

Research Article

Fosfomycin for Antibiotic Prophylaxis Prior to Transrectal Ultrasound-Guided Prostate Biopsy

Andrew Colhoun¹, Jessica Marinaro², Jay Sulek¹, Zachary McDowell³, Christopher Bednarz¹, Tyler Roseman¹, Adam Klausner¹, Michael Climo⁴, Leroy Vaughan⁴ and Baruch Mayer Grob^{1,5*}

¹Department of Surgery/Urology, Virginia Commonwealth University School of Medicine, Richmond, USA

²Department of Urology, Georgetown University, Washington, D.C., USA

³Department of Urology, Baylor University School of Medicine, Houston, USA

⁴Infectious Disease Service, Hunter Holmes McGuire VA Medical Center, Richmond, USA

⁵Urology Service, Hunter Holmes McGuire VA Medical Center, Richmond, USA

Abstract

Introduction

Infectious complications are known risks of Transrectal Ultrasound (TRUS) prostate biopsy. Increasing fluoroquinolone resistance creates a need for novel prophylactic agents. Fosfomycin is an oral bactericidal agent with high urinary and prostatic tissue concentrations. This study aims to assess the efficacy of fosfomycin in preventing infectious complications after prostate biopsy.

***Corresponding author:** Baruch Mayer Grob, Department of Surgery/Urology, Virginia Commonwealth University School of Medicine, Richmond, USA; Urology service, Hunter Holmes McGuire VA Medical Center, Richmond, USA, Tel: +1 8048285320; E-mail: baruch.grob@vcuhealth.org

Citation: Colhoun A, Marinaro A, Sulek J, McDowell Z, Bednarz C, et al. (2018) Fosfomycin for Antibiotic Prophylaxis Prior to Transrectal Ultrasound-Guided Prostate Biopsy. Arch Urol 1: 004.

Received: May 14, 2017; **Accepted:** October 17, 2018; **Published:** October 31, 2018

Copyright: © 2018 Colhoun A, 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.

Methods

Under the advice of the infection control service at our hospital, prostate biopsy prophylaxis transitioned from ciprofloxacin to fosfomycin in July 2013. A prospective quality assurance database was maintained. Retrospective review of the periprocedural infectious complications within 30 days of biopsy was performed comparing prophylaxis with ciprofloxacin prior to initiation of fosfomycin prophylaxis and the new fosfomycin regimen. All patients received phosphate enemas prior to biopsy.

Results

Among the 414 patients treated with fosfomycin and 400 patients treated with ciprofloxacin over 26 months, there was no difference in number of biopsy cores obtained or history of prior prostate biopsy. Positive post-biopsy urine cultures occurred in 0.75% and 1.21% of patients in the ciprofloxacin and fosfomycin groups, respectively ($p=0.73$), and positive post-biopsy blood cultures in 0.75% and 0.72% of patients in the ciprofloxacin and fosfomycin groups, respectively ($p=1.0$). Bacterial cultures in the ciprofloxacin group demonstrated a significantly higher rate of fluoroquinolone resistance compared to cultures in the fosfomycin group (66% vs. 0%, $p=0.015$).

Conclusion

Fosfomycin is an effective agent for antimicrobial prophylaxis in patients undergoing TRUS prostate biopsy, comparable to standard therapy. It could be an alternative prophylactic agent particularly in centers with high fluoroquinolone resistance.

Keywords: Antibiotic prophylaxis prostate; Biopsy; Fluoroquinolones; Fosfomycin

Introduction

Transrectal Ultrasound-Guided (TRUS) needle biopsy is routinely employed to obtain tissue for prostate cancer diagnosis and is recommended for patients with abnormal digital rectal examination findings or an elevated serum prostate-specific antigen level. TRUS Prostate Biopsy (TRUSPB) provides a definitive, histopathologic diagnosis with sensitivities between 75% and 90% [1]. The majority of TRUSPB are performed on an outpatient basis with minor complications of hematuria and hematospermia; however, major complications including prostatitis, urosepsis or even septic shock can occur [2,3]. In an attempt to mitigate risks of TRUSPB, the American Urological Association recommends routine antibiotic prophylaxis prior to all prostate biopsies with either a fluoroquinolone, cephalosporin or trimethoprim-sulfamethoxazole [4]. Worldwide, ciprofloxacin is the most frequently prescribed drug for TRUSPB antibiotic prophylaxis due to its broad spectrum of activity, enteric administration and high prostatic tissue concentrations [5,6].

