



Imran Ali Shaikh^{1*}, Naila Masood² and Tariq Zaffar Shaikh³

¹Professor of Medicine Liaquat University of medical and health sciences Jamshoro Sindh, Pakistan

²Associate Professor of Medicine Liaquat University of medical and health sciences Jamshoro Sind, Pakistan

³Assistant Professor Liaquat University of medical and health sciences Jamshoro Sindh, Pakistan

Received: 05 March, 2019

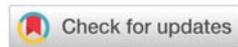
Accepted: 13 March, 2019

Published: 14 March, 2019

***Corresponding author:** Dr, Imran Ali Shaikh, Professor of Medicine, Liaquat University of Medical and Health sciences Jamshoro, A-81, Qasim nagar, Qasimabad. Hyderabad, Pakistan, Tel: +923332662415; E-mail: imran2naila@yahoo.com

Keywords: PPI; Young; Semen; Hyderabad

<https://www.peertechz.com>



Research Article

Do proton pump inhibitors harm to semen? Hyderabad Sindh based study

Abstract

Background: Proton pump inhibitors (PPIs) are widely used over counter drugs in Pakistan. Unjustified use of PPI is increasing. One concern of their use is spermatogenesis and male fertility.

Objective: To observe the detrimental effects of proton pump inhibitors on various parameters of semen of younger individuals of Hyderabad Sindh Pakistan.

Duration of study: 1st June to 25th Dec 2017.

Place of study: private Clinics of sadder Hyderabad Sindh Pakistan.

Methodology: 109 patients were selected as per inclusion criteria. All were young subjects, age was 24 ± 7.6 years. Mean duration of PPI was 2.5 ± 2.7 months. None of subject was diagnosed infertility or sub fertility. Five parameters were assessed before and after PPI use. Sampling technique was non probability convenience. Statal software was SPSS 16. Student paired t test was used to calculate p value before and after PPI use. P value was considered <0.05 significant.

Results: There was no significant impact noted over five parameters of semen p value was only significant in semen volume <0.05.

Conclusion: There is no negative impact of PPI over five parameters of semen and male fertility.

Introduction

Enormous data is supporting proton pump inhibitors (PPI) are the best option for treatment of peptic ulcer disease, non-ulcer dyspepsia and erosive esophageal diseases. Omeprazole marketed first, was high selling drug over counter for one decade. Then many different molecules having strong potency and less side effects marketed over next 20 years and Dexlansprazole launched recently, claimed superior to other PPIs.

Regarding PPI, inhibitor of H⁺/K⁺ ATPase enzyme in gastric mucosal parietal cells, which are responsible acid production, so reducing total burden of acid over gastric mucosa [1].

Due to relieving effects of PPI, its easily misused as over the counter drug everywhere in world. In Pakistan its reported that more than fifty percent of patients on Proton pump inhibitors were without a definite indication [2], Other study demonstrated >40% of discharged cards prescribed PPI with many antibiotics without any indication [3].

The association of PPI to male fertility is debatable. Many

studies have shown concern over use of PPI in fertile male due to impaired absorption, achlorhydria and false facts.

Regarding Infertility is divided in to: primary infertility, secondary infertility and lifetime infertility.

The primary infertility is no conception after one year of unprotected intercourse. Secondary infertility is the inability to become pregnant after first conception and permanent infertility is unable to become pregnant with a live birth within five years of unprotected intercourse without any contraceptives [4].

Infertility is not uncommon, it affects more than 60 million couples all over world and problem is increasing [5]. Infertility is a common problem in Pakistan affecting about 21.9% in total, with 3.5% primary and 18.5% secondary infertility [6].

Among couples, males are responsible for 20 to 25% for infertility [7]. The common contributory factors could be some environmental factors like smoking, pollution, medical conditions like diabetes, any cancer treatment, mumps in past, genital surgery and multiple sexually transmitted diseases,

genital Tuberculosis, scrotal , recent or chronic testicular problems also contributors of male infertility [8].

The PPI impairs sperm DNA synthesis is unclear. One explanation was impaired pH due to PPI use led to vitamin B12 deficiency which could inhibit DNA maturation and hence reduced sperm production [9].

In 2012, a study suggested that treatment using a PPI regimen, improves sperm motility in semen of infertile men [10] In contrast a small study showed abstinence from PPI is required for male partners who need a baby.

One researcher [11], suggested that use of PPI is not harmful to sperm directly and not acute one. It will reduce sperm quantity after 3 months or more and could be due to reduced semen B12 levels.

