LITERATURE REVIEW

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Molecular therapy for ectopic pregnancy

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ABSTRACT

Aim: The study aims to compare a combination of both gefitinib and methotrexate to methotrexate only in ectopic pregnancy.
Review: Ectopic pregnancies are a serious condition that can be fatal, so the prompt therapeutic is essential. There were some recent studies explained the combination is more effective inducing placental cell death. They can rapidly resolve ectopic tubal pregnancy than single methotrexate only. If a large clinical randomized control trial confirms these finding, these combinations could become a new medical option for ectopic pregnancy.
Conclusion: The combination of gefitinib and methotrexate is more effective than methotrexate one in ectopic pregnancy.

Keywords: ectopic pregnancy, gefitinib, methotrexate

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INTRODUCTION

An ectopic pregnancy is a life-threatening condition that occurs when the fertilized ovum implants outside the endometrial cavity. Many of ectopic pregnancy is often asymptomatic or present with non-specific symptoms. Most of them are treated surgically,[1] and even though it's safe, several possible risks can occur such as abdominal obstruction, vessel injury and other complication. Alternative treatment has been increasingly applied to treat it since 90's using methotrexate for small ectopic pregnancy with serum hCG concentration <1500 IU/l.[1,2] It acts as an agonist antifolate as well as blocks both RNA synthesis and DNA replication. It rapidly lead thropoblast detached due to its sensitivity. Although, when we use it, it has an unacceptably high rate of failure. Once the serum hCG was >1500 IU/ I, the cost does not more effective.[2]

REVIEW

Placenta has the highest expression of the epidermal growth factor receptor (EGFR) compared with all other tissue types. Furthermore, the placenta relies on EGFR signalling heavily which promotes the cytotrophoblast motility, blocks apoptosis, and protects placental cells when exposed to stressors. Therefore, inhibiting EGFR signalling could negatively affect placental survival and could be a novel approach to treat ectopic pregnancy.[3-7]

Gefitinib is a molecular-targeted drug that selectively blocks EGFR signalling by inhibiting the tyrosine kinase domain of EGFR.[8] There is an undertaken programme of translational research to examine whether gefitinib could be combined with methotrexate to enhance its efficacy.[7] Combining both methotrexate and gefitinib was significantly more effective in inducing placental cell death than using methotrexate one.[9] Adding gefitinib to methotrexate induced significantly greater decreases in JEG3 tumour volume xenografted s.c. in NOD/SCID mice, compared with methotrexate alone. Furthermore, these agents increase the rates of resorption of eutopic fetuses in immunocompetent mice, compared with either drug alone. The preclinical data supported the exciting premise that combining them may be a promising treatment for ectopic pregnancy in the future.[7]

Postmarketing surveillance of 31,045 people exposed to gefitinib had been reported to the FDA.[10] Common side effects include a transient skin rash and diarrhoea. Gefitinib is associated with a rare but significant side effect of interstitial lung disease (ILD), a thickening of the lung parenchyma (0.3% incidence). As for these reasons, administering a short course of gefitinib to women will help to avoid all these risk factors for ILD and is likely to be a safety agenda. This trial yielded highly encouraging efficacy data. The median of post-treatment serum hCG levels over 7 days was less than one-fifth of levels observed among 71 prevalence controls treated with methotrexate alone. Notably, the median time for the ectopic pregnancies to resolve with combination therapy was 34% shorter compared with methotrexate alone (21 as against 32 days). A participant was treated successfully for ectopic pregnancy just in her remaining Fallopian tube (the other tube having been removed previously as a treatment for a prior ectopic pregnancy). She got subsequently pregnant

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spontaneously and delivered a healthy child at term. Its situation means that the fallopian tubes exposed to the combination have still remained fertile.[7]

CONCLUSION

The combination of methotrexate and gefitinib could be a novel treatment in ectopic pregnancy and can reduce the number of women treated by surgical and its risks. It also allows for a more rapid resolution of ectopic pregnancies and even decreases the high rates of maternal losses caused by an ectopic pregnancy.

REFERENCES

1. Jurkovic D, and Wilkinson H. Diagnosis and management of ectopic pregnancy. *BMJ* 2011; 342: 3397.
2. Mol F, Mol BW, Ankum WM, van der Veen F, Hajenius PJ. Current evidence on surgery, systemic methotrexate and expectant management in the treatment of tubal ectopic pregnancy: a systematic review and meta-analysis. *Hum Reprod Update* 2008; 14: 309-319.
3. Ferretti C, Bruni L, Dangles-Marie V, Pecking AP, Bellet D. Molecular circuits shared by placental and cancer cells, and their implications in the proliferative, invasive and migratory capacities of trophoblasts. *Hum Reprod Update* 2007; 13:121-141.
4. LaMarca HL, Dash PR, Vishnuthevan K, Harvey E, Sullivan DE, Morris CA, Whitley GS. Epidermal growth factor-stimulated extravillous cytotrophoblast motility is mediated by the activation of PI3-K, Akt and both p38 and p42/44 Horne AW, Duncan WC, Critchley HO. The need for serum biomarker
5. Johnstone ED, Mackova M, Das S, Payne SG, Lowen B, Sibley CP, Chan G, Guilbert LJ. Multiple anti-apoptotic pathways stimulated by EGF. In: Nilsson UW, Johns TG, Wilmann T, Kaitu'u-Lino T, Whitehead C. Cytotrophoblasts. *Placenta* 2005; 26: 548-555.
6. Wolff GS, Chiang PJ, Smith SM, Romero R, Armant DR. Epidermal growth factor-like growth factors prevent apoptosis of alcohol-exposed human placental cytotrophoblast cells. *Biol Reprod* 2007; 77: 53-60.
7. Stephen T, Monika MS, Andrew WH. Molecular Diagnostic and Therapeutics for Ectopic Pregnancy. *Molecular Human Reproduction* 2015; 21: 126-–135
8. Herbst RS, Fukuoka M, Baselga J. Gefitinib—a novel targeted approach to treating cancer. *Nat Rev Cancer* 2004; 4: 956-965.
9. Nilsson UW, Johns TG, Wilmann T, Kaitu'u-Lino T, Whitehead C, Dimitriadis E, Menkhorst E, Saglam B, Gao Y, Greenall SA et al. Effects of gefitinib, an epidermal growth factor receptor inhibitor, on human placental cell growth. *Obstet Gynecol* 2013; 122: 737-744. *BMJ* 2011; 342: 3397.
10. Cohen MH, Williams GA, Sridhara R, Chen G, McGuinn WD Jr., Morse D, Abraham S, Rahman A, Liang C, Lostritto R et al. United States Food and Drug Administration Drug Approval summary: gefitinib (ZD1839; Iressa) tablets. *Clin Cancer Res* 2004; 10: 1212-1218.