Despite the use of antibiotic prophylaxis, infectious complications following TRUSPB continue to increase, almost tripling from 1991 to 2007 based on Medicare data and increasing six-fold in Canada from 1996 to 2005 [7-10]. This increase in infectious complications has been found to parallel an increase in Fluoroquinolone-Resistant (FQR) *E. coli* isolates [9,11]. FQR infections following TRUSPB

have risen from 0.6% to 2.6% from 2004 to 2006, an approximate 4-fold increase in 2 years [11]. Specifically, patients colonized with FQR rectal flora demonstrated a seven-fold increase in post-TRUSPB infection rate compared to patients with FQ-sensitive rectal flora [12]. Multiple studies estimate the prevalence of FQR rectal flora among all men to be between 17% and 24% [12-14]. Given these increased rates of colonization and infection with FQR pathogens, there is a pressing need for novel antimicrobial prophylaxis that is easily administered, is well tolerated and is effective against FQR organisms.

Fosfomycin is a broad-spectrum, oral bactericidal agent that is approved in the United States for the treatment of uncomplicated acute cystitis caused by *E. coli* and *E. faecalis* and is used in Europe for prophylaxis prior to endourologic and transurethral procedures [15,16]. Fosfomycin is administered orally as a water-soluble powder and is distributed in high concentrations to the kidneys, bladder wall, prostate and seminal vesicles within 1-4 hours of consumption [17,18]. The mechanism of action involves inactivation of enolpyruvyl transferase, an enzyme essential for bacterial cell wall synthesis [16,19]. Urinary concentrations remain bactericidal for over 24 hours after administration and the drug is generally well-tolerated, with the most frequent adverse reactions being diarrhea (10.4%), headache (10.3%) and nausea (5.2%) [16]. In an *in vitro* study comparing fosfomycin to other antibiotics commonly used to treat urinary tract infections, fosfomycin was found to be the most effective drug against *E. coli* (99% of strains susceptible) with only 88% of *E. coli* strains showing susceptibility to ciprofloxacin [20]. Fosfomycin has also demonstrated activity against both FQR and extended-spectrum beta-lactamase producing strains of *E. coli* [19,21]. Additionally, fosfomycin resistance is uncommon with only 1-3% of *E. coli* strains worldwide demonstrating resistance [19].

To our knowledge, no study has compared infectious complications from standard prophylaxis and fosfomycin prophylaxis prior to TRUSPB in a North American population. We aim to determine if fosfomycin is an effective agent for antibiotic prophylaxis prior to TRUSPB.

Materials and Methods

Patients who underwent TRUSPB at the Hunter Holmes McGuire VA Medical Center received a standard prophylactic antibiotic regimen of oral ciprofloxacin 500mg twice daily for 3 days (day before, day of and day after biopsy). In July 2013 hospital epidemiology and the infectious disease service recommended transitioning to a one-time dose of oral fosfomycin 3g approximately 2 to 3 hours prior to TRUSPB instead of the traditional ciprofloxacin regimen due to increasing prevalence of FQR bacterial infections at our institution. Specifically, 3g of Fosfomycin Tromethamine powder mixed with 3-4 oz was administered. A quality assurance database was prospectively maintained to monitor patients for signs and symptoms of infection within 30 days of biopsy after initiation of the new fosfomycin regimen. An infectious complication was defined as any positive blood or urine bacterial culture (irrespective of CFU/mL or presenting symptoms). After Institutional Review Board approval, a retrospective review of the quality assurance database was performed from July 2013 through August 2014 as well as retrospective review of patients undergoing TRUSPB during the 12 months prior to the antibiotic transition who received prophylaxis with ciprofloxacin. All patients received phosphate enemas prior to TRUSPB. Patients were excluded

