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Differences in Influence between Intravenous Methylprednisolone and Intramuscular Progesterone toward Erectile Function After Operation Transurethral Resection of the Prostate (TUR-P) in Patients Benign Prostate Hyperplasia (BPH)

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ABSTRACT

Background: Erectile function is an important factor for all men in an active sexual condition, as well as to assess the quality of sex life with their partners. Transurethral Resection of the Prostate (TURP) is a gold standard action for Benign Prostate Hyperplasia (BPH). The researcher tried to study to investigate the effect of corticosteroid and progesterone on erectile function in BPH patients who have done TURP surgery by using Erection Hardness Score (EHS). The purpose of this study was to investigate the effect of intra venous methylprednisolone on post-operative erection function of TURP in BPH patients. To investigate the effect of intra-muscular progesterone on postoperative erectile function of TURP in BPH patients. To investigate the different effect between methylprednisolone and progesterone on post-operative erection function of TURP in BPH patients.
Subjects and Method: Subjects of all BPH patients who performed TUR-P surgery in the urology sub-section of Dr. Moewardi Hospital, Surakarta. The sampling technique in this study was incidental sampling. This study was a clinical experimental study using Pre and Post-test design-Only Control Design. 3 groups were divided to get different treatment, the first group was given methylprednisolone, the second group was given progesterone and the third group was given TURP therapy protocol only.
Results: After 1 month of TURP treatment in BPH patients, the result obtained for the EHS which on a scale of 2 and 3. EHS on scale 2 for the methylprednisolone group was 9 patients (69.2%), the progesterone group had 6 patients (46.2%), and the control group had 8 of patients (66.7%). Meanwhile, EHS on scale 3 for the methylprednisolone group was 4 patients (30.8%), there were 7 patients (53.8%) of the progesterone group, and the control group had 4 patients (33.3%). After 3 months of TURP treatment in BPH patients, EHS on scale 2 in the methylprednisolone group there were 2 patients (15.4%), the progesterone group there were 0 patients (0.0%), and the control group there were 6 patients (50.0%). The methylprednisolone group had 9 patients (69.2%) on EHS 3 scale, the progesterone group had 4 patients (30.8%), and there were 6 patients (50.0%) in the control group. While, EHS scale of 4 the total of the patients in the methylprednisolone group was 2 patients (15.4%), the progesterone group had 9 patients (69.2%), and the control group had 0 patients (0.0%).
Conclusion: the methylprednisolone improved the erectile function in post-operative TURP patients. Progesterone improved erectile function in post-operative TURP patients. Therefore, it can be concluded that progesterone was better than methylprednisolone.

Keywords: Erectile dysfunction, Methylprednisolone, Progesterone
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BACKGROUND

Erectile function is an important factor for all men in an active sexual condition, as well as to assess the quality of sex life with their partners. The higher the level of erection hardness is, the higher the sexual satisfaction is and it could improve the

whole quality of life (Goldstein et al., 1998; Mulhall, 2008).

According to the United States National Institutes of Health and the American Urological Association, Erectile Dysfunction (ED) is defined as the inability to achieve or maintain an adequate erection for sexual satisfaction. According to the International Journal of Impotence Study (IJIR) in 2013, the effect of TURP on erectile function is still controversial and the available data is still under debate.

Transurethral Resection of the Prostate (TURP) is a gold standard action for Benign Prostate Hyperplasia (BPH). One of the complications after surgery that can be generated after the patient gets the action is DE (Thorpe et al, 1999; Florator et al 2001). Some patients suffer temporary ED right after TURP and the returning of erection ability with ranges from 1 to 6 months right after TURP. The effects of ED for in patients right after TURP are still controversial, one of the possible causes of ED is the result of heat trauma to the erectile nerves (Jaidane 2010; Poulakis et al, 2006).

Corticosteroid has anti-inflammatory and immunosuppressive effects by decreasing the coming out cells and the function of inflammatory cells and the permeability of blood vessels in the inflammatory part. Corticosteroid also inhibits the synthesis of prostaglandins and leukotrienes by inhibiting the release of arachidonic acid from phospholipids. With this mechanism, corticosteroids protects organs from damage (Priyanka et al, 2008).

