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A Comparative Study to Evaluate the Efficacy and Safety of Injection Placentrex as Compared to Conventional therapy in Pelvic Inflammatory Disease

Authors
Dr Sujata Sharma[1], Dr Upasana[2], Dr Amarjeet Kaur[3]
[1]Professor & Head, Department of Obstetrics and Gynaecology, Govt. Medical College, Amritsar, 143001, India
[2]Lecturer, Department of Obstetrics and Gynaecology, Govt. Medical College, Amritsar, 143001, India
[3]Senior Resident, Department of Obstetrics and Gynaecology, Govt. Medical College, Amritsar, 143001, India

Abstract
Background: *Pelvic Inflammatory Disease (PID) is the infection of upper female genital tract and is one of the major causes of gynaecologic morbidity. Appropriate and prompt treatment can prevent the complications of PID. The objective of this study is to evaluate the efficacy and safety of injection placentrex as compared to conventional therapy in pelvic inflammatory disease.*
Methods: *This is a randomized prospective study conducted on 90 patients with diagnosis of PID in a tertiary care centre over a period of one year. Patients were divided into three groups with 30 patients in each group. Group I, II and III were given injection placentrex, doxycycline and injection placentrex plus doxycycline respectively. Treatment was given treatment for 14 days. Final evaluation was done at the end of 2 weeks according to Clinical Global Impression (CGI) scale.*
Results: *Final assessment of efficacy of three groups was done according to Clinical Global Impression (CGI) scale. Excellent response was seen in 19(67.85%) cases in group I, 14(50%) cases in group II and 25(86.20%) cases in group III. Good response was seen in 5(17.85%) cases in group I, 2(7.14%) cases in group II and 2 (6.89%) cases in group III. Poor response was seen in 4 (14.28%) cases in group I, 12 (42.85%) cases in group II and 2(6.89%) cases in group III. The difference was statistically significant between group 1 versus 2 (p-0.049) and highly significant between group 2 versus 3 (p- 0.006).*
Conclusion: *Placentrex injection given from day one of diagnosis of PID is a better option for treating PID and in preventing complications of PID as compared to conventional antibiotics.*
Keywords: *PID, CGI scale, Placentrex.*

Introduction

PID refers to the infection of the upper female genital tract, including the endometrium, fallopian tubes, ovaries and pelvic peritoneum[1]. PID occurs most often through bacterial infection and from Sexually Transmitted Disease (STD's). It is one of the major causes of gynaecologic morbidity, such as infertility, ectopic pregnancy and chronic pelvic pain[2].

PID commonly occurs in women less than 35 years of age. It rarely occurs before menarche, after menopause or during pregnancy. Risk factors for PID include multiple sexual partners, previous history of PID, use of an intrauterine

contraceptive device, presence of bacterial vaginosis or a bacterial sexually transmitted disease (STD)[3]. Many different organisms can cause PID, but most of the cases are associated with gonorrhea and Chlamydia infection. The incidence of PID is on the rise because of increased incidence and reportage of STDs caused by chlamydia[4]. Incidence among the sexually active women is 1-2% per year. Among sexually active females of reproductive age group, about 85% infections are spontaneous. Rest 15% occurs after procedures which help the organisms to ascend up.

Symptoms may vary from none to severe. Clinical diagnosis of PID is often imprecise and potential of damage is there even in mild infection. Lower abdominal pain is the most common symptom. Other signs and symptoms include fever, vaginal discharge, dysmenorrhea, dyspareunia, irregular menstrual bleeding, forniceal tenderness and less commonly, pain in the right upper abdomen. However, because of non-specific symptoms, PID often goes unrecognized by women and healthcare providers. Lower genital tract microscopy, culture and serology is also inconclusive.

Various types of antibiotics can cure PID. Treatment with antibiotics can prevent severe damage to reproductive organs. However, antibiotic treatment does not reverse any damage to reproductive organs. The longer is the delay in treatment for PID, the more likely is the occurrence of complications. Even after treatment with appropriate antibiotics mentioned by CDC (Centers for Disease Control and Prevention), the clinical course of PID remains varied.

CDC recommends treatment for even mild cases of PID [5,6]. Therapeutic goal in management of PID is to prevent chronic residual disease[7]. As the antibiotic therapy cannot prevent sequelae of salpingitis, there is a need of additional therapy along with antibiotics.