if they received any type of antibiotic prophylaxis other than the two regimens listed or if they took the prescribed antibiotic regimen incorrectly. Demographics and pertinent medical history were obtained including patient age, number of biopsy cores obtained, history of prior TRUSPB and susceptibility to infection (i.e. diabetes mellitus, HIV and immunosuppressive medications). In the event of an infectious complication symptoms and causative organisms were recorded. Statistical analysis was performed using a two-tailed student's t-test to compare means and Fisher's exact test to compare event frequency between groups.

Results

A total of 868 consecutive patients were identified over 26 months, 54 were excluded for not meeting criteria. Demographics between the ciprofloxacin group (n=400) and the fosfomycin group (n=414) were similar and are listed in table 1.

	Fosfomycin	Ciprofloxacin	p
n	414	400	
Average age (years)	64	64	0.28
Diabetes mellitus (%)	128 (31)	108 (27)	0.25
Immunocompromised (%)	7 (2)	4 (1)	0.55
Average number of biopsy cores (range)	11 (10-20)	11 (10-20)	0.71
History of prior prostate biopsy (%)	118 (29)	132 (33)	0.17

Table 1: Patient demographics.

There was not a significant difference in the number of post-TRUSPB infections between the two groups (Table 2). A total of 8 (1.93%) infectious complications were identified in the fosfomycin group and 6 (1.50%) infectious complications were identified in the ciprofloxacin group which was not significantly different (p=0.47). Three patients in both the fosfomycin arm (0.72%) and ciprofloxacin arm (0.75%) developed bacteremia (p=1.0), all six of these patients were hospitalized. No infectious complications were observed in patients with suspected or confirmed immune compromised status. There were no deaths from infection within 30 days of the biopsies.

	Fosfomycin	Ciprofloxacin	p
Patients (%)	8 (1.93)	6 (1.50)	0.47
Positive urine culture (%)	6 (1.45) 2 <i>Enterobacter</i> 3 <i>K. pneumoniae</i> 1 FQS <i>E. coli</i>	4 (1.00) 3 FQR <i>E. coli</i> 1 Group B Strep	0.75
Positive blood culture (%)	3 (0.72) 1 FQS <i>E. coli</i> 2 <i>K. pneumoniae</i>	3 (0.75) 1 FQS <i>E. coli</i> 2 FQR <i>E. coli</i>	1.0
Patients with FQR isolates (%)	0 (0)	4 (66)	0.02
Relative risk of post-biopsy infection in patients with history of prior biopsy [95% CI]	2.51 [0.64-9.87]	2.03 [0.42-9.92]	NS

Table 2: Infectious complications.

Note: FQS: Fluoroquinolone-Sensitive; FQR: Fluoroquinolone-Resistant.

The majority of patients with infectious complications in the fosfomycin group (5/8) demonstrated only bacteriuria and 2 of these 5 patients had chronic kidney disease stage III or greater. The majority of infectious complications in the ciprofloxacin group (66%) were secondary to FQR *E. coli* isolates. All 8 infectious complications in the fosfomycin group were secondary to Gram negative rods (*Enterobacter* sp., *E. coli* and *K. pneumoniae*) with 50% demonstrating only ampicillin resistance and the remainder demonstrating pan-sensitivity on susceptibility testing. The ciprofloxacin group demonstrated a significantly higher rate of FQR complications when compared to the fosfomycin group (66% vs. 0%, $p=0.02$). Of note, 2 of the 3 patients developing bacteremia in the ciprofloxacin group had a prior TRUSPB and blood cultures at time of presentation demonstrated FQR *E. coli*.

Patients with history of prior TRUS prostate biopsy demonstrated a relative risk of 2.03 (95% CI [0.42-9.92], $p=0.38$) for the ciprofloxacin group and 2.51 (95% CI [0.64-9.87], $p=0.19$) for the fosfomycin group for developing post-biopsy infectious complications when compared to biopsy-naïve patients in their respective cohorts.