Some journals mention the mechanism of progesterone. It has a protective effect on peripheral nerves. Its action mechanism is an example of a regulation of neurotropin expression which is able to help cells survive. In addition, main metabolic outcomes of progesterone such as allopregnanolone are reported taking a part in neuroprotective effects.

SUBJECTS AND METHOD

1. Study design/ the design of the study

This study is a clinical experimental study using Pre and Post-test design-Only Control Design. In this design, the subjects were divided into 3 groups, the first group was given the TURP + methylprednisolone therapy protocol, the second group was given the TURP + progesterone therapy protocol, and the third group was given TURP therapy protocol only. Then, that will be assessed before TURP during 1 to 3 months after TURP assessed erectile function before TURP, 1 month and 3 months after TURP by using Erection Hardness Score (EHS).

The study was conducted in the sub-section of urology Section RSDM Surakarta, started in December 2016 - May 2017. The population of this study were all BPH patients who have done TUR-P surgery in the sub-section of urology RSUD Dr. Moewardi Surakarta.

2. Population and sample

The sampling technique in this study was incidental sampling. The subject size was determined by using the subject formula for a cross-sectional study (a single subject to test the hypothesis of a population) that is:

$$n = \frac{(\frac{Z\alpha}{2} + Z\beta\sqrt{P.Q}}{(P - \frac{1}{2})}$$

$$n = \frac{(1{,}96 + 80\%\sqrt{0{,}75X0{,}25}}{(0{,}75 - 0{,}5)}$$

$$n = 38$$

Information:
N: Minimum number of subjects required

Zα: 95% confidence level ◊ Z = 1.96
Zβ: Power 80%
P: R / (1 + R)
Q: 1 - P8
R: Estimated Odds Ratio = 3
Restriction Criteria:
1. Inclusion criteria
a. The BPH diagnosed patients and post-TURP surgery
b. BPH patients between the range of 50 and 70 years
c. Patients are willing to attend study and fill out informed consent
d. BPH patients with normal erectile function before TURP.
2. Exclusion criteria
a. Patients of BPH who have done previous TURP surgery
b. Patients suspected of prostate cancer
c. BPH patients with a history of erectile dysfunction prior to TURP surgery
d. BPH patients with diseases:
   1) Hypertension
   2) Diabetes mellitus
   3) Heart failure
   4) Stroke
   5) Spinal Trauma

3. Data Analysis

The analytical test was implemented in this study, because comparing 3 different groups which are independent each other and the scale of variable data measured on a nominal scale, thus v the statistical test used was *Kruskal Wallis* test.

RESULTS

The age of the patients given the intervention of Metilprednisolon was averaged 65.00 + 3.94 years, meanwhile the age of the patients given the Progesterone intervention averaged 61.85 + 5.63 years, and the patient age in the control group averaged 64.83 + 3.27 years, the value (p> 0.05) there is no significant difference.

The prostate volumes before TURP in patients who have been given the intervention of methylprednisolone was averaged 58.00 + 7.56 g, while patients given an average Progesterone intervention was 58.60 + 8.17 g, and the patients in the control group were 58.00 + 7.54, the score (p>0.05).

TURP prostate volumes in patients with methylprednisolone intervention were on averaged 51.54 + 8.99 g, while non-methylprednisolone patients were an average progesterone intervention were 51.92 + 8.55 g, and the patients in the control group were averaging 50.00 + 7.39, > 0.05).

