Research Article

Comparative Analysis of Efficacy, Cost Analysis and Prevalence of Urinary Tract Infection in Type II Diabetic Patients Exposed to Dapagliflozin, Dapagliflozin Propanediol Monohydrate, Dapagliflozin with Metformin Prospective Observational Study

Ramesh Petchi. R[1]*, Devika.G.S.[2], Nandini P[3], Reshma B[3], Prasanth V S[3]

1. Professor and HOD, Department of Pharmacology, Cherraan's College of Pharmacy, 521 Siruvani Main Road, Telungupalayam Pirivu, Coimbatore-641039, Tamil Nadu, India.
2. Professor and HOD, Department of Pharmaceutical Analysis, Cherraan's College of Pharmacy, 521 Siruvani Main Road, Telungupalayam Pirivu, Coimbatore-641039, Tamil Nadu, India.
3. Doctor of Pharmacy, Cherraan's College of Pharmacy, 521 Siruvani Main Road, Telungupalayam Pirivu, Coimbatore-641039, Tamil Nadu, India.

***Corresponding author's E-mail:** rameshpetchi28@gmail.com

Received: 25-07-2024; **Revised:** 26-11-2024; **Accepted:** 08-12-2024; **Published on:** 15-12-2024.

ABSTRACT

Background: Type 2 diabetes mellitus(T2DM) is a chronic metabolic disorder carrying an enormous burden of morbidity and mortality because of its characteristic complications, many of which are preventable with strict glycemic control. Initial management of T2DM consists of non -pharmacological interventions; if those fail, an oral anti-diabetic drug, most typically metformin is started. Combination therapy is initiated only when monotherapy fails to achieve glycemic control. Currently, Dapagliflozin may be considered a second line agent to treat patients with T2DM and has the potential to provide a first line option particularly for patients with contraindications or lack of glycemic control on metformin, the conventional first line agent.

Methods: A prospective observational study was conducted for 150 patients and their records from 2023-2024 were included in this study based on the inclusion and exclusion criteria. The case records were reviewed and evaluated on the basis of gender, age, efficacy results, prevalence of urinary tract infections and cost analysis results were collected. The collected data was entered and analyzed by using Microsoft Excel and the statistical calculation were also conducted by using ANOVA.

Results: A total of 150 patients were included in our study. On comparing three group of subjects with different drugs Group A which was provided with Dapagliflozin Propanediol Monohydrate involved 20 male patients and 20 female patients, Group B which was provided with Dapagliflozin involved 18 male subjects and 22 female subject and Group C which was provided with Dapagliflozin with Metformin include 22 male subjects and 18 female subjects. The majority of reduction or most efficacious is Group C. Also, by comparing three group of drugs for its prevalence of UTI GROUP C indicates less prevalence rate as compared to Group A and Group B.

Conclusion: In conclusion, this study effectively compares the efficacy and cost analysis of three diabetic drugs in managing type 2 diabetes, with a particular focus on their impact on the prevalence of UTI. Our findings suggests that Dapagliflozin with metformin has highest efficacy and also cost effectiveness compared to Dapagliflozin Propanediol Monohydrate and Dapagliflozin. Similarly, Dapagliflozin with metformin has lowest prevalence for UTI as compared to Dapagliflozin Propanediol Monohydrate and Dapagliflozin. These results provide critical insights for clinicians when selecting antidiabetic medications, emphasizing the importance for considering UTI risk alongside glycaemic control. Further research is recommended to explore long term outcomes and potential strategies for mitigating UTI risk in diabetic patients.

Keywords: SGLT2i, UTI, Dapagliflozin, Metformin, Combination Therapy.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a widespread, progressive disease that demands ongoing innovation in therapeutic options to enhance management and improve patient outcomes[1]. It is primarily managed through lifestyle changes and medications, starting with metformin. When metformin alone isn't effective, additional drugs, like SGLT2 inhibitors, are introduced. SGLT2 inhibitors, including dapagliflozin, work by reducing glucose reabsorption in the kidneys, which increases glucose excretion in the urine[2]. Dapagliflozin raise glucose levels in the urine, creating conditions that support bacterial growth and potentially increase the risk of urinary tract infections (UTIs)[2]. Managing T2DM focuses on maintaining glycemic control to prevent complications. With continued advancements in T2DM therapies, patients can achieve better outcomes and quality of life.