Discussion

Infectious complications are serious sequelae of TRUSPB and increased efforts are needed to mitigate the risks of infection. Patients hospitalized for post-TRUSPB infectious complications have a significantly greater 30 day mortality risk when compared to patients hospitalized for noninfectious complications [7]. An increase in FQR infections after TRUSPB indicates that novel prophylactic agents or approaches are necessary [11]. Some groups have demonstrated improved rates of infection with the addition of intravenous or intramuscular antibiotics to augment standard prophylaxis and provide targeted therapy directed at FQR bacteria discovered on pre-TRUSPB rectal cultures [22-24]. Other studies have demonstrated efficacy of rectal povidone-iodine preparation prior to TRUSPB, although this method does not provide any prophylactic benefit to the prostate tissue itself since the antiseptic agent is contained in the rectal vault [25].

Fosfomycin tromethamine is a bactericidal agent that is particularly effective against *E. coli*, *E. faecalis*, *Citrobacter*, *Proteus*, *Enterobacter*, *Klebsiella*, *Serratia* and *Enterococcus* species. In the oral form, it has a bioavailability of 34-41% [26]. Once absorbed Fosfomycin has no metabolic transformation and is primarily excreted in the urine. Doses used in this study were sufficient enough to have bactericidal effects [26].

Preliminary studies have already investigated the efficacy of fosfomycin as a prophylactic antibiotic prior to TRUSPB in Europe. Ongun et al., performed a retrospective analysis comparing the rates of infectious complications among patients who received either one 3g dose of oral fosfomycin, one 500mg dose of oral levofloxacin or 5 days of 500mg oral ciprofloxacin BID prior to TRUSPB. The rate of febrile Urinary Tract Infection (UTI) following fluoroquinolone prophylaxis was 3.4%; in contrast, the rate of febrile UTI following fosfomycin prophylaxis was only 0.9%, although this was not statistically significant [26]. Another study by Lista et al., randomized patients to receive either two 3g doses of fosfomycin or ten 500mg doses of ciprofloxacin as antibiotic prophylaxis prior to TRUSPB with no significant difference in the rates of post-TRUSPB febrile episodes [27].

Recent research has also shown favorable evidence for the use of fosfomycin prophylaxis prior to TRUSPB in Mediterranean populations. Roberts et al., investigated efficacy through a meta-analysis that was comprised of three prospective randomized trials and two retrospective cohorts. Results from the meta-analysis demonstrated a decreased relative odds of infection in patients treated with fosfomycin trometamol compared to fluoroquinolone prophylaxis for TRUSPB (OR 0.22, 95% CI [0.09-0.54]) [28].

In the present study, we incurred similar rates of infectious complications between patients treated with ciprofloxacin prophylaxis and those treated with fosfomycin prophylaxis for TRUSPB. Our overall prevalence of post-TRUSPB infectious complications requiring hospitalization was similar to larger series [29]. Although there was not a significant difference in infectious complication rates between the two groups, a significantly higher number of patients in the ciprofloxacin group developed FQR infections. Our findings of an increased risk of infectious complications among patients with a history of prior TRUSPB and that 66% of patients who developed bacteremia in the ciprofloxacin group grew FQR *E. coli* suggests these patients may harbor FQR organisms in their rectal vault as sequelae of prior biopsy. Therefore, fosfomycin may be considered a reasonable alternative for antibiotic prophylaxis prior to TRUSPB, especially in areas with high FQR or in patients with history of prior TRUSPB.

Fosfomycin was well-tolerated and no adverse events were reported after patient self-administration. The ease of administration 2-3 hours prior to TRUSPB is similar to a one-time oral quinolone. However, when compared to ciprofloxacin (approximately \$5 for one 500mg tablet), fosfomycin has significantly higher monetary costs (approximately \$72 for a one-time 3g dose) [30-32]. In centers with high percentages of FQR organisms, the cost of administration of intravenous antimicrobials including advanced generation cephalosporins prior to TRUSPB and the expense and morbidity of a hospital stay may balance the cost of the drug.

