

Results of Prolonged Use of Intrauterine Device in Endometrium and Eosinophil Leukocytes

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Abstract; We aim to evaluate the effects of prolonged use of IUD (Intrauterine device) in endometrium curettage materials and the relationship between the use of IUD and eosinophils. Between 2018 and 2020, the pathology preparations of 38 patients who applied to our hospital with abnormal uterine bleeding and had IUD, and 30 patients with abnormal uterine bleeding alone as the control group were examined by a single pathologist. Histopathological diagnosis in the curettage materials with a light microscope, eosinophil leukocyte, neutrophil, plasmocyte counts, and accompanying histopathological findings were re-evaluated in 10XHMF (High magnification fields) in compact areas without destruction findings. In our study, the eosinophil presence rate of 38 patients using IUD was 81%. The average duration for IUD use in these patients was seven years. The average duration of IUD use for seven patients who had no eosinophils detected was two years. The average duration of IUD use for 31 patients with eosinophils was 7.5 years. In the control group patients who were not using IUD with abnormal uterine bleeding, the eosinophil presence rate was found to be 36%. The use of IUD does not always cause an increase in eosinophils in the endometrium but is accompanied by high rates. However, we can say that the number of eosinophils increases as the IUD carrying time increases. It should be kept in mind that eosinophil leukocytes, monitored by gynecopathologists in curettage materials, may be associated with prolonged IUD use.

INTRODUCTION

It is known to all gynecopathologists that the use of IUD (intrauterine device) causes histopathological changes in the endometrium. The histological features associated with the use of IUD are usually due to mechanical action. The micropapillary formation, focal reactive changes, nuclear enlargement, mild nuclear atypia, small nucleoli, and cytoplasmic vacuolization, as well as rarely stromal microcalcification, can be seen on the surface. Polymorphs, lymphocytes, histiocytes, plasma cells, foreign body type giant cells, and inflammatory cell infiltration can also be seen. Long-term use of IUD may also be associated with actinomyces infection¹.

Until today, there were several studies about the number of eosinophils in the endometrium.

These studies were generally performed in endometritis to help configuring out the confusion between plasma cells, which are the diagnostic cell of endometritis, and plasmacytoid stroma cells²⁻³.

However, the relationship of eosinophil leukocytes with IUD has never been studied in the literature.

MATERIAL and METHOD

Ethical approval

This study was approved by the Ethical Committee in Konya Training and Research Hospital, Turkey (02 July 2020, 48929119/774)

Patients and study design

A single pathologist reviewed pathology preparations of 68 patients (38 using IUD and 30 not using IUD) who had abnormal uterine bleeding during the reproductive period and applied to our hospital between 2018-2020. Histopathological diagnosis in the curettage materials with a light microscope, eosinophil leukocyte, neutrophil, plasmocyte counts, and accompanying histopathological findings were re-evaluated in 10 high magnification fields from compact areas without destruction findings. The methodology of this study is descriptive-analytical method, and data is analyzed using the statistical software SPSS 20.

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RESULTS

In this study, a total of 68 patients with abnormal uterine bleeding in the reproductive period were examined. Thirty patients were not using IUD, while 38 had IUD. The patients' age range was between 25 and 46 years, with a mean age of 37.

In the histopathological diagnosis of 38 patients using IUD during curettage; endometritis was detected in 13 patients, proliferative endometrium in 5 patients, disorder proliferative endometrium in 4 patients, early secretory endometrium in 3 patients, endometrial polyp in 4 patients, progesterone effect in 3 patients, glandular stromal destruction in 3 patients, *Enterobius vermicularis* infestation in 1 patient. Six of our patients used the Mirena coil, while 32 of them used copper-wire IUD. The duration of IUD use in our patients varied between 3 months and 15 years, and the mean use was seven years (Table 1). In 31 of 38 patients (81%) with abnormal uterine bleeding and using IUD, eosinophils were detected in curettage materials. Among them, eosinophils were detected in 85% (11/13) of cases, which were detected to have endometritis and in 80% (20/25) of cases without endometritis