Placentrex is a drug containing Peptides (FNP-III, CRF), Nucleotides (PDRN) & Glutamate. It is derived from an extract of fresh term, healthy, human placenta. Placentrex has been indicated in the treatment of PID as an adjuvant to primary antibiotic therapy. It has significant anti inflammatory effect involving chemical mediators of immunological response[8-12]. It does not produce any significant adverse reaction and is generally considered quite safe. Effect of placentrex is well documented in wound healing and in treatment of burns and radiation effects. It has been recommended for prescription for PID.

Materials and Methods

This is a randomized prospective clinical study conducted in the department of Obstetrics and Gynaecology, Govt. Medical college, Amritsar from March, 2017 to March 2018. A total of 90 patients of PID within the reproductive age group 20-45 years were recruited. PID was diagnosed by history and clinical examination.

Inclusion criteria:

- Women of childbearing age.
- Patients freshly diagnosed to have PID or had suffered not more than 3 episodes in the last 12 months.
- Willingness to receive 14 doses of intramuscular injection (one each day).
- Willingness to provide informed and writtens consent for participation in the study.

Exclusion criteria:

- Post menopausal women or women outside the reproductive age group.
- Subjects who are pregnant or breastfeeding
- Subjects on active treatment or with evidence of active tuberculosis or sexually transmitted diseases.
- Subjects with endometriosis.
- History of more than 3 episodes of documented PID or bacterial STDs.
- Any other pathology, apart from chronic PID, that may explain the patient's presenting signs and symptoms.
- Any significant hepatic and renal impairment.
- Any severe or serious disorder of other vital organs.

- Any disorder requiring treatment with anti-inflammatory drugs on a continous or regular basis.
- Any other investigational drug treatment being received concomitantly.
- Patients unlikely to comply with trial protocol.

A total of 90 subjects were randomized into three groups. The treatment was continued for 14 days. Each group containing 30 patients received medication and doses as follows:

GROUP 1: Injection Placentrex in the dose of 2 ml IM daily.

GROUP 2: Doxycycline oral capsule 100 mg. in the dose of 1 capsule twice daily in the first week and then 1 capsule once daily in the next 2 weeks.

GROUP 3: Injection Placentrex IM 2ml daily + Doxycycline oral capsule 100mg. in the dose of 1 capsule twice daily in the first week and then 1 capsule once daily in the next 2 weeks.

Subjects were followed up at the end of every week i.e. week 1, week 2 and week 3 from the date of randomization during the treatment period. Subjects underwent a complete physical examination at all follow-ups. Besides, laboratory examination were also be performed at baseline and at the end of study and noted in the case record form (CRF), along with assessment of treatment emergent adverse events and compliance with study medication.

Primary efficacy variables were appropriate clinical recovery end points like disappearance of abdominal pain and tenderness and constitutional symptoms like dysmenorrhoea, dyspareunia, dysuria and improvement in patients quality of life.

The final evaluation was done at the end of 2 weeks of the prescribed treatment according to the Clinical Global Impression (CGI) scale as follows:

1. Excellent: Resolution of the majority of presenting symptoms and marked improvement in QoL.
2. Good: Majority of presenting symptoms unresolved but adequately controlled and QoL better than before.
3. Poor: Minimal improvement or worsening in presenting symptoms and QoL.

Adverse events were quantified by simple descriptive statistics.

Results

A total of 90 patients of PID were recruited, 30 in each group. Mean age of the patients were 34.5 years in group 1, 32.8 years in group 2 and 36.5 years in group 3. At the end of 2 weeks, 28 patients left in both group 1 and group 2 and 29 patients left in group 3. Following observations were noted in the study.

Table 1 Response According to CGI Scale at 2 Weeks

	Group I (n=28)	Group II (n=28)	Group III (n=29)	Group I vs Group II p value	Group I vs Group III p value	Group II vs Group III p value
Excellent	19 (67.85%)	14 (50%)	25 (86.20%)	0.049*	0.252	0.006*
Good	5 (17.85%)	2 (7.14%)	2 (6.89%)			
Poor	4 (14.28%)	12 (42.85%)	2 (6.89%)			

*p<0.05; Significant

Excellent response was seen in 19(67.85%) cases in group I, 14(50%) cases in group II and 25(86.20%) cases in group III. Good response was seen in 5(17.85%) cases in group I, 2(7.14%) cases in group II and 2 (6.89%) cases in group III. Poor response was seen in 4 (14.28%) cases in group I, 12 (42.85%) cases in group II and 2(6.89%) cases in group III.