Garem et al [12], investigated thousands of semen for H.Pylori antibodies. He and colleagues suggested that treatment with PPI is beneficial for males who are planning for kid.

Many drugs used by males can be contributory for derangements of semen parameters A study showed that 26.65% infertile men have been unidentified multivitamins while herbal medicine users were 12.41% and over counter medicine users were 10.03%. Mixed types of medicines user reported in 4.49% [13]. This clearly shown that many drugs have toxic effects over sperms.

The rationale of this study to evaluate adverse effects of PPI on semen parameter of semen of healthy and young males of Hyderabad.

Methodology

109 healthy sexually active males were included which were on the PPI for at least 3 weeks before semen collection. The age was 19 to 45 years .The study as cross sectional observational. The pateints were not to advised for stopping PPI because of certain indications and unilligness to stop.

The procedure of semen analysis was explained and collected by masturbation in bottle provided by laboratory after written consent.

At least 2 ml of semen was collected after abstinence from coitus or masturbation for 7 days. Sample send to different laboratories of sadder to reduce the bias.

Following parameters were calculated

Sperm count: > 15 million sperm per milliliter is considered normal, can be measured within 60 minutes of collection [14].

Total sperm motility: Grade a – d. These are the strongest, weakest, non-motile or sluggish in semen.

Sperm morphology: > 4% will have normal morphology.

Semen volumes: 2-4 ml is normal.

Normal pH: 7.1-8.0.

Liquefaction of semen, within 60 minutes is normal.

Total motile spermatozoa.

Total motile sperm count (TMSC) is a combination of sperm count, motility and volume.

In our study we have considered normal when 20 million sperm/ml, motility grade c or d and 75% of sperm cells alive.

TMSC. $\geq 20 \times 10^6$ was considered normal.

Two samples of semen were collected one before study and second after 6 months of PPI therapy. Confidentiality and secrecy was maintained by assigning number to subjects rather names.

Data are presented as mean \pm standard deviation, median and percentages as appropriate. Linear regression used for age were used to test the on semen parameters pre and post PPI. Effect estimates and their 95% confidence intervals (CIs) are reported, and significance was assessed at the 0.05 level. Student unpaired t test used for p value.

Inclusion criteria was male 19-45 years and taking PPI in therpeutic doses at least 3 eeks before study. The dose of PPI for esomeprazole 40mg/day, rabeprazole 20mf/day and patoprazole 40mg /day.

Exclusion criteria included Age <18 years or >45 years, Azoospermia, consumption of any known spermatotoxic medication during the 3-month period before semen collection i.e medications included: testosterone, 5-alpha-reductase inhibitors, alpha-blockers, anticancer medications, anti-hypertensive medications, anti-depressants and psychoactive medication.

Results

General characteristics of the 109 subjects include median age as 24 ± 7.6 , mean duration of PPI use was 2.5 ± 2.7 months. Only 34% were addicted except alcohol and sex practice including coitus and masturbation was observed in 55%, other parameters are shown in table 1.

NO significant differences were observed in the general characteristics.

The sperm volume, ejaculate volume, total sperm count, sperm motility, normal head morphology and TMSC was observed (no p value was significant) table 2.

The use of PPI was although not statistically significantly associated with any other parameter except small decreased observed in semen volume of 1 ml /ejaculate $p < 0.05$, table 2.

Discussion

This is an exceptional study done by us over healthy young males assessing the effects of PPI use on semen parameters. In our study 55% were married an doing coitus at least once a week, 45% were unmarried. 40% subjects were smoker and average BMI was 24 ± 4.3 .

Table 1: Characteristics of 109 subjects.

Characteristic of patients	Percentage%		Mean
Age (years)			
Group 1(21 subjects)	21±4.6	20%	24±7.6
Group 2(44subjects)	28±5.7	40%	
Group 3(44 subjects)	39±4.2	40%	
Addictions except alcohol	34%		
BMI	27±3.9		24±4.3
Duration of PPI use(months)	2.2±1.8		2.5±2.7
Marital status married	55%		
Unmarried	45%		
Sex practice	55%		40±6.5
Use of PPI(seprescribed)	45		
Prescribed	55		
Smoker	40		
Non smokers	60		

Table 2: Semen analysis before and after use of PPI in 109 subjects.