Diabetes Uncovered: Exploring the Types, Triggers, and Key Risk Factors [4]

1. **Type 1 Diabetes Mellitus (T1DM):** This form arises from the body's inability to produce sufficient insulin. Previously known as "insulin-dependent diabetes mellitus" (IDDM) or "juvenile diabetes," the cause of T1DM remains unknown.
2. **Type 2 Diabetes Mellitus (T2DM**): T2DM starts with insulin resistance, where cells do not respond effectively to insulin. Over time, insulin production may also decrease. It was once termed "non-insulin-dependent diabetes mellitus" (NIDDM) or "adult-onset diabetes." The primary risk factors include

excess body weight and insufficient physical activity.

3. **Gestational Diabetes:** This form occurs in pregnant women who have no prior history of diabetes but develop elevated blood glucose levels during pregnancy.

In type 2 diabetes mellitus (T2DM), high blood sugar is mainly due to either an absolute or, more often, a relative lack of insulin. Relative insulin deficiency generally results from the body's inability to sufficiently counteract insulin resistance, which can stem from both genetic and metabolic factors. The most common contributor to insulin resistance is central obesity, which is often linked to metabolic syndrome. This syndrome encompasses several related metabolic disturbances, such as impaired glucose tolerance, high blood pressure, a specific dyslipidemia (typically high triglycerides and low HDL cholesterol), and a heightened risk of cardiovascular disease. Together, these factors increase cardiovascular risk in individuals with T2DM, underscoring the need for lifestyle changes and medical treatment that focus on managing insulin resistance and associated risks.[5]

Comprehensive Non-Insulin Therapies for Effecive Type 2 Diabetes Management [6]

Type 2 Diabetes Mellitus (T2DM) is managed through various non-insulin oral therapies that target different aspects of glucose regulation:

1. Insulin Secretagogues: Sulfonylureas (e.g., Glibenclamide, Glipizide) stimulate insulin release from pancreatic β-cells. While effective, they may cause hypoglycemia and weight gain.
2. Biguanides: Metformin is the primary drug in this class, enhancing insulin sensitivity and reducing hepatic glucose production. It does not typically cause weight gain or hypoglycemia but may lead to gastrointestinal issues and long-term vitamin B12 deficiency.
3. Insulin Sensitizers: Thiazolidinediones (e.g., Pioglitazone) improve cellular response to insulin, enhancing glucose uptake. Side effects include weight gain, edema, and increased risk of fractures.
4. Alpha-Glucosidase Inhibitors (AGIs): Drugs like Acarbose slow carbohydrate digestion in the intestines, reducing postprandial blood glucose spikes. They are unsuitable for individuals with certain digestive disorders.
5. Incretin Mimetics: GLP-1 receptor agonists and DPP-IV inhibitors enhance insulin secretion and suppress glucagon release, effectively lowering blood glucose levels. Common side effects include nausea and appetite loss.
6. Amylin Analogues: These agents delay gastric emptying and suppress glucagon secretion, helping to stabilize blood glucose levels.
7. SGLT2 Inhibitors: Medications such as Canagliflozin and Dapagliflozin prevent renal glucose reabsorption, promoting glucose excretion through urine and lowering blood sugar levels.

These non-insulin therapies provide a multifaceted approach to managing T2DM, allowing for personalized treatment plans based on individual patient needs and tolerances.

Key Risk Factors for Type 2 Diabetes: Are You at Risk?

Key risks for type 2 diabetes include being overweight, abdominal fat, inactivity, family history, certain ethnic backgrounds, age (over 45), low HDL, high triglycerides, and conditions like prediabetes or polycystic ovary syndrome**.**

Serious Complications of Type 2 Diabetes: Protect Your Health

Complications like cardiovascular disease, neuropathy, and retinopathy. Additional complications include damage to the nervous system, dental disease, limb amputations, and ketoacidosis [3].