(figure 1). While the average number of eosinophils observed in 10 HMF is 5.8 in patients with endometritis, it is 5 in patients without endometritis. The average duration of IUD use for eight patients who were observed to have no eosinophils was two years. The average duration of IUD use for patients who were found to have eosinophils was six years. In addition to these findings, actinomyces were observed in 2 patients (figure 2). *Enterobius vermicularis* was detected in 1 patient. Metaplastic changes were observed in 17 of our patients (14 eosinophilic, two squamous, one tubal) (figure 3). One patient had dystrophic calcification (figure 3). Pigment-laden histiocytes draw attention in 8 patients. (Table 1-2)

Eosinophils were observed in 11 (36%) of 30 patients in the control group with abnormal uterine bleeding who did not use IUD. Histopathological diagnoses in the control group were found as proliferative endometrium in 20 patients and disordered proliferative endometrium in 10 patients. Eleven patients who had eosinophils in the control group had an eosinophil average of two in 10 HMF.

Table 1. Results of our patients using IUD

IUD-Usage-duration	M-C-IUD	Pathologic diagnosis	NPL/10 HPF	Plasmocyte/10 HPF	EOS/ 10 HPF	Metaplasia
10 year	+	Progesterone effect	0	0	8	0
10 year		Endometritis	15	5	5	Squamous metaplasia
3 year		DPE	5	0	5	Eosinophilic metaplasia
2 year	+	Progesterone effect, endometritis	0	2	0	Tubal metaplasia
3 month		Endometrial polyp	5	0	0	0
12 year		Proliferative endometrium	10	0	3	Eosinophilic metaplasia
3 year		Endometritis	5	5	3	0
4 year	+	Progesterone effect	3	1	3	0
9 year		Early secretory endometrium	5	0	3	Eosinophilic metaplasia
1 year		Endometrial polyp	10	0	0	0
5 year		Endometritis	1	3	1	Eosinophilic metaplasia
2 year		DPE	5	0	0	Eosinophilic metaplasia
14 year		Endometritis	20	20	15	Squamous metaplasia
5 year		Early secretory endometrium	20	5	10	0
10 year		DPE	20	5	5	0
7 year	+	Progesterone effect	10	3	10	0
12 year		Endometritis	5	4	5	Eosinophilic metaplasia
15 year		Endometritis	10	10	10	Eosinophilic metaplasia
4 year		Endometritis	10	5	5	Eosinophilic metaplasia
4 year		Endometritis	10	10	3	Eosinophilic metaplasia
3 year	+	Progesterone effect	5	5	5	0
4 year		Endometritis	10	5	15	Eosinophilic metaplasia
5 year		Endometritis	10	5	10	0
4 year	+	Progesterone effect	0	0	0	0
3 year		Endometrial polyp	10	5	10	Eosinophilic metaplasia
1,5 year		Endometrial polyp	15	2	10	0
5 year		PE	5	0	5	0
7 year		Endometritis	5	5	5	0
1 year		Endometrial polyp	5	3	5	0
4 year		Early secretory endometrium	1	2	4	0
1.5 year		PE	5	5	0	0
5 year		PE	5	2	7	0
4 year		Endometritis	2	7	2	Eosinophilic metaplasia
18 year		DPE	10	2	10	Eosinophilic metaplasia
2 year		G/S br.	0	0	0	Eosinophilic metaplasia
11 year		G/S br.	5	5	5	Eosinophilic metaplasia
10 year		G/S br.	7	5	3	0
5 year		PE	5	0	4	Eosinophilic metaplasia

(M-C-IUD: Mirena- coil intrauterine device, PE: Proliferative endometrium, DPE:Disorder proliferative endometrium, G/S br.(Glandulo stromal breakdown)

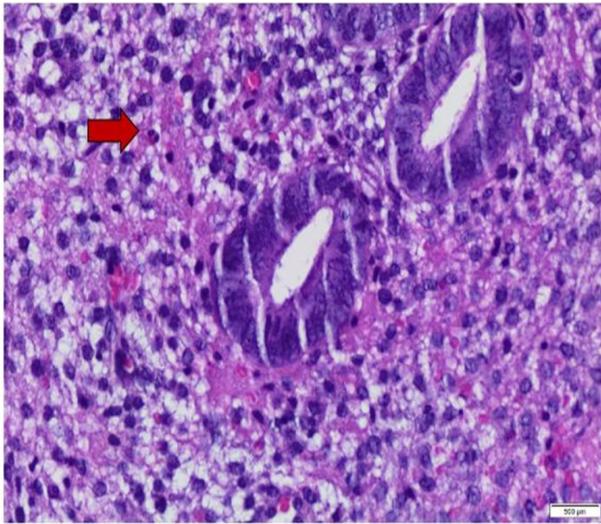


Figure 1. Eosinophil on the proliferative endometrium background (red arrow) 400X H&E Stain

