Effectiveness, acceptability and safety of LEEP in Kerala, India: beginners' experience

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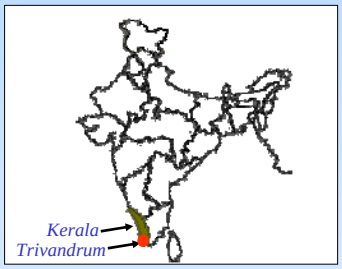
Background:

Loop Electrosurgical Excision Procedure (LEEP) involves excision of cervical intraepithelial neoplasia (CIN) using a thin tungsten wire loop electrode activated by radiofrequency electric current from an electrosurgical generator. The effectiveness and safety of LEEP in the treatment of CIN has been widely evaluated in developed countries. However, there have been extremely limited evaluations of LEEP in low-resource settings in developing countries.

We now present preliminary findings on the effectiveness and safety of LEEP in the context of a collaborative cervical cancer screening study in Kerala State, India, jointly organised by the Regional Cancer Centre, Trivandrum, India and the International Agency for Research on Cancer of the World Health Organization , Lyon, France.

Study location: Kerala, India:



Notional map showing Kerala, India

Objective:

Investigate the effectiveness of LEEP in curing CIN and to document its safety and acceptability profile in a screening project.

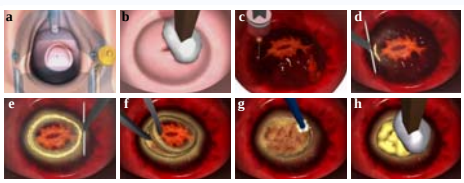
LEEP equipment

Methods:

During January 2000-March 2006, **21 370** women aged 25-59 years were screened by visual inspection with acetic acid (VIA). Among the **2 956** women with positive VIA, **337** diagnosed with different grades of CIN were advised LEEP. The indications for LEEP were: large lesions not suitable for cryotherapy; lesions involving endocervical canal; cryotherapy failures.

Detailed medical history was taken to exclude uncontrolled hypertension, diabetes, bleeding disorders, exposure to diethyl stilbesterol, pregnancy and active genital tract infection before doing LEEP.

After counselling and obtaining informed consent, LEEP was done under local anaesthesia as a day care procedure. Single or multiple passes or two layer excisions were carried out depending on the extent of lesion.



(a) Speculum insertion exposing the cervix; (b) Application of acetic acid; (c) Local anaesthesia; (d) Beginning of one pass LEEP procedure; (e) Ending of one pass LEEP procedure; (f) Removal of the LEEP specimen; (g) Coagulation; (h) Application of Monsel's paste.

Women were advised on home care, abstinence from sexual intercourse for 4 weeks after treatment, signs and symptoms on which they should report back for a problem visit and were prescribed presumptive antibiotics. They were advised to come for routine follow-up at 6 months and 1 year from treatment. Women completing 1-year follow-up are included in this study.

Follow-up:

At follow-up the cervix was assessed with VIA, colposcopy and directed biopsies as indicated. No evidence of CIN at 6 to 12 months from treatment was defined as cured and presence of CIN at follow-up was categorized as failure. Women with failures were advised subsequent treatment with repeat LEEP, conization or hysterectomy (mostly by patient choice).

Acceptability and safety definition:

The following side-effects (indicator of **acceptability**) were assessed during or within 1 month from treatment: mild pain/cramps, backache, excessive malodourous discharge, mild bleeding, more than usual bleeding during menses (menorrhagia) and fever lasting for more than 2 days. The following complications (indicator of **safety**) were recorded: severe pain/cramps requiring parenteral analgesics; local cervical infection; vaginal burns; severe bleeding requiring sutures, hospitalization, blood transfusion or hysterectomy; pelvic inflammatory disease requiring intravenous antibiotics and true functional stenosis.