Figure 1

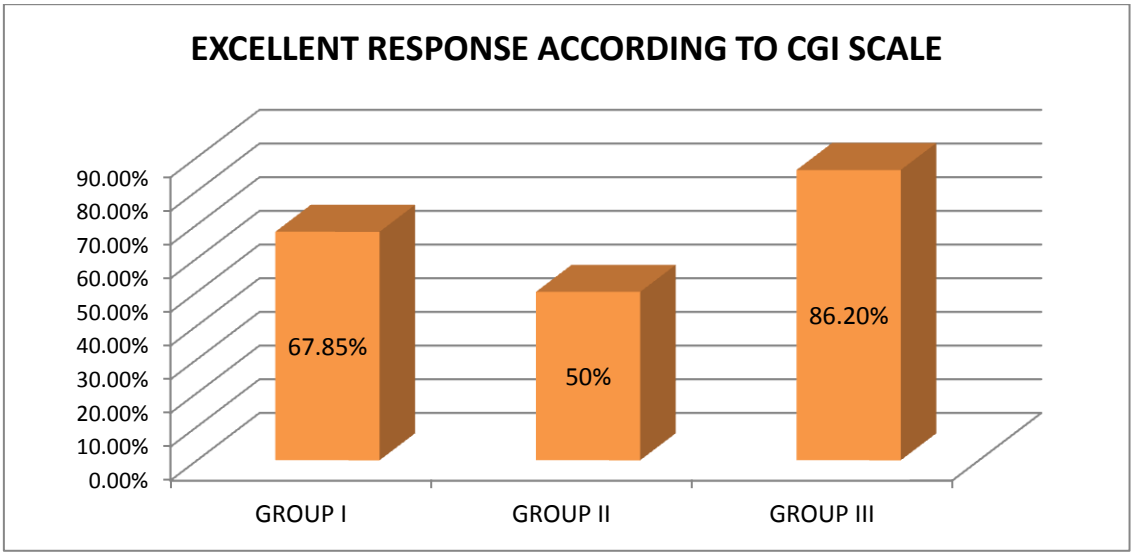

Figure 2

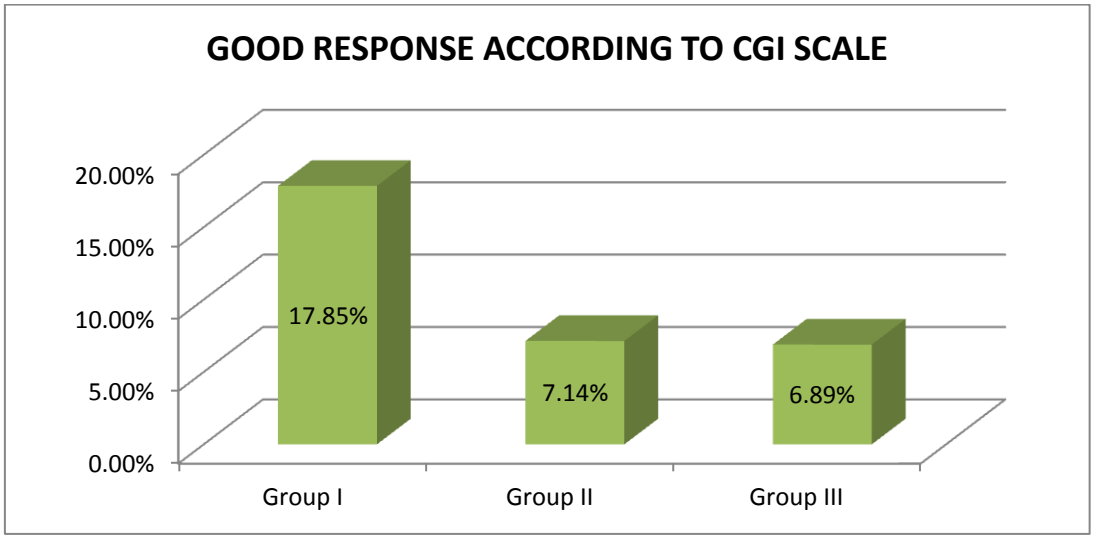

Figure 3

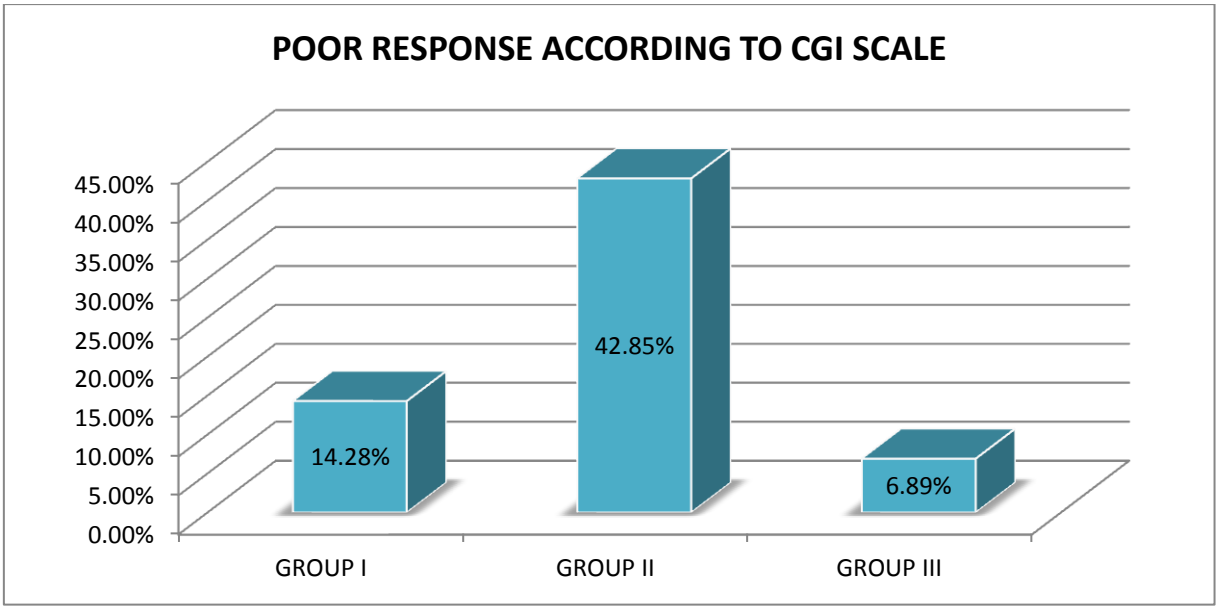

Table 2 Safety Profile

Side effects	GROUP I	GROUP II	GROUP III
Minor	1	2	1
Major	0	0	0

Minor side effects were seen in 1 case in group I, 2 cases in group II and 1 case in group III. There was no major side effect reported in any group.

Table 3 Need of Rescue Treatment

	GROUP 1	GROUP 2	GROUP 3
NEED OF RESCUE TREATMENT	3	5	1

Rescue treatment i.e. other analgesics and anti-inflammatory drugs (whenever the subjects felt that symptoms were not relieved with trial medications) was required in 3 cases in group I, 5 cases in group II and 1 case in group III.

Discussion

PID is a frequent infection seen in the reproductive aged women. Despite availability of antibiotics, treatment of PID is not satisfactory. In our study we have evaluated efficacy and safety of placentrex injection as compared to doxycycline.

Final assessment of efficacy of three groups was done according to CGI scale. Excellent response was seen in 19(67.85%) cases in group I, 14(50%) cases in group II and 25(86.20%) cases in group III. Good response was seen in 5(17.85%) cases in group I, 2(7.14%) cases in group II and 2 (6.89%) cases in group III. Poor response was seen in 4 (14.28%) cases in group I, 12 (42.85%) cases in group II and 2(6.89%) cases in group III. The difference was statistically significant between group 1 versus 2 (p-0.049) and highly significant between group 2 versus 3 (p- 0.006).

Minor side effects were seen in 1 case in group I, 2 cases in Group II and 1 case in group III. There was no major side effects in any of the cases in the study.

There was need of rescue treatment in 3 cases in group I, 5 cases in group II and 1 case in group III.

In a study conducted by Prameela et al[13], comparison was done between the efficacy of injection placentrex (group I) and conventional therapy (group II). Overall patient satisfaction was better in placentrex group compared to conventional therapy. Complete remission with treatment at 2 weeks occurred in 12 cases (48%) in group I versus 8(34.8%) cases in group II. Lack of response at 2 weeks was seen in 5(20%) cases in group I versus 9 (39%) cases in group II. Their results were comparable to our study.