Limitations of this study include the nonrandomized nature and retrospective review of patient data. Although we demonstrated no significant difference between fosfomycin and quinolone prophylaxis, this study was underpowered to detect such a significant difference. However fosfomycin does appear to have similar efficacy and more rigorous study in a larger randomized trial appears warranted. Another limitation was the reliability of patient-reported compliance and time of fosfomycin administration. Although patients were educated on the proper administration of fosfomycin at their pre-biopsy appointment, actual administration times or noncompliance may have influenced drug bioavailability at time of biopsy and led to potentially avoidable infectious complications. Given the significant difference in the cost of fosfomycin compared to ciprofloxacin, there may be a cost barrier to widespread usage. Finally, the administration of fosfomycin to patients with renal insufficiency may not have allowed for adequate urinary concentrations at time of TRUSPB and predisposed these patients to infectious risks.

Conclusion

This is the first study in North America demonstrating that fosfomycin may be an effective agent for antimicrobial prophylaxis prior to TRUSPB when compared to standard prophylaxis. With a broad spectrum of activity against FQR organisms, fosfomycin could be considered as an alternative to standard prophylaxis in areas with high FQR.

References

1. Shariat SF, Roehrborn CG (2008) Using biopsy to detect prostate cancer. Rev Urol 10: 262-280.
2. Rodríguez LV, Terris MK (1998) Risks and complications of transrectal ultrasound guided prostate needle biopsy: A prospective study and review of the literature. J Urol 160: 2115-2120.
3. Raaijmakers R, Kirkels WJ, Roobol MJ, Wildhagen MF, Schrder FH (2002) Complication rates and risk factors of 5802 transrectal ultrasound-guided sextant biopsies of the prostate within a population-based screening program. Urology 60: 826-830.
4. Wolf JS Jr, Bennett CJ, Dmochowski RR, Hollenbeck BK, Pearle MS, et al. (2008) Best practice policy statement on urologic surgery antimicrobial prophylaxis. J Urol 179: 1379-1390.
5. Çek M, Tandoğdu Z, Naber K, Tenke P, Wagenlehner F, et al. (2013) Antibiotic prophylaxis in urology departments, 2005-2010. Eur Urol 63: 386-394.
6. Dan M, Golomb J, Gorea A, Braf Z, Berger SA (1986) Concentration of ciprofloxacin in human prostatic tissue after oral administration. Antimicrob Agents Chemother 30: 88-89.
7. Loeb S, Carter HB, Berndt SI, Ricker W, Schaeffer EM (2011) Complications after prostate biopsy: Data from SEER-Medicare. J Urol 186: 1830-1834.
8. Nam RK, Saskin R, Lee Y, Liu Y, Law C, et al. (2010) Increasing hospital admission rates for urological complications after transrectal ultrasound guided prostate biopsy. J Urol 183: 963-968.
9. Feliciano J, Teper E, Ferrandino M, Macchia RJ, Blank W, et al. (2008) The incidence of fluoroquinolone resistant infections after prostate biopsy--are fluoroquinolones still effective prophylaxis? J Urol 179: 952-955.
10. Zaytoun OM, Vargo EH, Rajan R, Berglund R, Gordon S, et al. (2011) Emergence of fluoroquinolone-resistant *Escherichia coli* as cause of post-prostate biopsy infection: Implications for prophylaxis and treatment. Urology 77: 1035-1041.
11. Williamson DA, Barrett LK, Rogers BA, Freeman JT, Hadway P, et al. (2013) Infectious complications following transrectal ultrasound-guided prostate biopsy: New challenges in the era of multidrug-resistant *Escherichia coli*. Clin Infect Dis 57: 267-274.
12. Roberts MJ, Williamson DA, Hadway P, Doi SA, Gardiner RA, et al. (2014) Baseline prevalence of antimicrobial resistance and subsequent infection following prostate biopsy using empirical or altered prophylaxis: A bias-adjusted meta-analysis. Int J Antimicrob Agents 43: 301-309.