Diet Modification for Type 2 Diabetes

Maintaining an ideal body weight through a nutritious diet, emphasizing plant-based foods, and reducing the intake of red meat, processed meats, sweets, high-fat dairy, and refined grains, is an effective way to lower diabetes risk. A Mediterranean-style diet, featuring olive oil, fruits, vegetables, whole grains, pulses, nuts, low-fat dairy, and moderate alcohol intake, is particularly beneficial for promoting metabolic health and preventing diabetes.[7]

General Cautions for Dapagliflozin[1]

1. Risk of Hypoglycemia
   - While dapagliflozin alone rarely causes hypoglycemia, its combination with insulin or insulin secretagogues (e.g., sulfonylureas) increases this risk. Regular blood sugar monitoring is advised.
2. Dehydration Potential
   - Increased urination caused by dapagliflozin can lead to dehydration. Patients should stay hydrated, especially in hot weather or after physical activity.
3. Infection Risk
   - Dapagliflozin raises the likelihood of urinary and genital infections. Signs like painful urination, frequent urination, fever, or unusual genital symptoms should be reported promptly.
4. Ketoacidosis Risk
   - Rarely, dapagliflozin may trigger ketoacidosis even if blood sugar levels are not significantly elevated. Symptoms like nausea, vomiting, abdominal pain, fatigue, or difficulty breathing require urgent medical care.

5. Kidney Function Monitoring
   - Kidney health should be checked regularly, as dapagliflozin may impair renal function. It is unsuitable for those with severe kidney impairment.
6. Low Blood Pressure
   - Dapagliflozin's diuretic effects may lower blood pressure, especially in patients on antihypertensives. Symptoms such as dizziness or lightheadedness, particularly when standing, should be noted.
7. Bladder Cancer
   - There is a possible link to bladder cancer. Symptoms like blood in urine or frequent, painful urination should be reported to a healthcare provider.

MATERIALS AND METHODS

This Prospective Observational study collects the patient specific data and compares the Efficacy, UTI prevalence, and Cost-effectiveness of three type 2 diabetes treatments: Dapagliflozin, Dapagliflozin Propanediol Monohydrate, and Dapagliflozin with Metformin. Key metrics include blood glucose reduction, UTI incidence, demographic analysis, and cost per 1% reduction in glucose levels for each treatment. Patient data was collected using a "chart review method," including demographics, medical history, and lab results. A total of 120 patients were divided into three groups: Group A (Dapagliflozin propanediol monohydrate 10mg), Group B (Dapagliflozin 10mg), and Group C (Dapagliflozin 10mg/Metformin 1000mg). Blood sugar levels and urine analysis were monitored. Inclusion criteria involves Type 2 diabetes patients using Dapagliflozin, Dapagliflozin propanediol monohydrate, or Dapagliflozin with Metformin, Type 2 diabetes patients irrespective of sex, person aged 30-70, or with other comorbid conditions. PublicationExclusion criteria involves Type 1 diabetes, pregnancy, recent SGLT2 inhibitor use, new diabetes diagnosis. Data collection is performed via patient case history and electronic medical records at Kumaran Medical Center, Coimbatore maintaining strict confidentiality[8]. Ethical approval for the study was obtained from the Institutional Ethics Committee (IEC) prior to data collection [9]. Fasting plasma glucose, post prandial glucose, HbA1C, Random blood glucose and urine analysis routine are the key clinical data points collected throughout the study.

RESULTS AND DISCUSSION

In the present study, a total of 120 medical records from the general medicine were reviewed and 120 DM cases were included in the study as per inclusion and exclusion criteria. The case records were reviewed and gender, age, efficacy, cost, ADR were collected.

Gender – Wise Distribution:

On comparing both the group of subjects given with different drugs, group (A) which was provided with Dapagliflozin propanediol monohydrate involved 20 male subjects and 20 female subjects, group (B) which was provided with Dapagliflozin includes 18 male subjects and 22 female subjects and group (C) which was provided with Dapagliflozin with metformin includes 22 male subjects and 18 female subjects.