Dahiya P et al[14] in their study also evaluated the efficacy and safety of injection Placentrex compared to doxycycline. Their study showed significant and persistant improvement of signs and symptoms of PID in women who received placentrex injection compared to conventional treatment.

In study conducted by Agrawal N et al[15], complete remission with treatment occurred in 21 (45.6%) cases in group I (doxycycline plus injection placentrex) versus 13 (28.9%) cases in group II (doxycycline) at the end of 2 weeks. 30 (68.2%) cases were having complete remission in group I versus only 6 (18.7%) in group II. There was no response in 11 (23.9%) cases in group I and 18 (40%) cases in group II at 2 weeks. There was no major side effects reported in their study which was comparable to our study.

R Garg et al[16] in their study also found significant and persistant improvement of signs and symptoms of PID in women treated with injection placentrex as compared with conventional therapy.

Conclusion

PID is one of the most frequent infections in women of reproductive age group. Conventional antibiotics does not provide maximum relief of symptoms and prevent its complications. Placentrex injection given from day one of diagnosis of PID is a better option for treating PID and in preventing complications of PID. The drug is safe without any major adverse event being reported.

References

1. Wiesenfeld HC, Sweet RL, Ness RB, Krohn MA, Amortegui AJ, Hillier SL. Comparison of acute and subclinical pelvic inflammatory disease. Sex Transm Dis. 2005;32(7):400–405. [PubMed]
2. Wiesenfeld HC, Hillier SL, Meyn LA, Amortegui AJ, Sweet RL. Subclinical pelvic inflammatory disease and infertility. Obstet Gynecol. 2012;120(1):37–43. [PubMed]
3. Bohm MK, Newman L, Satterwhite CL, Tao G, Weinstock HS. Pelvic inflammatory disease among privately insured women, united states, 2001–2005. Sex Transm Dis. 2010;37(3):131–6. [PubMed]
4. Taylor-Robinson D, Jensen JS, Svenstrup H, Stacey CM. Difficulties experienced in defining the microbial cause of pelvic inflammatory disease. Int J STD AIDS. 2012;23(1):18–24. [PubMed]
5. CDC. Pelvic Inflammatory Disease (PID) Atlanta, GA: Department of Health and Human Services; 2015.
6. CDC. Sexually Transmitted Disease Surveillance, 2013. Atlanta, GA: Department of Health and Human Services; 2014.
7. Trent M, Bass D, Ness RB, Haggerty C. Recurrent PID, subsequent STI, and reproductive health outcomes: findings from the PID evaluation and clinical health (PEACH) study. Sex Transm Dis. 2011;38(9):879–881. [PMC free article] [PubMed]
8. Bianchini P, Tellini N, Morani AM, Follono MG. Pharmacological Data on Polydeoxiribonucleotide of Human Placenta. Int.J.Tiss.Reac.1981;III,151-154.
9. Chakraborty PD, Bhattacharyya D. In vitro growth inhibition of microbes by human placental extract. Curr. Sc.2005; 88: 782-786.
10. Chakraborty PD, Bhattacharyya D. Isolation of fibrinectin Type III like peptide from human placental extract used as wound healer.J.Chromatogr.B 2005;818: 67-73.
11. Chakraborty PD, De D, Bandyopadhyay S, Bhattacharyya D. Human aqueous placental extract as a wound healer.J.Wound Care 2009;18:462-467.
12. Gupta R, Chattopadhyay D. Glutamate is the chemotaxis-inducing factor in placental extracts Amino Acids. 2010;39:615-618.
13. Prameela, Kavya D Sharma. Clinical efficacy of Placentrex Injection in pelvic inflammatory disease. Jr. of Obs & Gynae Research 2016; 3(1):65-67.
14. Dahiya P, Paul A. A randomized study to evaluate the efficacy and safety of placentrex injection in patients suffering from pelvic inflammatory disease. JIMA Vol. 111: 2013: 352-353.
15. Agarwal N, Kulshrestha V, Kriplani A. Clinical efficacy of placentrex injection in pelvic inflammatory disease. J Indian Med Assoc. 2010; 108: 117-118.
16. Garg R, Zahra F, Chandra JA, Vatsal P. A comparative study of injection Placentrex and conventional therapy in treatment of pelvic inflammatory diseases. J. Indian Med Assoc 2008: 106:463&467.