumirea de „peritiflită" şi erau atribuite inflamaţiei cecului. Doar în 1886 Reginald Fitz, bazându-se pe date morfopatologice, propune termenul „apendicită" şi recomandă înlăturarea apendicelui ca tratament curativ al acestei maladii. Prima apendicectomie în epoca chirurgiei contemporane a fost efectuată în 1884 de Krönlein, după recomandarea lui Miculitz. În a.1889 Charles McBurney descrie simptomatologia apendicitei acute, bazându-se pe 6 observaţii clinice, iar 5 ani mai târziu propune incizia, care respectă musculatura, vascularizarea şi inervaţia parietală[1,2,3].

Incidenţă. În Federaţia Rusă se consideră că apendicita acută afectează anual 4-5 persoane la 1000 locuitori, adică 400-500 la 100.000 populaţie (V.S. Saveliev, 2004), în Franţa 400-600 la 100,000. În Republica Moldova incidenţa apendicitei acute este de 220 : 100.000. În România este cea mai frecventă urgenţă abdominală (1/50-60 din locuitori prezintă în timpul vieţii apendicită acută) (A.Jecu, 2001). În S.U.A. incidenţa apendicitei acute este de 52 cazuri la 100.000 populaţie[1, 2,4,5,6]. Conform unui studiu efectuat în 1975-1991 frecvenţa apendicitei acute în SUA s-a micşorat de la 100 cazuri la 52 / 100.000 populaţie[2]. În Republica Moldova în perioada aa. 1982-2003 frecvenţa apendicitei acute s-a diminuat de la 320 la 220 cazuri la 100.000 populaţie[6]. Aceste diferenţe doar parţial pot fi explicate prin defecte de diagnostic. Menţionăm că în toată lumea se observă un declin al frecvenţei acestei patologii.

Conform studiului menţionat mai sus, în prezent în S.U.A. 84% din toate apendicectomiile se efectuează pentru patologie acută, iar 16% este rata apendicectomiei „normale" (tabloul clinic de apendicită fără schimbări patomorfologice în apendice)[2,15].

Etiologie şi patogenie. Cauza determinantă a apendicitei acute este infecţia microbiană (teoria infecţioasă şi afectul primar a lui Aschoff). Mecanismul predominant de declanşare al acestei patologii îl constituie obstrucţia lumenului apendiceal. Cauzele obstrucţiei în mod obişnuit sunt coproliţii, edemul şi hipertrofia ţesutului limfoid, bariul impactat din examinările radiologice precedente, diferiţi corpi străini, sâmburi de vegetale şi de fructe, paraziţii intestinali (oxiură, ascaride).

Lumenul apendicelui conţine în mod normal 0,1 ml de secret mucos. Obstrucţia duce la distensie şi la acumularea distal de bloc a unei secreţii de aproximativ 5 ml cu o presiune aproape de 60 ml H_2O. Această distensie şi valurile de peristaltism pentru depăşirea blocului sunt substratul şi cauza durerii viscerale (durerii periombilicale colicative). Astfel, obstrucţia provoacă stază, proliferare microbiană şi leziuni mucosale, iar hipertensia afectează vascularizarea parietală a apendicelui, cu apariţia focarelor de ischemie. Inflamaţia în scurt timp cuprinde tot apendicele, devenind flegmonoasă, se propagă la peritoneul parietal şi declanşează faza somatică. Zonele de ischemie duc la necroză (apendicita gangrenoasă) şi la perforaţie. Apendicita perforativă se complică cu peritonita locală (uneori cu formarea plastronului-abcesului) şi este generalizată[2,7].

Bacteriologie. Însămânţarea exudatului peritoneal a descoperit o varietate de aproximativ 10 diverse microorganisme: E.coli şi B.fragilis în majoritatea cazurilor, Peptostreptococcus (80%), Pseudomonas (40%), Bacteroides splanchnicus (40%) şi Lactobacillus (37%).