

INTRODUCTION

Dysfunctional uterine bleeding (DUB) is defined as a variety of bleeding manifestations in the absence of pathology or medical illness which results in prolonged estrogen stimulation to the endometrium without the opposed action of progesterone. This results in a thickened proliferative endometrium without structural support, the endometrium outgrows its blood supply, there is an increase in the release of prostaglandins resulting in vasospasm of spiral arterioles and ischaemia with elevated levels of hydrolytic enzymes and increase activation of the fibrinolytic system in the endometrium (*Cameron, 1989*). These events results in superficial breaks in the fragile endometrium and bleeding at various times. DUB is one of the most frequently encountered conditions in gynaecology. It represents 10% of out patients in hospital and private practice (*Davey, 1995*).

DUB can be either ovulatory or an ovulatory. Anovulatory DUB is most common at the two ends of reproductive age spectrum and is caused by prolonged unopposed estrogen which leads to endometrial hyperplasia and is presented as irregular prolonged excessive bleeding (*Fraser et al., 1996*).

Ovulatory (DUB) is cyclic bleeding and occurs in the reproductive age group and is caused by alteration in endometrial prostaglandin (*Ferenczy, 2003*). Heavy menstrual bleeding or menorrhagia may be a result of organic disease such as polyps, fibroids, pregnancy, infection or carcinoma but in the majority of cases no such underlying lesion can be found in which cases the diagnosis of (DUB) is made (*Fraser et al., 1973*).

Women complaining of excessive bleeding have objective menorrhagia with blood losses greater than 80 ml in each menstruation and this loss was measured by using two numerical systems; the first one called the total bleeding score per month and the second called bleeding index (*Magos et al., 1989 and Istre et al, 1991*).

Consequently much attention has been focused on the endometrium itself for it seems likely that local factors play an important part in the mechanisms controlling bleeding disorders (*Cameron, 1989*).

Indomethacin releasing copper intrauterine device:

Has a reasonable design to be able to effectively release indomethacin (IR Cu IUD) contains 6 Cu pearls of total surface area 300 mm². The content of indomethacin is equivalent 10% of the total weight of IUD and the release rate is 7-8 mg/year (*Liu et al., 1996*). It's capable of usage in the uterus for over 20 years with out aging and degeneration, threadless, no effect on sexual life, easy insertion and removal and with indomethacin to control increase of menstrual flow and other side effects like dysmenorrhea. In addition, it was observed that the inhibitory effect of indomethacin on the prostacycline (PGI₂) was stronger than that of Thromboxane A₂ (TXA₂) and the ratio of PGI₂ to TXA₂ decreased with the increase of dosage, suggesting that it is effective in reducing bleeding. (IR-Cu IUD) insertion didn't increase inflammatory cell number and in contrast, the total cell number was lower than that found in T shaped (Cu IUD) users (*Zhu et al., 1989*). This reduced inflammatory cell number most likely result in decreased production of plasminogen activator and PG. So IUD induced bleeding was reduced and the bleeding period was shortened.

Gelety and Chaudhuri, 1995 suggest that indomethacin prevents uterine bleeding by regulating the coagulation and endothelial cell function. IR. CuIUD insertion doesn't affect the endothelial complement factor level allowing the coagulation system to function normally and prevent uterine bleeding. Moreover, indomethacin doesn't affect endometrial growth and differentiation preventing local intrauterine bleeding. In addition, the endothelin possesses very strong contractive action on human endometrial blood vessel and uterine smooth muscles and can activate phospholipase A and phospholipase C in human endometrium to cause increased PG synthesis (*Ahmed, Cameron et al., 1992*).

Increased endothelin (ET) level leads to local ischaemia and degeneration, necrosis and denudation of tissues, thereby resulting in irregular bleeding. Indomethacin released by (IR.Cu IUD) can reduce the generation of the (ET) induced by copper bearing (IUD), thereby reducing the abnormal uterine bleeding. Also indomethacin can mitigate the stimulation of the foreign body and the damage to endometrium caused by (Cu IUDs). It's known that copper – bearing (IUD) can lead to aseptic inflammation and foreign body reaction, Cu^{2+} can change the biochemical composition of the cervical mucus and interrupt the implantation of the blastocyst by interfering endometrial enzyme systems, thus affecting the activity, capacitation and survival of the spermatozoa. So the release of Cu^{2+} directly influences the antifertility with efficacy of the (IUD). Indomethacin releasing – (Cu IUD) could promote Cu^{2+} release thereby enhancing contraceptive effect of (IUDS).

So, it is a point of consideration to determine to what extent the intrauterine release of indomethacin from (IR.Cu IUD) would reduce blood loss in women with menorrhagia or (D.U.B).