Table 2. Pathological effects of long-term use of IUD

Metaplastic changes	19/38 cases
Eosinophilic metaplasia	15
Squamous metaplasia	2
Tubal metaplasia	1
Hemosiderin pigments	8/38 cases
Actinomyces	2/38 cases (5 and 18 years usage of copperwire coil)
Dystrophic calcification	1/38 case (four years usage of mirena coil)
Endometritis	13/38 cases
Enterobius vermicularis	1/38 case (four years usage of mirena coil)
Hyperplasia-malignancy	None

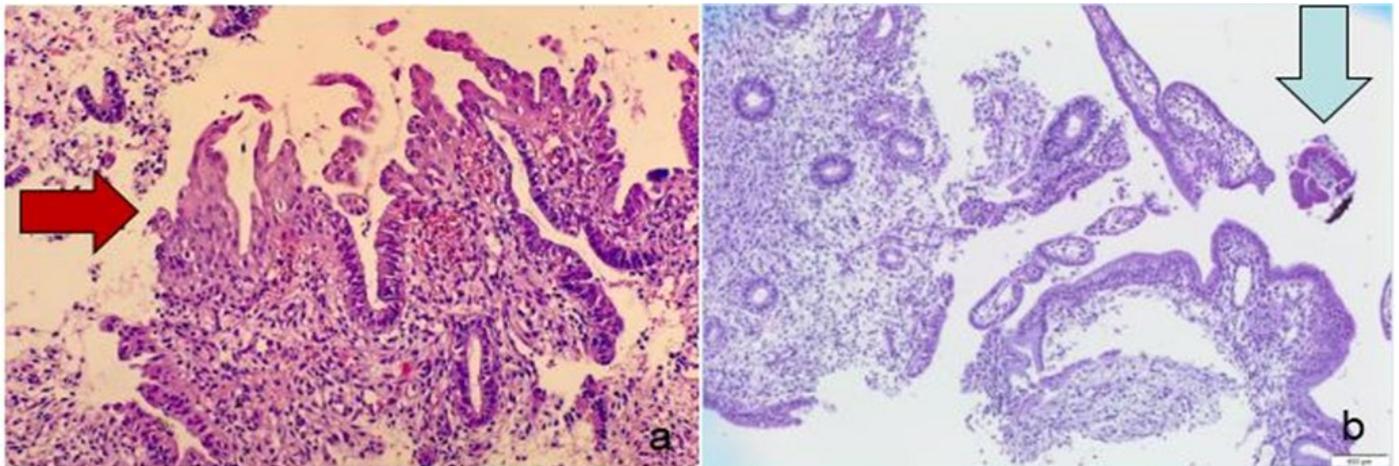


Figure 2. Squamous metaplasia of the endometrium (red arrow) 100X H&E Stain ,after usage of ten years copper -wire coil (a) Colonies of actinomyces (blue arrow) after usage of ten years copper -wire coil 100X H&E Stain (b)

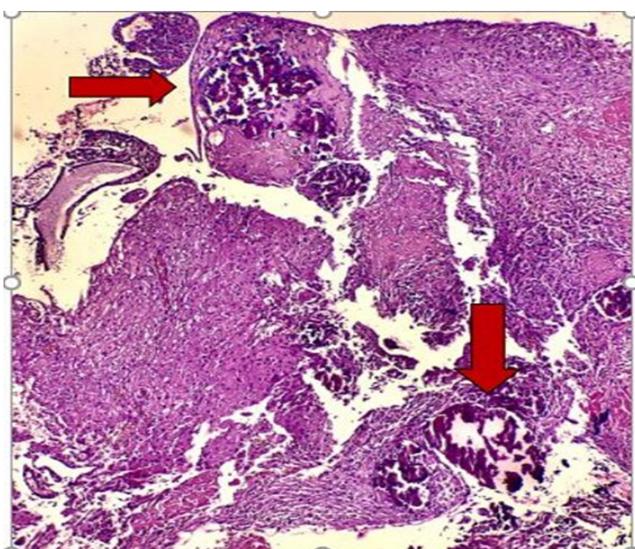


Figure 3. Microcalcifications of the endometrium (red arrows), after usage of four years Mirena coil 200X H&E Stain

