Prolonged use of oral contraceptive pill, a co-factor for the development of cervical cancer

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Abstract

This study was carried out to assess the use of oral contraceptive pill as a co-factor for the development of cervical cancer. Among the 100 participants, 71% used oral contraceptives pill. Maximum (40%) used oral contraceptive pill for >5 years whereas 31% for <5 years. Histopathologically diagnosed invasive squamous cell carcinoma was 84% and adenocarcinoma was 16%.

Introduction

In developing countries, the most common form of cancer is the cervical cancer and it is second most common cancer in the world as a whole after breast cancer. World health organization (WHO) estimated that incidence of cervical cancer in Bangladesh is 167 per 1,00,000 population and in every year 6,582 woman die in Bangladesh. But in India, incidence of cervical cancer is 20-35 per 1,00,000 woman. It is urgent to prevent and control cervical cancer. In developed countries due to well-developed screening program, the incidence of cervical cancer has been decreased. In Bangladesh cervical cancer is an acute problem because of poverty, early marriage, multiple marriages, high parity, illiteracy, poor nutrition. Histologically there are mainly two types of cancer. Invasive squamous cell carcinoma (75%) and adenocarcinoma (20%). In United States, most effective and reversible contraption is oral contraceptive pill which reduces the unwanted pregnancy. It is very much difficult to assess the association between oral contraceptive pill and cervical cancer because this disease has a long latency period. So, long time is necessary between the exposure of oral contraceptive and the diagnosis of cancer. Another difficulty is there is variation in oral contraceptive formulation which influence the association between cancer risk and oral contraceptive use. Furthermore, other factors, like gravity, breast feeding may influence the oral contraceptive use. Another problem is duration of oral contraceptive use or time after stopping use of oral contraceptive may modify the association of oral contraceptive pill with risk of cervical cancer. Cervical cancer can be detected or managed early because of screening. Screening is possible perfectly because cervix is a surface organ, easily accessible and it has a long premalignant phase. The aim of this study is to assess whether oral contraceptive pill is a cofactor for development of cervical cancer or not.

Materials and Methods

This study was carried out at the outpatient department from January 2016 to January 2018. Total 100 diagnosed cases of cervical cancer were included in this study. Patients were diagnosed as invasive cervical carcinoma and adenocarcinoma according to criteria as history, clinical sign, symptoms and histopathological examination of cervical tissues. Demographic and clinical presentations are collected. Demographic variables include age, parity, age at first marriage, socio-economic condition, number of marriage, extramarital relationship. The purpose of this research work was explained elaborately to the patient who fulfilled the enrollment criteria. Data were collected from the patient by interview, questions, clinical examination, histopathological report and history sheet of the patient.

Data analysis

All data were analyzed using statistical package for social science (SPSS).
Results

In this study, a total of 100 diagnosed cases were included. Majority (88%) of the participants age at marriage were less than 18 years and regarding parity 57% had parity >4 (Table I). Among 100 participants, 71% used oral contraceptive pill and 29% did not used the oral contraceptive pill. Among oral contraceptive pill users, 40% were used for more than 5 years and 31% were less than 5 years.

Discussion

This study shows either use of oral contraceptive pill is a co-factor for development of cervical cancer or not. In this study 88% of the participant’s age at first marriage were <18 years, 92% of the patient’s number of marriage were single and had no extra marital relationship. On the other hand, 58% husband’s marriage were single and only 11% had extra-marital relationship. These findings are well agreement to other studies. In developing countries, there are many risk factors for development of cervical cancer such as early marriage, early starting sexual activities, multiparity, low socio-economic condition and high incidence of sexually transmitted diseases and HPV infection.

This study shows that use of oral contraceptive for >5 years have a higher risk than nonusers. It also shows cervical cancer developed in those patients who use oral contraceptive pills <5 years than nonusers. We found in another study that risk of cervical cancer depends on duration of use. 10% increased risk for less than 5 years of use, 60% increased risk with 5-9 years of use and as doubling of risk with 10 or more years of use. But if the use of oral contraceptive is stopped, the risk of cervical cancer has been declined. This study shows that 84% were invasive squamous cell carcinoma and 16% were adenocarcinoma. Farley et al also shows that invasive squamous cell carcinoma is 75% cases and adenocarcinoma is about 20% cases. This study shows that both types of cervical cancer are associated with use of oral contraceptive pills. However if a women stop using oral contraceptives the risk of cervical cancer will decline. Long-term use of gestagens may be the cause of cervical cancer.

Human papilloma virus (HPV) initiates precancerous lesion of cervix and hormone receptors are known to affect the development of cervical cancer. Human papilloma virus (HPV) has an important role for development of cervical cancer and it is the principal cause of this disease and female hormones like oral contraceptive pill is a co-factor.