Table 1. characteristics of BPH patients

Variable	Intervention			p
	Methylprednisolone	Progesterone	Control	
Age	65.00 ± 3.94	61.85 + 5.63	64.83 ± 3.27	0.103
Prostat Volume	58.00 ± 7.56	58.60 ± 8.17	58.00 ± 7.54	0.971
Prostat TURP Volume	51.54 ± 8.99	51.92 ± 8.55	50.00 ± 7.39	0.806

Note: Kruskal Wallis test (numerical data is not normally distributed)

Before the TURP action on the 4th (entirely hard and fully strained) EHS BPH patient in the methylprednisolone group there were 8 patients (61.5%), the progesterone group had 9 patients (69.2%), there were 7 patients (58.3 %) in the control group. While the rest were on a scale of 3 (hard enough for penetration but not completely hard) is in the methylprednisolone group which the total patients were 5 patients (38.5%), there were 4 patients (30.8%) in

the progesterone group, and there were 7 patients (41.7%) in the control group.

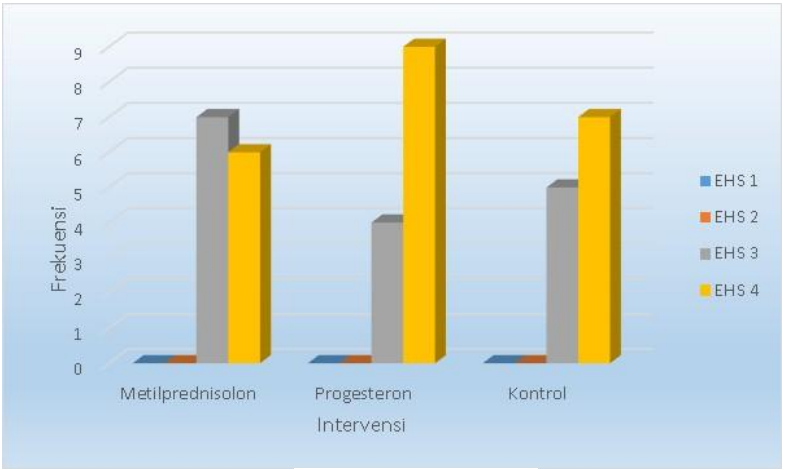
After 1 month of TURP treatment in BPH patients, EHS was on a scale of 2 (hard, but not hard enough for penetration) and 3 (hard enough for penetration but not completely hard). EHS met on scale 2 in the methylprednisolone group which was 9 patients (69.2%, the progesterone group obtained 6 patients (46.2%), the control group had 8 patients (66.7%). While EHS was on scale 3, the methylprednisolone group obtained 4 patients (30.8%), the progesterone had 7 patients (53.8%), and there were 4 patients (33.3%) in the control group.

Table 2. Differences erectile function before and after TURP action in BPH patients between Methylprednisolone, progesterone and control group

EHS	Scale	Intervention			p
		Methylprednisolone	Progesterone	Control	
Before	Scale 1	0 (0.0%)	0(0.0%)	0 (0.0%)	0.847
	Scale 2	0 (0.0%)	0 (0.0%)	0 (0.0%)	
	Scale 3	5 (38.5%)	4 (30.8%)	5 (41.7%)	
	Scale 4	8 (61.5%)	9 (69.2%)	7 (58.3%)	
1 month	Scale 1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0.432
	Scale 2	9 (69.2%)	6 (46.2%)	8 (66.7%)	
	Scale 3	4 (30.8%)	7 (53.8%)	4 (33.3%)	
	Scale 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	
3 months	Scale 1	0 (0.0%)	0 (0.0%)	0 (0.0%)	<0.001
	Scale 2	2 (15.4%)	0 (0.0%)	6 (50.0%)	
	Scale 3	9 (69.2%)	4 (30.8%)	6 (50.0%)	
	Scale 4	2 (15.4%)	9 (69.2%)	0 (0.0%)	
1vs3 month	p**	0.003	0.001	0.157	

