

# **EFFECT OF OZONE THERAPY in TREATING CHRONIC VAGINITIS**

# Vaginal Environment

- The vagina is a dynamic ecosystem that contains approximately  $10^9$  bacterial colony-forming units.
- Normal vaginal discharge is clear to white, odorless, and of high viscosity.
- Estrogen increase vaginal epithelial glycogen.
- Normal bacterial flora is dominated by lactobacilli that metabolize Glycogen into lactic acid – other potential pathogens present.
- Acidic environment (pH 3.8-4.2) inhibits the overgrowth of bacteria
- Some lactobacilli also produce  $H_2O_2$ , a potential microbicide present in 42-74% of females.  
Thought to be toxic to viruses like HIV.

# Important terms

- **Vaginitis** : significant inflammatory Response +many leukocytes in vag. Wall + Candida or Trichomonas.
- **Vaginosis** : minimal inflammatory Response + minimal leukocytes in vag. Wall + Bacteria.
- **Leucorrhoea** : non- infective , non-blood stained, physiological discharge.

# Vaginitis

- Usually characterized by:
  - **Vaginal discharge**
  - **Vulvar itching**
  - **Irritation**
  - **Odor**
- Common types
  - **Bacterial vaginosis (25-50%).**
  - **Vulvovaginal candidiasis (15-25%) .**
  - **Trichomonas vaginalis (5-15% ). STD.**

# Common causes

## A) Infective –not transmitted sexually :

1- **B. Vaginosis** ( 25-50%).

2- **Candida** (15-25%).

## B) Infective – transmitted sexually :

1-**Trichomoniasis** (5-15%) 2- **H. Simplex.**

3- **Chlamydia trachomatis.** 4- **Neisseria gonorrhoea.**

## C) Non Infective :

1- **F.B.** ( retained tampons, condom...).

2-**Cervical polyp.** 3- **Genital tract malignancy.**

4- **Fistula.** 5-**Allergic reaction.** 6-**Atrophic vaginitis.**

# VVC Epidemiology

- Affects most females during lifetime about 75% of women .
- 10% have recurrence.(saporiti AM , Rev Argent Microbial,2001).
- Most cases caused by *C. albicans* (85%-90%)
- Second most common cause of vaginitis
- Estimated cost: \$1 billion annually in the U.S.
- C. albicans.....87.5%
- C. glabrata.....08.6%
- C. krusei ,C.famata,C.tropicalis,C.cerevisiae.....3.9%
- C.albicans isolated in only 13.46% of cases resistant to Fluconazole.  
(Saporiti AM , Rev Argent Microbial,2001) .

# Mixed vaginal infection means presence of 2 out of the 3 common causes  
(Candida , Bacteria ,and Trichomonas), which occur in 38% of cases.  
(International Journal of Gynecology & Obstetric )

# CANDIDA Microbiology

- Candida species are normal flora of the skin and vagina.
- VVC is caused by overgrowth of *C. albicans* and other non-albicans species.
- Yeast grows as oval budding yeast cells or as a chain of cells (pseudo hyphae).
- Symptomatic clinical infection occurs with excessive growth of yeast.
- Disruption of normal vaginal ecology or host immunity can predispose to vaginal yeast infections.
- It is not STD.

# Complicated VVC

- Recurrent (RVVC) : Four or more episodes in one year.

## 1- Severe

- Edema.
- Excoriation / fissure formation.

## 2-Non-albicans candidiasis.

## 3- Pregnancy

## 4- Compromised host.

# After multiple occurrences, some consider empiric treatment of male sex partners to see if recurrence rate diminishes, but this approach has not been validated.



## **Most common Candidiasis :**

- 55% of women by mid twenties had VVC.
- Up to 75% of all women had at least 1 lifetime episode
- 58,4 million \$ /year its medication costs .(Foxman B, etal )
- Causative agents : C.albicans.....85 -90%,C.Glabrata .....5 -10% , others (C. tropicalis, C. Krusei, C. kefyr and Sachromyces cerevesiae).

## **Most common bacterial vaginitis :**

- 1)streptococci,
- 2)E.coli,
- 3)shigella sonnei.