Results:

- Women advised LEEP: **337**
- Women who accepted LEEP: **311** (92.3%)
- Women lost to follow-up: **28** (9%)
- Women included in the study: **283** (91%)
- Women cured of CIN: **240** (84.8%)
- Side effects were observed in **54** (19.1%) women
- Complications were observed in **8** (2.8%) women

Table 1: Side effects (acceptability)

Mild pain/cramps:	7
Foul discharge:	8
Mild bleeding:	24
Fever/chills:	3
Infection:	5
Menorrhagia:	7

Table 2: Complications (safety):

Severe bleeding:	1
Severe pain:	1
Vaginal burns:	1
pelvic inflammatory disease :	2

Table 3: Effectiveness : Follow-up based on histopathology or colposcopy at 12 months

Histopathology at base line (before Rx)	Total No. of LEEP performed	Follow-up status at 12 months			
		Cured of CIN (%)	Failure		
			CIN 1 (%)	CIN 2 (%)	CIN 3 (%)
CIN 1	156	141 (90.4%)	13	2	0
CIN 2	83	69 (83.1%)	10	3	1
CIN 3	44	30 (68.2%)	8	5	1
All grades	283	240 (84.8%)	31 (11.0)	10 (3.5)	2 (0.7)

Study profile:

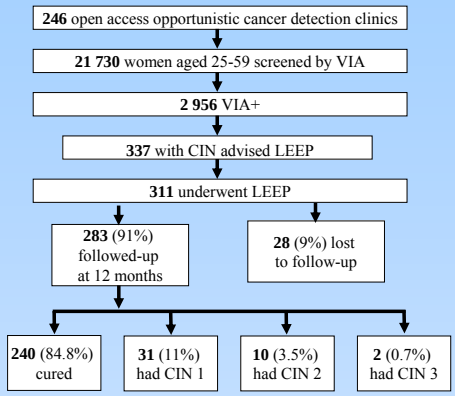


Table 4: Cure rates at follow-up according to characteristics of women at screening:

Characteristics	Cure rate	P-value for χ^2 Independence test
Age		< 0.05
< 35	85.7% (54/63)	
35-45	88.1% (156/177)	
> 45	69.8% (30/43)	
Area of involvement of TZ* of cervix		< 0.001
< 25%	91.2% (145/159)	
25-50%	81.2% (69/85)	
> 50%	66.7% (26/39)	
Endocervical canal involvement		< 0.001
Absent	91.6% (164/179)	
Present	73.1% (76/104)	
Margin involvement		< 0.001
Absent	87.7% (19/31)	
Present	61.3% (221/252)	
Grade of CIN		< 0.005
CIN 1	90.4% (141/156)	
CIN 2	83.1% (69/83)	
CIN 3	68.2% (30/44)	

***TZ**: transformation zone

Table 5: Comparison of our cure rates with early results from developed countries

Authors	Total	Cured	Reference
Prendiville *et al*	111	109 (99%)	*Br J Obstet Gynaecol. 1989, 96:1054-60*
Gunasekera *et al*	199	189 (95%)	*Br J Obstet Gynaecol. 1990; 97:995-8*
Luesley *et al*	557	506 (91%)	*BMJ 1990; 300: 1690-3*
Bigrigg *et al*	1 000	959 (96%)	*Lancet 1990; 336: 229-31*
Wright *et al*	*157*	*147 (94%)*	*Obstet Gynecol 1992; 79: 173-8*
Rema *et al*	283	240 (85%)	*Current poster*

Conclusions:

- LEEP is a safe procedure with minimal complications and acceptable cure rates.
- Cure rates were significantly lower for older women, large lesions, CIN 3 lesions, lesions with endocervical excision and incomplete excision in our study.
- Though our cure rates are satisfactory, they are lower than those reported from developed countries, possibly because our LEEP providers are 'beginners' in the field and in the learning curve.
- Side effects and complications are similar to published experience from developed countries.
- There are no reported cases of progression to invasive cancer at one-year follow-up, but duration of follow-up was not sufficient enough to evaluate long-term outcomes.
- Although one-year follow-up is a relatively short period, it does predict long-term success (most literature reports on 6-month cure rate only).

Acknowledgments:

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References:

- *Sellors JW and Sankaranarayanan R. Colposcopy and Treatment of Cervical Itraepithelial Neoplasia: A Beginners' Manual. IARC Non serial publication, Lyon 2003 (published in English, French, Spanish, Portuguese and Chinese).*
- *Zhang WH, Keskar V, Lucas E, Qiao YL, Sankaranarayanan R. A training course in Loop electrosurgical excision procedure (LEEP) - Digital learning series. IARC Screening Group, Lyon, 2006 (published in English, French, Spanish and Chinese).*

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