Semen analysis	Before PPI	After PPI	P value
semen volume (ml)	2.5±1.4	1.9±1.4	0.05
total sperm count 10 ⁶	37±14.5	25±4.5	0.5
total sperm motility	30±17	25±10	0.7
normal head morphology (percentage)	75±12.7	73±11	
Total motile sperm count (TMSC).	28±17	27±17	0.8

Our results suggest that using a PPI is not connected with bad effects on semen parameters. Our findings are comparable with animal studies suggesting that PPIs not having sperm damaging effect [15].

Previous studies done showed that *H. pylori* infection of semen is more common in infertile men is associated with reduced sperm quality [16].

In contrast to these findings, one researcher [17] highlighted that PPI use can badly affect semen quality by decreasing the total motile sperm count, he had chosen dutch population who were planning for pregnancy taking PPI since 6–12 months before semen collection, was associated with 3 fold risk of having a low total motile sperm count. The possible explanation in dutch based study was elder age of subjects and addiction practices which were not excluded by researcher

Our findings were not matchable to above mentioned study dutch men that we have not seen any reduction semen parameter except volume of semen.

In another study, the investigators included 40 sub fertile men taking medication for gastric acid related symptoms and compared the semen parameter to control. No significant difference was found in semen parameters between cases and controls [18]. Which is matched to our study in which only semen volume significantly decreased $p < 0.05$.

Proton pump inhibitors use with other non spermatotoxic drugs was not connected with harmful effects on five parameters of semen on sub fertile patients. Sperm harmful

effects have not been reported from any animal or human study by PPI and declared safe [19].

A pilot survey of short duration [20], supported these findings by showing that proton pump inhibitors at hyper therapeutic dose for 1 week, did not cause any significant cause any low level of testosterone, follicle-stimulating hormone, Luteinising hormone and prolactin, which are essential for spermatogenesis.

The role of BMI, Smoking and sex practice was not found in literature with connection of PPI use. However many studies done over a single variable like Smoking but not related to PPI and semen analysis.

PPI use is a not associated it sperm toxicity it's due to underlying other comorbidities which impairs quality of semen [21].

Conclusion

Proton pump inhibitors are quite safe in young males and do not cause semen abnormalities or sperm abnormalities.

References

- Sheen E, Triadafilopoulous G (2011) Adverse effects of long-term proton pump inhibitor therapy. *Dig Dis Sci* 56: 931-950. [Link: https://goo.gl/v9Vmhc](https://goo.gl/v9Vmhc)
- Shafi S, Soomro R, Abbas SZ (2011) Proton pump inhibitors-over-prescribed in a rural community. *Pak J Med Sci* 27: 300-302. [Link: https://goo.gl/9n5Ynp](https://goo.gl/9n5Ynp)
- Syed HA Naqvi, SM Saqib, WA Khan, IAA Syed (2014) Rising use of Proton Pump inhibitors: A Karachi perspective. *Sci Int* 26: 1941-1944. [Link: https://goo.gl/hxoECL](https://goo.gl/hxoECL)
- World Health Organization (2019) Infertility definitions and terminology. [Link: https://goo.gl/EjnXcX](https://goo.gl/EjnXcX)
- World Health Organization (2000) Manual for the standardised investigation and diagnosis of the infertile couple. Cambridge. Cambridge University Press. [Link: https://goo.gl/6wdLLk](https://goo.gl/6wdLLk)
- Shaheen R, Subhan F, Sultan S, Subhan K, Tahir F (2010) Prevalence of infertility in a cross section of Pakistani population. *Pak J Zool* 42: 389-393. [Link: https://goo.gl/ekcjqk](https://goo.gl/ekcjqk)
- Meacham RB, Hellerstein DK, Lipshultz LI (1993) Evaluation and treatment of ejaculatory duct obstruction in the infertile male. *Fertil Steril* 59: 393-397. [Link: https://goo.gl/3dWq3h](https://goo.gl/3dWq3h)
- Sandro C Esteves, Ricardo Miyaoka, Agarwal A (2011) An update on the clinical assessment of the infertile male. *Clinics (Sao Paulo)* 66: 691-700. [Link: https://goo.gl/m1BDmf](https://goo.gl/m1BDmf)
- Joel J (2013) Heidelberg Proton pump inhibitors and risk of vitamin and mineral deficiency: evidence and clinical implications. *Ther Adv Drug Saf* 4: 125-133. [Link: https://goo.gl/9Te13B](https://goo.gl/9Te13B)
- Nicole A, Huijgen MD, Maria AJ, de Ridder (2016) Are proton-pump inhibitors harmful for the semen quality of men in couples who are planning pregnancy. *Fertility and sterility* 106: 1666–1672. [Link: https://goo.gl/dg3fNj](https://goo.gl/dg3fNj)
- Huijgen NA, de Ridder MA, Verhamme KM, Dohle GR, Vanrolleghem AM, et al. (2016) Are proton-pump inhibitors harmful for the semen quality of men in couples who are planning pregnancy? *Fertil Steril* 106: 1666–1672. [Link: https://goo.gl/HP55fv](https://goo.gl/HP55fv)
- El-Garem Y, El-Sawy M, T Seminal M (2014) Helicobacter pylori treatment