But World Health Organization did not recommend to discontinue the use of oral contraceptive pill because its use is more beneficial than its risk. This study shows maximum (71%) participants has a history of taking oral contraceptive pill and 40% of users took oral contraceptive pill for more than 5 years. Several investigations including screening programs have suggested that the incident of cervical cancer is higher in women who have used oral contraceptives. In another study we found that use of oral contraceptives increase the risk of breast and cervical cancer.

The risk of cervical cancer rises where a women uses oral contraceptives pill for longer time. If a women infected with human papilloma virus (HPV), the long-term pill users are 2.5 times more prone to develop cervical cancer than non-users. The general finding of increasing risk of cervical cancer with increasing duration of pill use was found. Another study showed that long term oral contraceptives pill users had 50% higher risk of cervical cancer. Whether oral contraceptives pill is a cause of cervical cancer, it is debated. But many of the studies in the past 10 years found an association between OCP and CIN and CIS collectively called pre-invasive lesion.

The risk of cervical cancer will be increased by 2-fold only for those women who used oral contraceptives pill for 5 years or more.

Table I

Demographic characters of the study subject (n=100)

| Age of marriage (<18 years) | 88 |
| Wife |  |
| One marriage | 92 |
| Two marriage | 8 |
| Extra-marital relationship | 0 |
| Husband |  |
| One marriage | 85 |
| Two marriage | 15 |
| Extra-marital relationship | 11 |
| Para |  |
| <4 Children | 43 |
| ≥4 Children | 57 |
| History of taking oral contraceptive |  |
| None | 29 |
| Using for <5 years | 31 |
| Using for >5 years | 40 |
| Histopathological diagnosis |  |
| Squamous cell carcinoma | 84 |
| Adenocarcinoma | 16 |
Conclusion

Forty percent patients have used oral contraceptives pill for >5 years and 31% patient used <5 years. It may conclude from this study that prolonged use of oral contraceptives pill may be a co-factor for the development of cervical cancer.