## **Most common viruses :**

HSV especially HSV1 transmitted from oral mucosa .

:

# Vulvovaginal Candidiasis



Source: Health Canada, Sexual Health and STI Section, Clinical Slide Gallery

# Epidemiology

- B. Vaginosis is the most common cause of vaginitis
- - 5%-25% among college students .
  - 12%-61% among STD patients.
- Widely distributed Linked to premature rupture of membranes, premature delivery and low birth-weight delivery, acquisition of HIV, development of PID, and post-operative infections after gynecological procedures.
- Organisms do not persist in the male urethra

# Microbiology

- Overgrowth of bacteria species normally present in vagina with anaerobic bacteria
- BV correlates with a decrease or loss of protective lactobacilli:
  - Vaginal acid pH normally maintained by lactobacilli through metabolism of glucose/glycogen
  - Hydrogen peroxide ( $H_2O_2$ ) is produced by some *Lactobacilli*,sp.
  - $H_2O_2$  helps maintain a low pH, which inhibits bacteria overgrowth
  - Loss of protective lactobacilli may lead to BV

# BV Diagnosis: Amsel Criteria

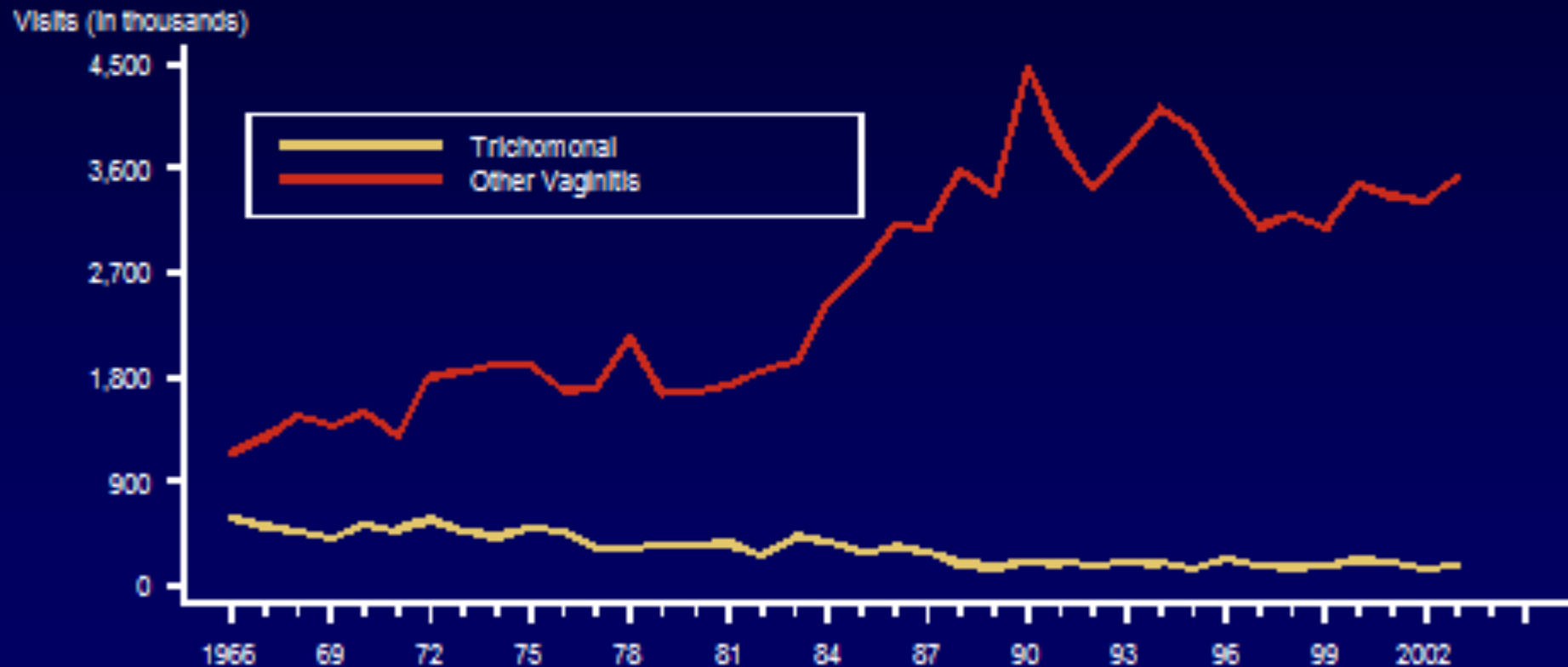
Amsel Criteria:  
Must have at least  
three of the  
following findings:

- Vaginal pH >4.5
- Presence of >20% per HPF of "clue cells" on wet mount examination
- Positive amine or "whiff" test
- Homogeneous, non-viscous, milky-white discharge adherent to the vaginal walls

# B.V. Recurrence

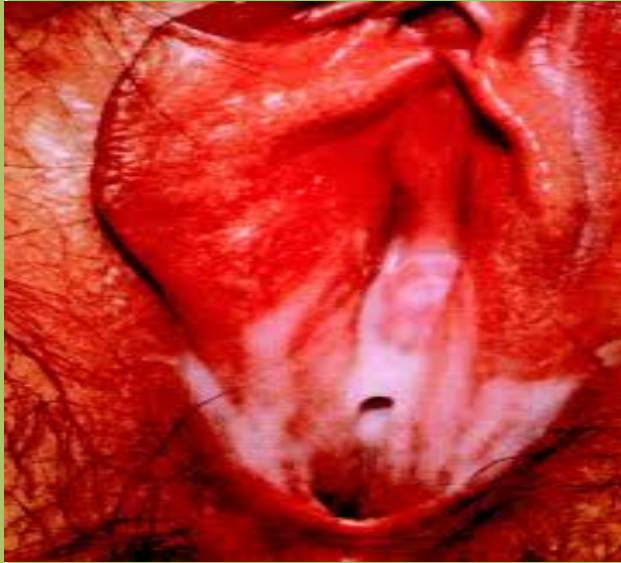
- 20% recurrence rate after 1 month
- Recurrence may be a result of persistence of BV-associated organisms and failure of lactobacillus flora to recolonize.
- Data do not support yogurt therapy or exogenous oral lactobacillus treatment.
- Under study: vaginal suppositories containing human lactobacillus strains

# Trichomoniasis and other vaginal infections — Initial visits to physicians' offices: United States, 1966–2003



SOURCE: National Disease and Therapeutic Index (IMS Health)