13. Liss MA, Chang A, Santos R, Nakama-Peeples A, Peterson EM, et al. (2011) Prevalence and significance of fluoroquinolone resistant *Escherichia coli* in patients undergoing transrectal ultrasound guided prostate needle biopsy. J Urol 185: 1283-1288.
14. Cohen JE, Landis P, Trock BJ, Patel HD, Ball MW, et al. (2015) Fluoroquinolone resistance in the rectal carriage of men in an active surveillance cohort: Longitudinal analysis. J Urol 193: 552-556.
15. Baert L, Billiet I, Vandepitte J (1990) Prophylactic chemotherapy with fosfomycin trometamol versus placebo during transurethral prostatic resection. Infection 18: 103-106.
16. Monurolo (R) (fosfomycin tromethamine) [prescribing information]. St. Louis, MO: Forest Pharmaceuticals
17. Rhodes NJ, Gardiner BJ, Neely MN, Grayson ML, Ellis AG, et al. (2015) Optimal timing of oral fosfomycin administration for pre-prostate biopsy prophylaxis. J Antimicrob Chemother 70: 2068-2073.
18. Gardiner BJ, Mahony AA, Ellis AG, Lawrentschuk N, Bolton DM, et al. (2014) Is fosfomycin a potential treatment alternative for multidrug-resistant gram-negative prostatitis? Clin Infect Dis 58: 101-105.
19. Raz R (2012) Fosfomycin: An old-new antibiotic. Clin Microbiol Infect 18: 4-7.
20. Marchese A, Gualco L, Debbia EA, Schito GC, Shito AM (2003) *In vitro* activity of fosfomycin against gram-negative urinary pathogens and the biological cost of fosfomycin resistance. Int J Antimicrob Agents 22: 53-59.
21. Falagas ME, Kastoris AC, Kapaskelis AM, Karageorgopoulos DE (2010) Fosfomycin for the treatment of multidrug-resistant, including extended-spectrum beta-lactamase producing, Enterobacteriaceae infections: A systematic review. Lancet Infect Dis 10: 43-50.
22. Losco G, Studd R, Blackmore T (2014) Ertapenem prophylaxis reduces sepsis after transrectal biopsy of the prostate. BJU Int 113: 69-72.
23. Adibi M, Hornberger B, Bhat D, Raj G, Roehrborn CG, et al. (2013) Reduction in hospital admission rates due to post-prostate biopsy infections after augmenting standard antibiotic prophylaxis. J Urol 189: 535-540.
24. Womble PR, Linsell SM, Gao Y, Ye Z, Montie JE, et al. (2015) A Statewide Intervention to Reduce Hospitalizations after Prostate Biopsy. J Urol 194: 403-409.
25. Abughosh Z, Margolick J, Goldenberg SL, Taylor SA, Afshar K, et al. (2013) A prospective randomized trial of povidone-iodine prophylactic cleansing of the rectum before transrectal ultrasound guided prostate biopsy. J Urol 189: 1326-1331.
26. Patel SS, Balfour JA, Bryson HM (1997) Fosfomycin tromethamine. A review of its antibacterial activity, pharmacokinetic properties and therapeutic efficacy as a single-dose oral treatment for acute uncomplicated lower urinary tract infections. Drugs 53: 637-656.
27. Ongün S, Aslan G, Avkan-Oguz V (2012) The effectiveness of single-dose fosfomycin as antimicrobial prophylaxis for patients undergoing transrectal ultrasound-guided biopsy of the prostate. Urol Int 89: 439-444.
28. Lista F, Redondo C, Meilán E, García-Tello A, Ramón de Fata F, et al. (2014) Efficacy and safety of fosfomycin-trometamol in the prophylaxis for transrectal prostate biopsy. Prospective randomized comparison with ciprofloxacin. Actas Urol Esp 38: 391-396.
29. Roberts MJ, Scott S, Harris PN, Naber K, Wagenlehner FME, et al. (2018) Comparison of fosfomycin against fluoroquinolones for transrectal prostate biopsy prophylaxis: An individual patient-data meta-analysis. World J Urol 36: 323-330.
30. Lundström KJ, Drevin L, Carlsson S, Garmo H, Loeb S, et al. (2014) Nationwide population based study of infections after transrectal ultrasound guided prostate biopsy. J Urol 192: 1116-1122.
31. Wolters Kluwer (2015) Fosfomycin: Drug information. uptodate.com.
32. Wolters Kluwer (2015) Ciprofloxacin (systemic): Drug information. uptodate.com.



