

# The Activity of Arylsulfatase A in Patients with Benign Ovarian Tumors

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## Abstract

The activity of Arylsulfatase A (ASA) is about two times higher in blood and urine of women with benign cystic ovarian tumors than in healthy subjects. It rises one week after surgical removal of tumor and falls four weeks later to the level before the surgery. Six months after the operation ASA activity reaches the same value as in the control group. ASA cannot be a marker of malignant ovarian neoplasms, because its activity rises also in benign ovarian tumors and during the process of healing after operation. These results agree with previous research showing that ASA is not a specific organ enzyme or tumor marker.

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## INTRODUCTION

Arylsulfatase, known as arylsulfate sulfohydrolase (ASA) EC 3.1.6.1, is a lysosomal enzyme which catalyses the hydrolysis of lipid and mucopolysaccharide sulfate esters. ASA is an acidic glycoprotein containing from 10 to 25 percent of carbohydrates with isoelectric point 3.8 and pH optimum 4.8-5.6. In the active center of the enzyme histidine and arginine, the amino acids, have been found. ASA consists of 2 sub-units which differ by several kDa. Its activity is inhibited by sulfates and phosphates.

The enzyme has been isolated from various human tissues and fluids (liver, placenta, urine, plasma). [1, 2, 3, 4] As the biochemical and immunological investigations were in progress, the attempts were made to examine the physiological role and clinical relevance of arylsulfatase A [2, 5, 6].

Arylsulfatase A is potentially important for clinical purposes because its activity changes in various physiological and pathological conditions. [3, 4] The main source of ASA for research is the urine. The estimation of ASA in blood is not very reliable, probably due to its low activity and the lack of a simple and routine method of its determination. It is also known that many diseases are accompanied by a significant

increase of ASA activity in urine. For example, a significant increase of its activity has been observed in leukemias, inflammations, and neoplasmas, particularly in patients with carcinomas of alimentary tract, breast and urogenital tract. [5, 6, 7, 8] ASA is not a specific organ enzyme [9].

The purpose of this study has been to find out if the activity of ASA changes also in benign ovarian tumors, which would indicate that it cannot be used in diagnosing ovarian cancer.

## MATERIAL AND METHODS

The specimens of blood and urine were collected from 30 women with suspected benign ovarian tumors. The patients were diagnosed and operated on in 1 Clinic of Gynecology and Obstetrics, Medical University of Wroclaw, in the years 2003-2006. For each woman the specimens were collected 4 times: before the operation, 1 week after the operation, 4 weeks after the operation and 6 months after the operation. The results of intrasurgery histopathological assessment and after surgery assessment confirmed benign ovarian tumors. The age of patients ranged from 16 to 42 years. The diameter of tumors ranged from 6 to 22 cm. Since intrasurgical histopathological examination confirmed the benign character of tumors (cystis serosa benigna ovari, adult teratoma) a conservative surgical operation was performed (enucleation of the whole cystic tumor with its wall integrity preserved). The control group was made up of 30 healthy women without any inflammatory or oncological disease

(WBC, CRP, liver enzymes, USG, and recent mammography were checked).

The activity of ASA was measured according to the Baum method using dipotassium salt of 2-hydroxy-5-nitrophenyl sulfate as substrate. The activity of ASA is expressed as units per liter in blood and units per mmol of creatinine in urine [10]. The creatinine was measured using a commercially available analytical kit form POCh (Gliwice, Poland).

The results were statistically analyzed using t-Student test. They are presented as average values (mean values) and standard deviations.

## RESULTS

As can be seen in table 1, the activity of ASA in urine of patients with benign ovarian tumors was twice as high as the one in the control group. 1 week after the surgery a significant increase in ASA activity was observed and 4 weeks after the operation it fell back to the same level as before the surgery. 6 months after the operation the activity of ASA declined further and its values approached those estimated for the control group.

**Figure 1**

Table 1: The activity of ASA in urine of patients before and after the surgery due to benign ovarian tumors.

Group	ASA activity/ creatinine (U/mmol)			
	before surgery	after surgery		
	(A)	1 week (B)	4 weeks (C)	6 months (D)
I - control	0.09 ± 0.03			
II - patients after surgery	0.22 ± 0.05	0.36 ± 0.10	0.19 ± 0.05	0.10 ± 0.04

Statistical analysis:

I/II A  $p < 0.001$  I/II B  $p < 0.001$

I/II C  $p < 0.001$

I/II D NS

II A/II B  $p < 0.001$

II A/ II C NS

II A/II D  $p < 0.001$

II B/II C  $p < 0.001$

II B/II D  $p < 0.001$

II C/II D  $p < 0.001$

As can be inferred from Table 2, similar changes in ASA activity were observed in the blood serum of the study group. Also here the activity of ASA in patients before the surgery was twice as high as that in the control group. 1 week after the operation the activity of ASA increased further and 6 months after the surgery in declined to the level similar to that of the control group.

**Figure 2**

Table 2: The activity of ASA in serum of patients before and after the surgery due to benign ovarian tumors.

Group	ASA activity (U/ml)			
	before surgery	after surgery		
	(A)	1 week (B)	4 weeks (C)	6 months (D)
I - control	1.9 ± 0.17			
II - patients after surgery	2.21 ± 0.42	2.76 ± 0.54	1.94 ± 0.41	1.25 ± 0.31

Statistical analysis:

I/II A  $p < 0.001$  I/II B  $p < 0.001$

I/II C  $p < 0.001$

I/II D NS

II A/II B  $p < 0.05$

II A/ II C NS

II A/II D  $p < 0.001$

II B/II C  $p < 0.001$

II B/II D  $p < 0.001$

II C/II D  $p < 0.001$

## DISCUSSION

About fifty years ago Dzialoszynski presented the results of his pioneer studies on sulfhydrolases, which paved the way for the application of arylsulfatase activity determination for clinical diagnostics [11]. Further biochemical and immunological studies, including the introduction of radioimmunoassay for the estimation of ASA concentration, led to the recognition of this lysosomal enzyme as a tumor marker, particularly in the diseases of lungs, kidneys, central nervous system and female genital tract [7, 8].

Despite the fact that the development of the research on ASA happened mainly due to the use of synthetic substrates the enzyme shows its affinity also to the substrates which are naturally present in tissues and body fluids. These compounds include glycosaminoglycans, such as keratan, heparin and dermatan sulfates as well as chondroitin4- and 6-sulfate, which was found in uterine myomas. [12, 13, 14] It is presumed that the enzyme regulates the level of steroid hormones and catecholamines acting on their sulfate derivatives.

The same authors emphasized that the possibility of heparan sulfate binding by various hormones, including estrogens, may provoke a significant growth of myomas. The changes of ASA activity in urine and serum of patients with benign ovarian tumors, described in this work, were statistically higher than in the control group. The differences between groups are greater than in the studies of Laidler et al. [7]

Although the increase in ASA activity one week after

surgery could be expected – as a result of post-surgery inflammatory reaction – its significant ( $p < 0.001$ ) decline 4 weeks after the surgery is worthy of notice. A further positive feature of enzymatic changes – the decrease in ASA activity 6 months after the surgery to the level not statistically different from that of the control group – suggests the possibility of an important diagnostic role of this marker.

## CONCLUSIONS

The obtained results correspond to the clinical data which show that when the activity of ASA in blood and urine decreases, no neoplastic process within the ovary structures are observed. On the other hand arylsulfatase A cannot be a marker of malignant ovarian neoplasms, because its activity rises also in benign ovarian tumors and during the process of healing after operation.

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