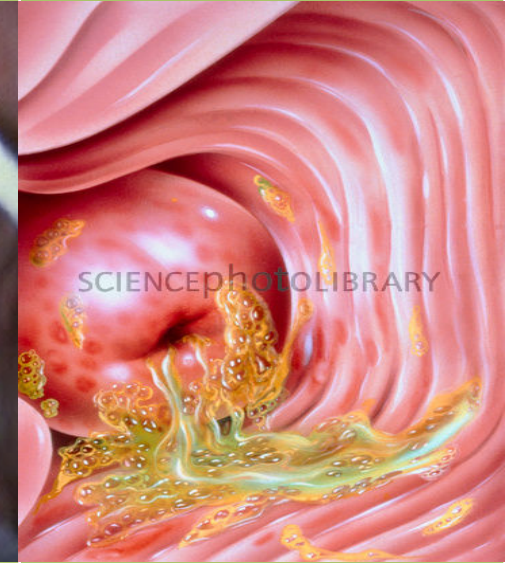
## CANDIDA



## BACTERIAL



## TRICHOMONAS



**DISCHARGE  
&**

**Cottage cheese, white,  
thick ,not offensive.**

**Thin ,white milky,  
homogenous  
,coating wall of  
vagina  
&vestibule ,FISHY  
OFFENSIVE**

**offensive,  
frothy ,copious ,  
white, gray, green  
or yellow**

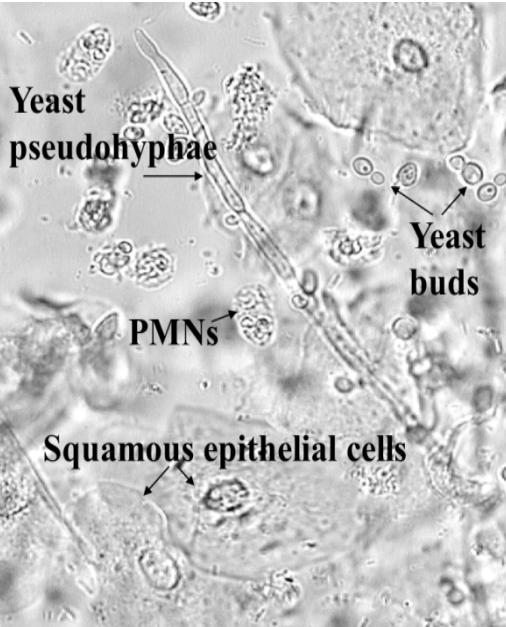
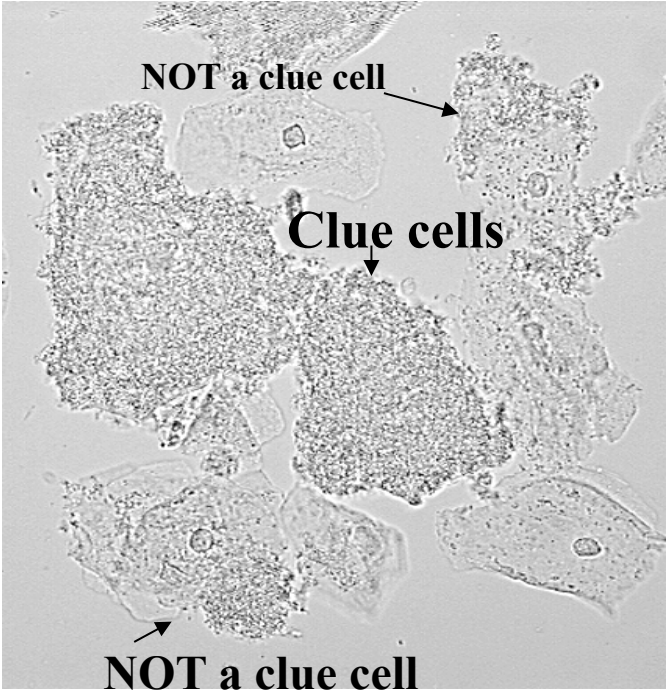
**VULVA**

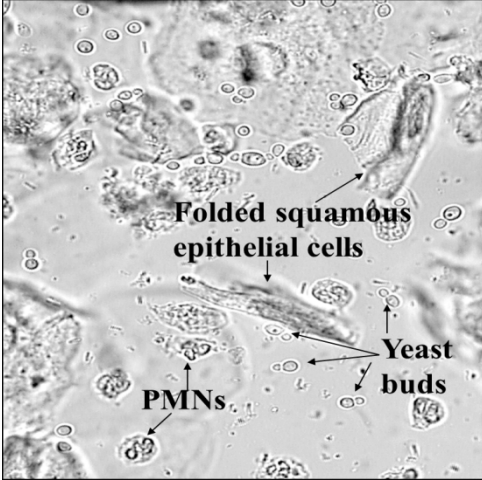
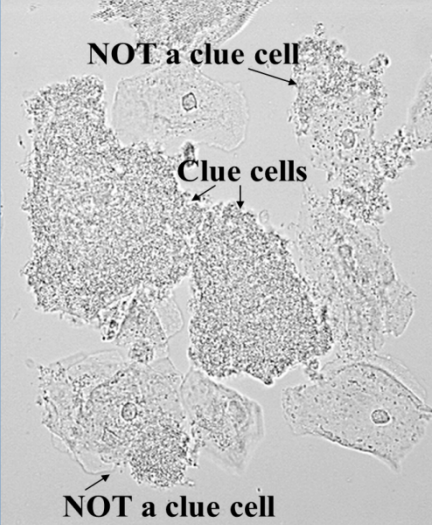
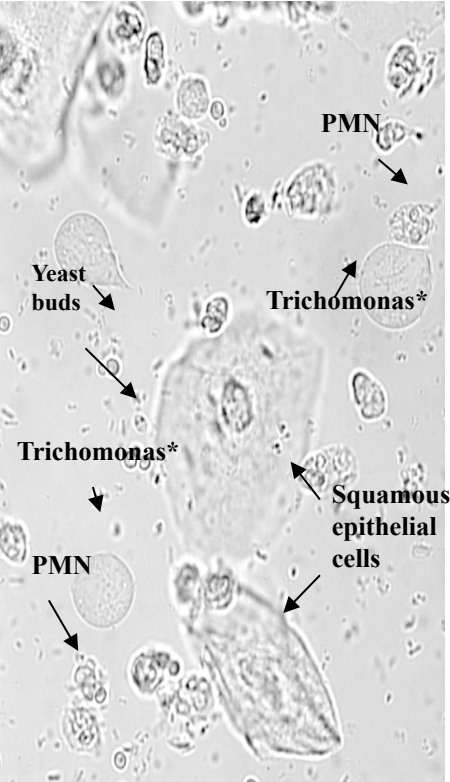
**Itching ,  
soreness ,dysuria ,  
dysparunia , satellite  
skin lesions**