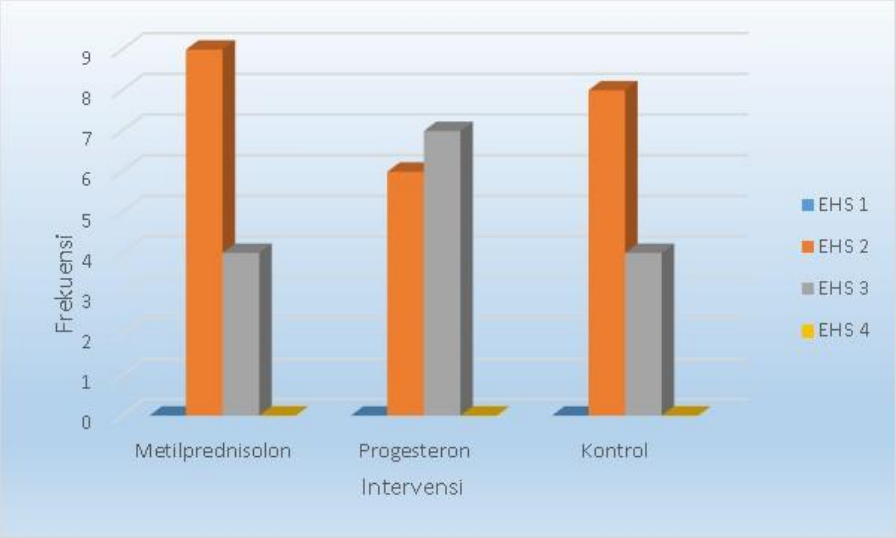
1. Note: * Unpaired group difference test; Kruskal Wallis (ordinal categorical data)
2. ** Pair group differential test; Wilcoxon (ordinal categorical data)

After 3 months of TURP action in BPH patients, EHS is on a scale 2 (hard, but not hard enough for penetration) and 3 (hard enough for penetration but not completely hard) and 4 (completely hard and fully strained) which is the methylprednisolone group had 2 patients (15.4%), the progesterone group obtained 0 patients (0.0%), and the control group had 6 patients (50.0%).

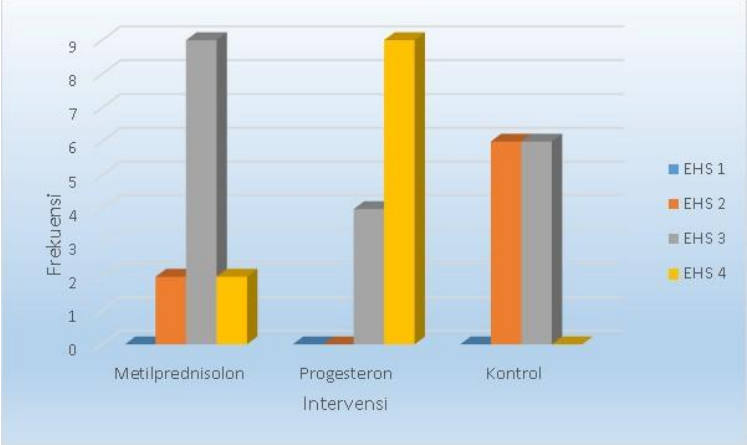


Before TURP

Patients were on scale 3 of EHS in the methylprednisolone group as many as 9 patients (69.2%), the progesterone group were 4 patients (30.8%), and the control group were 6 patients (50.0%). While patients were with EHS scale of 4 in the methylprednisolone group 2 patients (15.4%), the progesterone group obtained 9 patients (69.2%), and the control group obtained 0 patients (0%).



1 Month after



3 Months after

Picture 1. Comparison of erection function before and after TURP treatment for patients between the Methylprednisolone group, Progesterone, and Control

DISCUSSION

Based on the description above, it can be seen that BPH patients who got TURP treatment has the same conditions both from age and prostate volume before and after TURP treatment. The patients from these three treatments has decreased prostate volume after TURP action. Thus the patients' characteristic data among the methylprednisolone, progesterone, and control groups were not significantly diffirent or homogeneous.

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As it is known that TURP is the standard gold for surgery action for BPH. However, this action can cause erectile dysfunction that will be suffered by the patients. The previous studies have stated that erectile dysfunction is between 4% and 40%. A big difference in numbers can be caused due to the method used to assess the DE or the length of time the follow-up performed by the researcher. A number of patients had temporary DE post TURP and restored erection ability post TURP in 6 months (Taher, 2004; Poulakis et al. 2006). The cause of DE post-TURP is not known for certain, but it is estimated to be due to neurovascular bundle damage due to heat trauma when the treatment is on process (Taher, 2004; Poulakis et al., 2006).