- improves sperm motility in infertile asthenozoospermic men. *Urology* 84: 1347-1350. [Link: https://goo.gl/xxtBKN](https://goo.gl/xxtBKN)
13. Vliet EP, Otten HJ, Rudolphus A, Knoester PD (2008) Inappropriate prescription of proton pump inhibitors on two pulmonary medicine wards. *Eur J Gastroenterol Hepatol* 20: 608-612. [Link: https://goo.gl/M9b7B3](https://goo.gl/M9b7B3)
 14. Cooper TG, Noonan E, von Eckardstein S, Auger J, Baker HW, et al (2010) "World Health Organization reference values for human semen characteristics" . *Human Reproduction Update* 16: 231-245. [Link: https://goo.gl/PwwHVx](https://goo.gl/PwwHVx)
 15. Banihani SA (2016) Omeprazole and semen quality. *Basic Clin Pharmacol Toxicol* 118: 181-183. [Link: https://goo.gl/LfL4zR](https://goo.gl/LfL4zR)
 16. El-Garem, El-Garem Y, El-Sawy M, Mostafa T (2014) Seminal Helicobacter pylori treatment improves sperm motility in infertile asthenozoospermic men. *Urology* 84: 1347-1350. [Link: https://goo.gl/R15K14](https://goo.gl/R15K14)
 17. Huijgen NA, Goijen HJ, Twigt JM, Mulders AG, Lindemans J, et al. (2017) Effect of medications for gastric acid-related symptoms on total motile sperm count and concentration: a case-control study in men of subfertile couples from the Netherlands. *Drug Saf* 40: 241-248. [Link: https://goo.gl/DeRzEv](https://goo.gl/DeRzEv)
 18. Keihani S, James R, Craig, Zhang C (2018) Proton-pump inhibitor use does not affect semen quality in subfertile men. *Asian J Androl* 20: 290-293. [Link: https://goo.gl/qdVzws](https://goo.gl/qdVzws)
 19. Sachs G, Scott D, Reuben M (1990) Omeprazole and the gastric mucosa. *Digestion* 47: 35-38. [Link: https://goo.gl/nr2PJE](https://goo.gl/nr2PJE)
 20. MacGilchrist AJ, Howden CW, Kenyon CJ, Beastall GH (1987) The effects of omeprazole on endocrine function in man. *Eur J Clin Pharmacol* 32: 423-425. [Link: https://goo.gl/QUQAXt](https://goo.gl/QUQAXt)
 21. Eisenberg ML, Li S, Behr B, Pera RR, Cullen, MR (2015) Relationship between semen production and medical comorbidity. *Fertil Steril* 103: 66-71. [Link: https://goo.gl/DLH5W3](https://goo.gl/DLH5W3)

Discover a bigger Impact and Visibility of your article publication with Peertechz Publications

Highlights

- ❖ Signatory publisher of ORCID
- ❖ Signatory Publisher of DORA (San Francisco Declaration on Research Assessment)
- ❖ Articles archived in worlds' renowned service providers such as Portico, CNKI, AGRIS, TDNet, Base (Bielefeld University Library), CrossRef, Scilit, J-Gate etc.
- ❖ Journals indexed in ICMJE, SHERPA/ROMEO, Google Scholar etc.
- ❖ OAI-PMH (Open Archives Initiative Protocol for Metadata Harvesting)
- ❖ Dedicated Editorial Board for every journal
- ❖ Accurate and rapid peer-review process
- ❖ Increased citations of published articles through promotions
- ❖ Reduced timeline for article publication

Submit your articles and experience a new surge in publication services (<https://www.peertechz.com/submit>).

Peertechz journals wishes everlasting success in your every endeavours.

Copyright: © 2019 Shaikh IA, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.