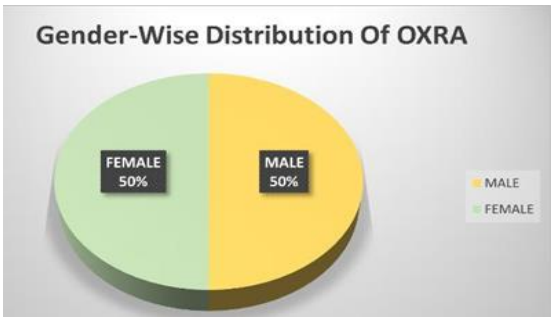

Figure 1: Gender wise Distribution of OXRA

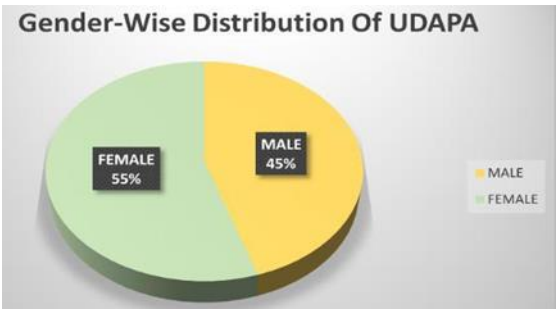

Figure 2: Gender wise Distribution of UDAPA

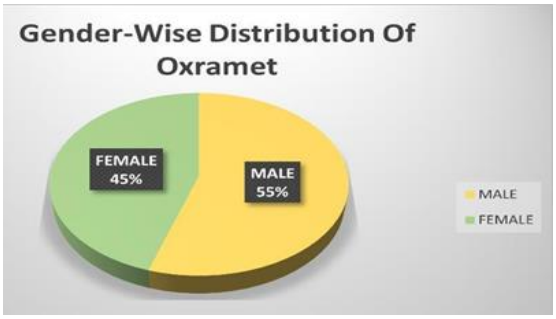

Figure 3: Gender wise Distribution of OXRAMET

Age – Wise Distribution:

In groups A, B, and C, the majority of participants were aged 60-70 (42.5%-45%), followed by 50-60 (32.5%). Smaller percentages were in the 40-50 (15%-20%) and 30-40 (5%-7.5%) age groups, showing a trend of older age predominance across all groups.

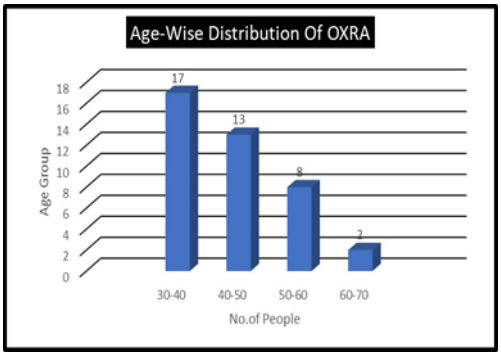

Figure 4: Age wise Distribution of OXRA

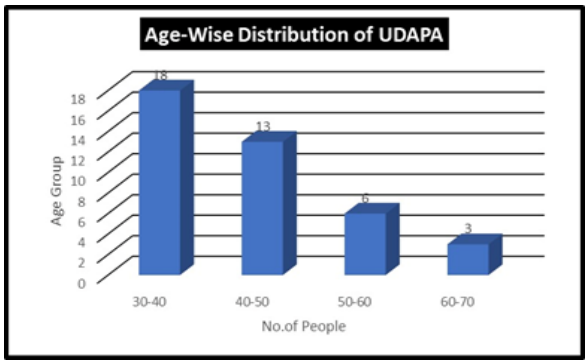

Figure 5: Age wise Distribution of UDAPA

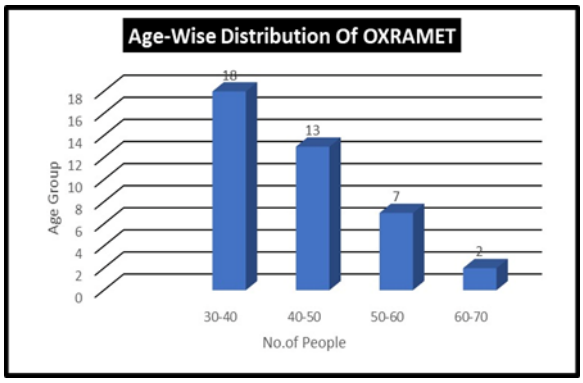

Figure 6: Age wise Distribution of OXRAMET

Efficacy Results:

Over 60 days, mean reductions were 26.5% (FBS) and 31.6% (PPBS) for Group A, 16.9% (FBS) and 29.3% (PPBS) for Group B, and 27.3% (FBS) and 49.8% (PPBS) for Group C. ANOVA results ($p < 0.05$) confirmed significant efficacy differences among the treatments.