DISCUSSION

Eosinophils are inflammatory cells that are popularly known to

be involved in allergy-related responses. However, eosinophils are also known to play an important role in the pathogenesis of late-type inflammation. Previous studies have shown that eosinophils are absent in the normal endometrium, except for immediately before menstruation, or they may be associated with endometrial instrumentation³. Also, inflammatory infiltration can sometimes be accompanied by eosinophils in endometritis²⁻³. Adegboyega et al. stated that eosinophil leukocyte infiltration in the endometrium may occur in curettage materials after surgical intervention and may sometimes be seen without an underlying abnormality. In the study of Phillips et al., only patients using Mirena coils were examined, and it was found that 59 of 75 samples had stromal inflammatory cell infiltration, which is usually with a mixture of lymphocytes, neutrophils, histiocytes, and eosinophils⁴.

In the study in which Perlman et al. aimed to find the

rate of eosinophils in endometritis, eosinophils were found in 68% in the endometritis group and 38% in the control group (1). In our study, this rate was found to be 85% in the endometritis group who were using IUD, and 80% in the group using IUD without endometritis.

The eosinophil presence rate (36%) found in our control group was found to be similar to that of the control group in the study of Perlman et al. In our study, the rate of eosinophil monitoring rate of 36% for non-endometritis and non-IUD control group indicates that IUD use alone may cause an increase in the number of eosinophil leukocytes without endometritis. The reason for separately evaluating endometritis and non-endometritis groups in the group using IUD is to prevent misleading because eosinophils may accompany plasma cells in endometritis.

As per our findings, the average duration of IUD use for seven patients, for whom no eosinophils were detected in the histopathological examination, was two years. The average duration of IUD for patients who had eosinophils was 7.5 years. Although the use of IUD does not always cause an increase in eosinophils in the endometrium, we can say that the rate of eosinophils increases as the duration of IUD use increases.

In our study, we added neutrophils along with eosinophils and observed that neutrophils usually accompany (30/31) eosinophils. However, we know that lymphocytes and neutrophils may be a regular component of the endometrium, depending on the menstrual cycle stage. Also, we did not detect any eosinophilic micro-abscess in any of our patients.

In addition, metaplastic changes have been observed in 17 of our cases, and 8 of them had hemosiderin pigment-laden histiocytes, and in the literature, metaplastic changes and hemosiderin pigments were associated with the use of IUD in endometrial curettage materials ⁵.

The dystrophic calcification observed in one of our cases was found to be seen in 10% of the patients using Mirena coil in the literature. In our results, it was observed in only one out of six patients who were using the Mirena coil ⁵. In a recent study, they stated that endometrial benign calcifications may be multifactorial but progesterone plays an important role ⁶. The fact that the only case we detected calcification used mirena coil for four years supports this thesis .

Once again, Enterobius vermicularis was present in one of our cases, which was associated with chronic pelvic inflammatory diseases in the literature, and its association with

IUD has not been previously defined²⁻⁷.

Although at low rates, hyperplasias have been reported in the literature related to Mirena coil use. There were no findings suggesting malignancy or hyperplasia in our patients ⁵.

Our study is valuable since it is the first study in the literature investigating the number of eosinophils in curettage materials of patients using an intrauterine device (IUD).

CONCLUSION

The prolonged use of IUD causes many histopathological changes in the endometrium. According to the results of our study, the use of IUD does not always cause an increase in eosinophils in the endometrium but is accompanied by high rates. Also, we can say that the number of eosinophils increases as the IUD usage time increases. It should be kept in mind that increased eosinophil leukocytes monitored by gynecopathologists in curettage materials, may be associated especially with prolonged IUD use.

Conflict of interest

The authors declare that they have no conflict of interest.

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