**No vaginitis**

**\*itching , irritation,  
dysuria , abdominal  
discomfort ,  
Strawberry cervix**



PH	<4.5	>4.5	>4.5
MICROSCOPY	<p>WBCs ,Yeast Epithelial cells , mycelia or pseudo mycelia in 80%</p> 	<p><b>Clue cells, Rare WBCs ,lactobacilli outnumbered by profuse mixed flora including Gram + cocci and coccobacilli</b></p> 	<p>WBCs , in 80% of cases motile trichomonas can be detected</p>

	Candida	Bacteria	Trichomonas
KOH (whiff) test	NEGATIVE -ve	POSITIVE +ve	POSITIVE (often) +ve
Na Cl Wet Mount	Few RBC's	NO, or Few RBC's + Clue cells $\geq$ 20%.	Many RBC's + Motile Flagellated Protozoa
KOH Wet Mount  ( ABUBAKR ELNASHAR)	<p>PSEUDOHYPHAE – OR- Spores if not <i>C. albicans</i>.</p> 		

**C****B****T****PREDISPOSING  
Factors**

- **Antibiotics,**
- **DM uncontrolled**
- **Sugary diet**
- **Tight fitting**
- **synthetic clothing**
- **douching, local**
- **irritants as shower gels and shampoos in bath**

- **Douching**
- **Smoking**
- **IUCD**
- **New /Multiple partners**
- **Unprotected sexual intercourse**
- **Increased dose of spermicide eg : nonoxynol 9**
- **Use of Shower gel and shampoo in bath**

- **More Sexual intercourse with infected partner**
- **Multiple sexual partners FACTORS**
- **Unprotected sex (condom is not used by male partner)**
- **Skin**

# Treatment

C	B	T
<p>1) Miconazole cream 4% vaginally applied once for three days .</p> <p>2) Nystatin Tablet 100,000units 1/d for 14 days .</p> <p>3) Ticonazole 6.5% or Terconazole . 4% cream 5 gms 1/d .for a day and 5gms 1/d .for one week respectively</p>	<p>1) Metronidazole 500mgX2X7 d.</p> <p>2) Tinidazole 2gm 1/d for two days .</p> <p>3) Clindamycin 300mgx2x7days (Dalacin-C).</p>	<p>1) Metronidazole or Tinidazole : 2 gms X 1 X1 d.</p> <p>2) Metronidazole 500mg X2 X7 d .</p> <p>3) If above ttt failed amoxaycillin or Erythromycin are used to eradicate Beta heamolytic streptococci before metronidazole.</p>

- Chronic Vaginitis : when recurrence occurred 4 or more times / year.
- Causes of recurrence:
  - 1- Wrong diagnosis.
  - 2- Persistence of predisposing factors.
  - 3- Inadequate ttt. (A) Duration.  
(B) Dose.  
(C) Drug.