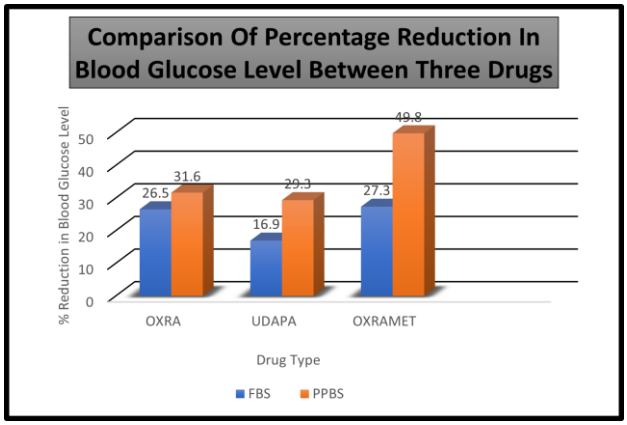

Figure 7: Efficacy Comparison Between Three Drugs

Prevalence Of UTI:

The study assessed the prevalence rates of urinary tract infections (UTIs) among three groups, A, B, and C, each comprising 35 individuals. Group A reported a UTI prevalence rate of 37%, with 13 cases out of 35. Group B had a higher prevalence rate at 54%, with 19 UTI cases identified. In contrast, Group C showed the lowest prevalence at 34%, with 12 cases. These findings reveal notable variations in UTI prevalence across the groups, with Group B showing a considerably higher rate of UTIs compared to Groups A and C.

The differences in prevalence rates may be due to varying factors associated with each group, potentially including underlying health conditions, differences in immunity, or treatment protocols. Such differences underscore the importance of targeted UTI prevention and treatment approaches based on individual or group-specific risk factors.

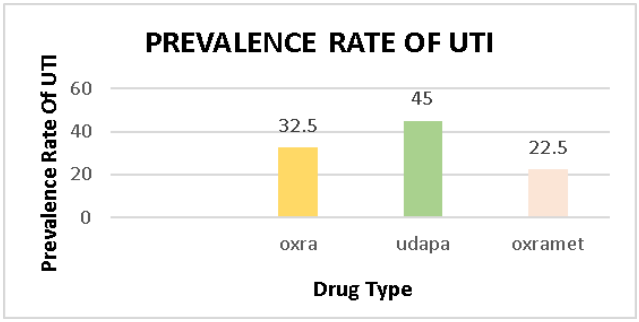

Figure 8: Prevalence Rate of UTI

Cost – Analysis Results:

The cost analysis of three therapies over 30 days reveals significant differences in cost-effectiveness. Dapagliflozin Propanediol Monohydrate costs 321.3 rupees for 30 days, with a 1% reduction in FBS costing 12.12 rupees and PPBS costing 10.16 rupees in Group A. Dapagliflozin costs 378 rupees for 30 days, with Group B's 1% reduction in FBS costing 22.3 rupees and PPBS costing 12.9 rupees. Dapagliflozin with Metformin is the most cost-effective, at 228 rupees for 30 days, with a 1% reduction in FBS costing 8.35 rupees and PPBS costing 4.57 rupees in Group C.

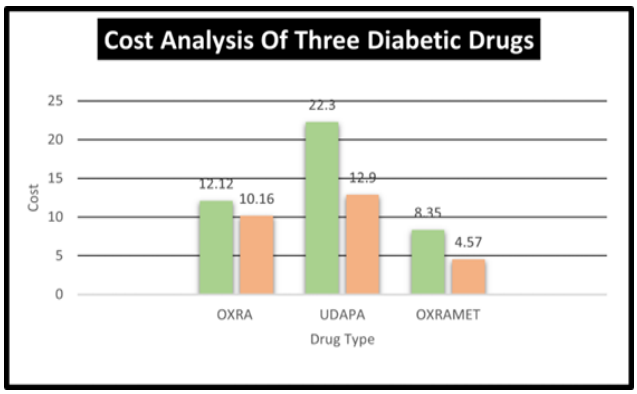

Figure 9: Cost- Analysis of Three Diabetic Drugs

CONCLUSION

Our analysis compares the efficacy, cost, and side effects of Dapagliflozin, Dapagliflozin propanediol monohydrate, and add-on therapy with metformin for diabetes management. All three demonstrate robust efficacy in controlling blood glucose levels, with add-on therapy outperforming the others. Despite its higher efficacy, add-on therapy is also the most cost-effective, while Dapagliflozin incurs the highest cost, potentially affecting patient adherence.