The results showed that methylprednisolone and progesterone were effecttive in improving erectile dysfunction which was suffered by BPH patients who got TURP treatment. For the methylprednisolone group, the ratio of erectile function between 1 month after TURP and 3 months after TURP get the result of wilcoxon test with value ($p < 0.05$) which means there is a significant difference of erection function between 1 month and 3 months after TURP, so there was a significant improvement in the methylprednisolone group. Hence, the hypothesis (H1) which states "There is an effect of intra venous methylprednisolone on postoperative erection function of TURP in BPH patients. The giving of methylprednisolone will improve the erection function of post-operative TURP patients "proven.

The comparison of erectile function between 1 month and 3 months after TURP in progesterone group got wilcoxon test result with value ($p < 0.05$) which means there is significant difference of erection function between 1 month and 3 months after TURP, thus there is improvement which is significant in the progesterone group. Thus the hypothesis (H2) states "There is an effect of intra muscular progesterone on postoperative erectile function of TURP in BPH patients.
The giving of progesterone will improve the erectile function in patients post-TURP surgery" proven.

Progesterone is more effective than methylprednisolone in improving erectile function. After 3 months of TURP treatment in patients with BPH erectile function (EHS) in the majority group of methylprednisolone on scale 3, there were 9 patients (69.2%), in the majority progesterone group with scale 4, there were 9 patients (69.2%), and the control group had 6 patients (50.0%) with the scale of 2 and 3. Kruskal wallis' statistical results obtained values ($p < 0.05$), meaning that there was a significant difference in erectile function 3 months after TURP action in BPH patients between methylprednisolone, progesterone, and control. As it can be seen that the progesterone group is better than methylprednisolone and control group, and methylprednisolone is better than control group. Thus the hypothesis H3 which states "There is a difference in the effect of intravenous and progesterone methylprednisolone on post-operative erection function of TURP in BPH patients. Progesterone is better than methylprednisolone. "Proven.

Methylprednisolone is a class of synthetic steroids derived from glucocorticoid that has biological activity to reduce antiinflammatory effects after lesions (Nash et al., 2002). By inhibiting the production of various inflammatory materials such as chemotaxis, lysosomal enzyme, inhibiting an enzyme phospholipase A's activity, the next will lead to decrease in arachidonic acid cascade metabolite production, then

decrease free radical formation, decrease TNF-α expression, decrease activity of nuclear factor that will decrease inflammatory response.

Whereas progesterone is known produced in the central nervous system and the peripheral nervous system, and is considered as a neurosteroid. The responsible enzyme in progesterone biosynthesis is localized in the glia and Schwann cells of the central nervous system. Progesterone biosynthesis occurs in the mitochondria, the synthesis of progesterone in the nervous system has an important role in the regulation of myelin formation and the modulation of GABA type A receptor function (Milani et al., 2010). The progesterone synthesis plays an important role in the regulation of myelin formation and the modulation of GABA type A receptor function. Progesterone stimulates myelinization by stimulating activation of gene code expression for myelin protein transcription and indirectly regulating myelin formation by influencing gene expression in neurons and supporting regeneration of neurons with some ways include: reducing inflammation, edema and apoptosis, by stimulating the life-enhancing neurons through the formation of new myelin sheaths (Milani et al., 2010).

Based on the description above, it can be seen that giving intra vena methylprednisolone and progesterone effect on erection function post-surgery TURP in BPH patients. Thus, progesterone is better than methylprednisolone.

Based on the results of the study which has been done on 38 patients with BPH treated in RSUD Dr Moewardi Surakarta and TURP surgery, it can be concluded as follows. Giving methylprednisolone will improve the erection function of post-operative TURP patients. The giving of Progesterone improves the erectile function of patients with postoperative TURP. Thus, progesterone is better than methylprednisolone.

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