References

1. Papri FS, Khanam Z, Islam F, Hakim MM. Knowledge and awareness about risk factors of cervical cancer, its screening and vaccination among the women attending Chittagong Medical College Hospital. Chattagram Maa-O-Shishu Hosp Med Coll J. 2015; 14: 57-60.
2. Khutun SF, Homaira R, Khutun S, Sharmin F, et al. Performance of VIA (Visual inspection with acetic acid) and colposcopic biopsy as a method of screening in detecting preinvasion and early cancerous lesion of the cervix. Med Today. 2011; 23: 13-14.
3. R Sultana, N Sultana. Clinical profile and treatment protocol of invasive carcinoma of cervix. Bangladesh Med J (Khulna). 2012; 45: 11-14.
4. Perkin DM, Bray FI, Devesa SS. Cancer burden in the year 2000: The global picture. Eur J Cancer. 2004; 37: 566.
5. Ferlay J, Shin HR, Bray F. Estimates of worldwide burden of cancer in 2008: GLOBOCAN. Int J Cancer. 2008; 127: 2893-917.
6. Jemal A, Bray F, Center MM. Global cancer statistics. CA Cancer J Clin. 2001; 61: 69-90.
7. Smith HO, Tiffany MF, Qualls CR, Key CR. The rising incidence of adenocarcinoma relative to squamous cell carcinoma of the uterine cervix in the United States: A 24-year population-based study. Gynecol Oncol. 2000; 78: 97-105.
8. Liu S, Semenciw R, Mao Y. Cervical cancer: The increasing incidence of adenocarcinoma and adenosquamous carcinoma in younger women. CMA. 2001; 164: 1151-52.
9. Mathew A, George PS. Trends in incidence and mortality rates of squamous cell carcinoma and adenocarcinoma of cervix-worldwide. Asian Pac J Cancer Prev. 2009; 10: 645-50.
10. Wang SS, Sherman ME, Hildesheim A, Lacey JV, Devesa S. Cervical adenocarcinoma and squamous cell carcinoma incidence trends among white women and black women in the United States for 1976-2000. Cancer 2004; 10: 1035-44.
11. Mosher WD, Jones J. Use of contraception in the United States: 1982-2008. Vital Health Stat. 2010; 23: 1-44.
12. Dinger J, Do Minh T, Buttmann N, Bardenheuer K. Effectiveness of oral contraceptive pills in a large U.S. cohort comparing progestogen and regimen. Obstet Gynecol. 2011; 117: 33-40.
13. Dinger JC, Cronin M, Mohner S, Schellschmidt I, Minh TD, Westhoff C. Oral contraceptive effectiveness according to body mass index, weight, age and other factors. Am J Obstet Gynecol. 2009; 201: 263.e1-9.
14. Gierisch JM, Coeytaux RR, Urrutia RP, Havrilesky LJ, Moorman PG, Lowery WJ, Dinan M, McBroom AJ, Hasselblad V, Sanders GD, Myers ER. Oral contraceptive use and risk of breast, cervical, colorectal, and endometrial cancers: A systematic review. Cancer Epidemiol Biomarkers Prev. 2013; 22: 1931-43.
15. Smith JS, Green J, Berrington de Gonzalez A, Appleby P, Peto J, Plummer M, et al. Cervical cancer and use of hormonal contraceptives: A systematic review. Lancet 2003; 361: 1159-67.
16. Moorman PG, Calingaert B, Palmieri RT, Iversen ES, Bentley RC, Halabi S, et al. Hormonal risk factors for ovarian cancer in premenopausal and postmenopausal women. Am J Epidemiol. 2008; 167: 1059-69.
17. Kumar P, Narendra Mahotra, Jeffcoate’s Principles of gynaecology. 7th ed. London, Arnold, 2008: 465-86.
18. Akhter PS, Uddin MM, Sharia SK. Patterns of Malignant neoplasm: A three year study. Bangladesh Med J. 1998; 27: 29-32.
19. Kulkarni PV, Jaiswal SS, Rathod SB, Khalique A, Kulkarni RR. Profile of malignancies at Medical College, Ambajogai: 15 years retrospective study. Indian J Cancer. 1996; 33: 31-36.
20. Banerjee AK, Bhattacharya N, Chowdhury MK, Chatto Padthyay R, Sengupta J. Incidence of malignancy in Bankura. J Indian Med Assoc. 1994; 92: 400-02.
21. Sharma RG, Ajmera R, Saxena O. Cancer profile in Eastern Rajasthan. Indian J Cancer. 1994; 31: 166-73.
22. Hug SF. Common cancers of Bangladesh: Their trends through last three decades. Bangladesh Med J. 1988; 17: 55-63.
23. Ashrafunessa, L Shamsuddin, TA Chowdhury, development of cancer cervix screening programme in Bangladesh 9. WHO workshop on cancer control programme. Report of ministry of Health New Delhi, Ministry of Health, 1992.
24. WHO workshop on cancer control programme, report of ministry of Health New Delhi, Ministry of Health 1992.
25. International Collaboration of Epidemiological Studies of Cervical Cancer, Appleby P, Beral V, et al. Cervical cancer and hormonal contraceptives: Collaborative reanalysis of individual data for 16,573 women with cervical cancer and 35,509 women without cervical cancer from 24 epidemiological studies. Lancet 2007; 370: 1609-21.
26. Roura E, Travier N, Waterboer T, et al. The influence of hormonal factors on the risk of developing cervical cancer and pre-cancer: Results from the EPIC Cohort. PLoS One. 2016; 11: e0147029.

27. Iversen L, Sivasubramaniam S, Lee AJ, Fielding S, Hannaford PC. Lifetime cancer risk and combined oral contraceptives: The Royal College of General Practitioners' Oral Contraception Study. Am J Obstet Gynecol. 2017; 216: 580.e1-e9.

28. Monsonego J, Magdelenat H, Catalan F, Coscas Y, Zerat L, Sastre X. Estrogen and progesterone receptors in cervical human papillomavirus related lesions. Int J Cancer. 1991; 48: 533–39.

29. Moodley J. Combined oral contraceptives and cervical cancer. Curr Opin Obstet Gynecol. 2004; 16: 27-29.

30. World Health Organization. Oral contraceptives and neoplasia. Report of WHO Scientific Group. World Health Organization Technical Report series 817. Geneva, WHO, 1992.

31. Burkman R, Schlesseman JJ, Zieman M. Safety concerns and health benefits associated with oral contraception. Am J Obstet Gynaecol. 2004; 190 (Suppl): S5-22.

32. Gadducci A, Barsotti C, Cosio S, Domenici L, Riccardo Genazzani A. Smoking habit, immune suppression, oral contraceptive use and hormone replacement therapy use and cervical carcinogenesis: A review of the literature. Gynecol Endocrinol. 2011; 27: 597.

33. Brinton LA, Tashima KT, Lehman HF, et al. Epidemiology of cervical cancer by cell type. Cancer Res. 1987; 47: 1706-11

34. International Agency For Research Of Cancer. IARC Monographs on the evaluation of the carcinogenic risk to humans. Vol. 72. Hormonal contraception and post menopausal hormonal therapy. Lyon, IARC, 1999.