Dapagliflozin shows a higher incidence of urinary tract infections (UTIs), making it less suitable for patients with infection risks. In contrast, add-on therapy with metformin has fewer side effects, making it safer for broader use.

Clinicians should balance efficacy, cost, and side effect profiles when prescribing. For patients at risk of UTIs, add-on therapy or Dapagliflozin propanediol monohydrate are preferable. A personalized approach will enhance outcomes, reduce complications, and improve quality of life, aligning care with patient-specific needs.

ACKNOWLEDGEMENT

We would like to express our sincere gratitude to Kumaran Medical Centre, Coimbatore, for providing the resources and support necessary for the completion of this study. Special thanks to the physicians and medical staff for their invaluable assistance in data collection and patient care. We are also grateful to all those who offered their guidance and encouragement throughout this work.

Source of Support: The author(s) received no financial support for the research, authorship, and/or publication of this article

Conflict of Interest: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

REFERENCES

1. Sarah L. Anderson, Dapagliflozin efficacy and safety: a perspective review. Therapeutic Advances in Drug Safety. 2014. https://doi.org/10.1177/2042098614551938

2.Frequency of Urinary Tract Infections in Type 2 Diabetic Patients Taking Dapagliflozin Sarfaraz Khan, Mubashar Sultan Hashmi, Muhammad A Rana, Ghulam Mujtaba Zafar, Sadia Asif, Muhammad Talha Farooq, Sarmad Zahoor, Cureus. 2022;14(1):e21720. PMID: 35251794, PMCID: PMC8887691 DOI: 10.7759/cureus.21720

3. The Safety and Efficacy of Combination Therapy of Dapagliflozin and Metformin in Patient with Type 2 Diabetes Mellitus: A Review Study Saif K. Alkhanferi, Khadeejah H. Alhuraiz, Hussein S. Alyami, Sultan L. Alenazi, Mohammed F. Aldhaban, Naif Alrowedann, Yazeed Y. Albedaiwi, Nawal Alnazawi, Abrar Bokhamseen, Fatimah A. Talaqof King Abdulaziz Medical City, National Guard Health Affairs, Riyadh, Saudi Arabia. King Abdullah International Medical Research Center, Riyadh, Saudi Arabia. Imam Abdurrahman Bin Faisal Hospital, National Guard Health Affairs, Dammam, Saudi Arabia. Qassim Primary Health Care Center, National Guard Health Affairs, Qassim, Saudi Arabia. Journal of Diabetes Mellitus, 2022;12(4):271-283. DOI: 10.4236/jdm.2022.124022

4. A review on diabetes mellitus: type 1 & type 2 Roshan Kumar, Purabi Saha, Yogendra Kumar, Soumitra Sahana, Anubhav Dubey and Om Prakash. World Journal of Pharmacy and Pharmaceutical Sciences, 2020;9(10):838-850.

5. Understanding the cause of type 2 diabetes Publication History: Published July 19, 2024 DOI: 10.1016/S2213-8587(24)00157-8

6. Update on the treatment of type 2 diabetes mellitus Juan José Marín-Peñalver, Iciar Martín-Timón, Cristina Sevillano-Collantes, Francisco Javier del Cañizo-Gómez, World J Diabetes 2016 Sep 15;7(17):354–395. DOI: 10.4239/wjd.v7.i17.354

7. The role of diet in the prevention of type 2 diabetes Author links open overlay panelJ. Salas-Salvadó, M.Á. Martinez González, M. Bulló, E. Ros,2011;21(2):B32-B48. https://doi.org/10.1016/j.numecd.2011.03.009

8. Improving the Quality and Design of Retrospective Clinical Outcome Studies that Utilize Electronic Health Records Oliwier Dziadkowiec, Jeffery Durbin, Vignesh Jayaraman Muralidharan, Megan Novak, Brendon Cornett PMCID: PMC10324708 PMID: 37424712 HCA Healthc J Med 2020 Jun 27;1(3):131–138. doi: 10.36518/2689-0216.1094

9. World Medical Association Declaration of Helsinki. Ethical principles for medical research involving human subjects Bull World Health Organ 2001;79(4):373-4. PMID: 11357217 PMCID: PMC2566407