- Journal of Anesthesia & Clinical Care
- Journal of Addiction & Addictive Disorders
- Advances in Microbiology Research
- Advances in Industrial Biotechnology
- Journal of Agronomy & Agricultural Science
- Journal of AIDS Clinical Research & STDs
- Journal of Alcoholism, Drug Abuse & Substance Dependence
- Journal of Allergy Disorders & Therapy
- Journal of Alternative, Complementary & Integrative Medicine
- Journal of Alzheimer's & Neurodegenerative Diseases
- Journal of Angiology & Vascular Surgery
- Journal of Animal Research & Veterinary Science
- Archives of Zoological Studies
- Archives of Urology
- Journal of Atmospheric & Earth-Sciences
- Journal of Aquaculture & Fisheries
- Journal of Biotech Research & Biochemistry
- Journal of Brain & Neuroscience Research
- Journal of Cancer Biology & Treatment
- Journal of Cardiology & Neurocardiovascular Diseases
- Journal of Cell Biology & Cell Metabolism
- Journal of Clinical Dermatology & Therapy
- Journal of Clinical Immunology & Immunotherapy
- Journal of Clinical Studies & Medical Case Reports
- Journal of Community Medicine & Public Health Care
- Current Trends: Medical & Biological Engineering
- Journal of Cytology & Tissue Biology
- Journal of Dentistry: Oral Health & Cosmesis
- Journal of Diabetes & Metabolic Disorders
- Journal of Dairy Research & Technology
- Journal of Emergency Medicine Trauma & Surgical Care
- Journal of Environmental Science: Current Research
- Journal of Food Science & Nutrition
- Journal of Forensic, Legal & Investigative Sciences
- Journal of Gastroenterology & Hepatology Research
- Journal of Gerontology & Geriatric Medicine
- Journal of Genetics & Genomic Sciences
- Journal of Hematology, Blood Transfusion & Disorders
- Journal of Human Endocrinology
- Journal of Hospice & Palliative Medical Care
- Journal of Internal Medicine & Primary Healthcare
- Journal of Infectious & Non Infectious Diseases
- Journal of Light & Laser: Current Trends
- Journal of Modern Chemical Sciences
- Journal of Medicine: Study & Research
- Journal of Nanotechnology: Nanomedicine & Nanobiotechnology
- Journal of Neonatology & Clinical Pediatrics
- Journal of Nephrology & Renal Therapy
- Journal of Non Invasive Vascular Investigation
- Journal of Nuclear Medicine, Radiology & Radiation Therapy
- Journal of Obesity & Weight Loss
- Journal of Orthopedic Research & Physiotherapy
- Journal of Otolaryngology, Head & Neck Surgery
- Journal of Protein Research & Bioinformatics
- Journal of Pathology Clinical & Medical Research
- Journal of Pharmacology, Pharmaceutics & Pharmacovigilance
- Journal of Physical Medicine, Rehabilitation & Disabilities
- Journal of Plant Science: Current Research
- Journal of Psychiatry, Depression & Anxiety
- Journal of Pulmonary Medicine & Respiratory Research
- Journal of Practical & Professional Nursing
- Journal of Reproductive Medicine, Gynaecology & Obstetrics
- Journal of Stem Cells Research, Development & Therapy
- Journal of Surgery: Current Trends & Innovations
- Journal of Toxicology: Current Research
- Journal of Translational Science and Research
- Trends in Anatomy & Physiology
- Journal of Vaccines Research & Vaccination
- Journal of Virology & Antivirals

Submit Your Manuscript: <http://www.heraldopenaccess.us/Online-Submission.php>