**# Better to do C. & S. of vaginal discharge for each case.**

# Aim Of Study

- **To evaluate effect of ozone therapy in treating chronic vulvo-vaginitis due to mixed candida and bacterial infection.**
- **And to compare and evaluate 2 different lines of ozone therapy after trying uneventful conventional ttt.**

# Why mixed recurrent infection

- 1- It represent 38% of recurrent vulvovaginitis.
- 2- Bacterial vaginitis is mostly offensive so patients asking for new tools to get rid of their recurrent problems.
- 3- Bacterial vaginitis is most common cause (25-50%) & Candidiasis is second common cause (15-25%) of V .V infections.

# SUBJECTS

- **30 female patients age between 25-40 years.**
- **They have mixed chronic vaginitis ,(candida + streptococci) .**
- **They received the proper medical treatment for 3 times or more before.**
- **Their body mass index did not exceed 36 Kg. / m<sup>2</sup>.**
- **They are randomly assigned into 2 groups each is 15 patients**



# Subject (continue)

<ul style="list-style-type: none"> <li>Group (A): are treated by</li> </ul>	Group(B): are treated by
<ul style="list-style-type: none"> <li>1- R.I. (20,25,30,35,40mcg.) 300 ml. 4/W. for 6W.</li> </ul>	<ul style="list-style-type: none"> <li>1-Ozone Sauna ( HOCATT) 4/W. for 6W.(O3 =</li> </ul>
<ul style="list-style-type: none"> <li>27min.&amp;CO2=3min)</li> </ul>	
<ul style="list-style-type: none"> <li>2- Vag.I.(20,25,30,35,40mcg./ml) 500ml. 4/W. for 6W.</li> </ul>	<ul style="list-style-type: none"> <li>2-Vag. I. 4/W. for 6W. for 27 min. (1<sup>st</sup> 3min. Is CO2 inside cabinet)</li> </ul>
<ul style="list-style-type: none"> <li>3- Ozonated olive oil cream applied to External Genitalia once daily 6 W. in both groups.</li> </ul>	

**# C & S of vag. Discharge before ttt in all 30 cases.**

**# follow up for 6 months to all cured cases and repeating C&S for uncured cases to know cause of recurrence**

# Ozone Steam Sauna (HOCATT)

- **Skin has a multiform antioxidant defense system .  
so can't be overwhelmed , provided attacks of ozone &UV  
are not too harsh .(oxidants and antioxidants in cutaneous biology-  
J. Thiele & P. Elsener 2001) .**
- **study demonstrates that CO2 bathing of ischemic lower limb  
causes the induction of local VEGF (vascular endothelium growth  
factor) synthesis, resulting in an NO-dependent new capillary  
formation associated with mobilization of endothelial progenitor  
cell. (Hidekazu Irie Etal , 2005)**
- **Carbonic acid which penetrates the skin leads to more O2**
- **released to the tissues according to Bohr's theory .**

# Ozone Steam Sauna (HOCATT)

“continue”

**Bohr's theory : haemoglobin's oxygen binding affinity is inversely related both to acidity and to the concentration of carbon dioxide.**

- # Thermal stress increases absorption of ROS & LOPs .**
- # Skin vasodilatation enhances transfer of O<sub>2</sub>, CO<sub>2</sub>, ROS, LOPs**

# HOCATT

- Hyperthermia.
- Ozone.
- Carbonic acid.
- Transdermal
- Therapy.

HOCATT advantages:

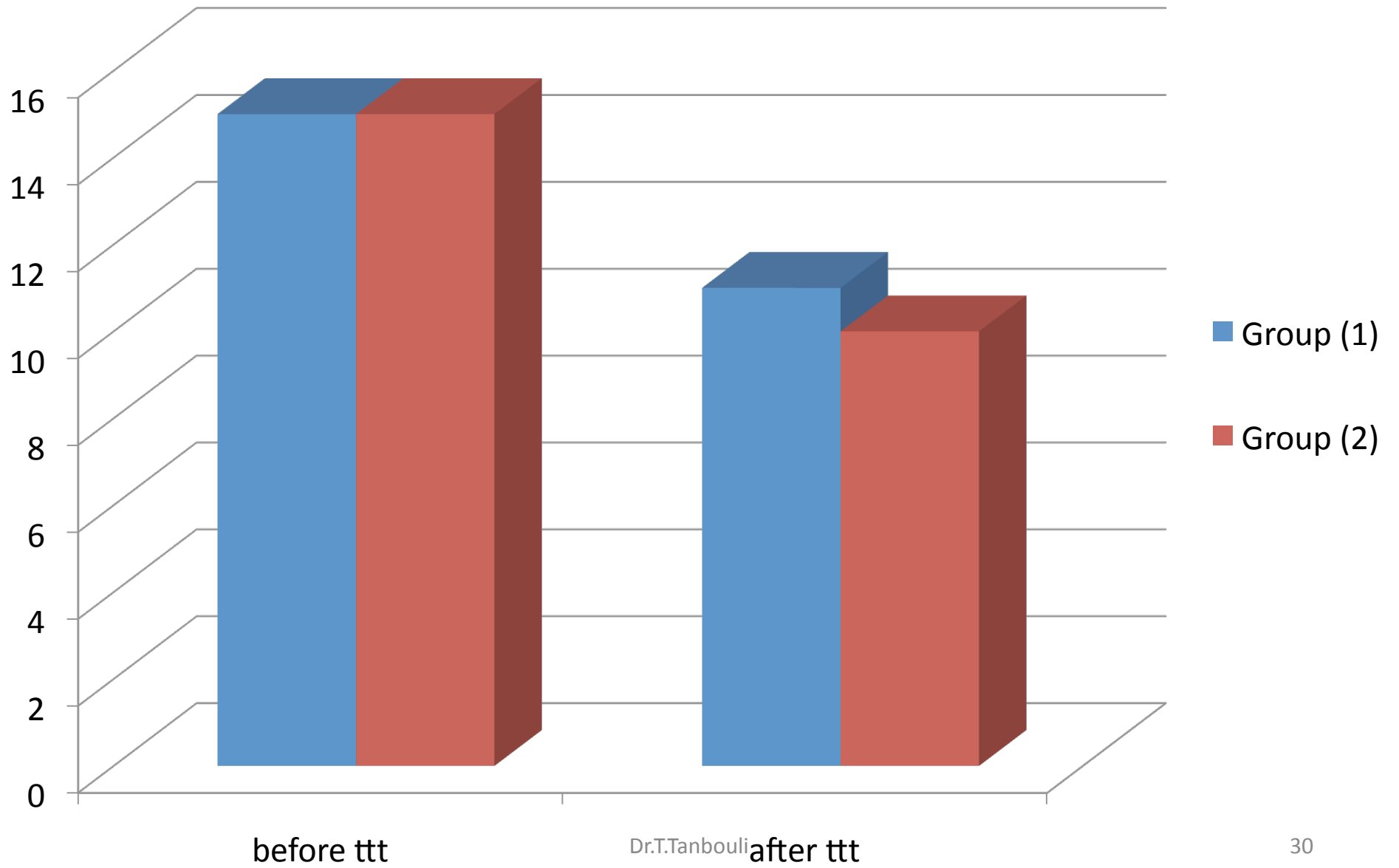
1) O<sub>3</sub> destructor with automatic suction at end of session.

2) Ability of use of vaginal insufflation during ttt session.



# RESULTS

- **Group (A):**  
**11 pt. are cured and don't have recurrence 6 months or more after ttt. (73.3%)**
- **Group (B):**  
**10 pt. are cured and don't have recurrence 6 months or more after ttt. (66.6%)**



# Conclusion

- Ozone therapy can help a lot in treating chronic vulvovaginitis , which is a resistant medical condition .
- There is no significant difference between using the classical rectal ozone insufflation ( as a systemic ozone therapy ) & the use of ozone sauna instead .
- A larger scale study that includes larger number of patients is needed to confirm this study result.
- Further studies are needed to prove the systemic effect of ozone sauna.