

SERMs as Contraceptives – A Scoping Review

Jessy Jindal¹, Chloe Curtis¹, Clara Portwood¹, Sharon Dixon^{1,2}

¹University of Oxford, ²Nuffield Department of Primary Health



UNIVERSITY OF
OXFORD

MOTIVATION

Selective estrogen receptor modulators (SERMs) are a class of drugs with differential, heterogenous effects on estrogen receptors.¹

Established in the treatemnt of breast cancer (ie. tamoxifen) and menopause related symptoms (ie. raloxifene), SERMs also have application as contraceptives, and already licensed in parts of the world.^{1, 3, 4}

Hormonal contraception has well documented contra-indications, risks and side effects.² **SERMs may offer a different, beneficial profile, but little is known about these variances.**

This scoping review is the first to synthesise evidence on SERMs as contraceptives and map research gaps.

METHODS

Scoping review methodology was used.³

Terms “SERM OR Selective Estrogen Receptor Modulator” AND “Contraception OR Contraceptive” were searched across EmBase, PubMed, Cinahl and Global Index Medicus.

Specific drug names identified in scoping were integrated.

Analysis ongoing, we are reporting our interrim results.



Full Protocol Here

References

1. James, P. (2014). Use of SERMs in clinical practice. Climacteric, 17, 45. <https://doi.org/doi:https://dx.doi.org/10.3109/13697137.2014.893731>

2. FSRH Clinical Guideline: Combined Hormonal Contraception (January 2019, Amended November 2020)

3. Hilary Arksey & Lisa O'Malley (2005) Scoping studies: towards a methodological framework, International Journal of Social Research Methodology, 8:1, 19–32, DOI: [10.1080/1364557032000119616](https://doi.org/10.1080/1364557032000119616)

4. Kamboj, V. P., Ray, S., & Anand, N. (2018). Centchroman: A safe reversible postcoital contraceptive with curative and prophylactic activity in many disorders. Front Biosci (Elite Ed), 10(1), 1–14. <https://doi.org/doi:10.2741/e807>

5. Han X, Weng L, Xiao B. [Emergency contraception with mifepristone and anordrin]. Zhonghua Fu Chan Ke Za Zhi. 1996 Sep;31(9):526–9. Chinese. PMID: 9275422.



Saheli (Centchroman) - available for free as part of Indian family planning services as well as over-the-counter in Indian pharmacies ⁴

Paper breakdown

482 identified by search

209 for full text screening

143 included

Inclusion criteria

- Studies looking at SERMs as contraceptives
- English language
- No restriction on study type

Types of studies

- Clinical trials: 30 papers
- Laboratory research papers: 70 papers
- Reviews: 30 papers
- Others: 8 papers

SERMs currently in use as contraceptives

- **Centchroman (India): 73 papers**
- Once a week, regular use contraceptive
- **Estetrol (EU, USA, UK) : 44 papers**
- Daily use contraceptive in combination with Drospirinone
- **Anordrin (China): 9 papers.**
- Emergency, post-cotial contraceptive in combination with Mifepristone

RESULTS TO DATE

Mechanism of action and role

- Centchroman: primarily prevents implantation, some delay of ovulation
- Estetrol: primarily inhibits ovulation
- Anordrin: inhibits ovulation and implantation

Efficacy

- Centchroman: 96% to 98% in clinical trials and 93% to 100% in observational studies
- Estetrol [in combination with Drospirinone]: Pearl Index in pooled phase III trials (pregnancies/100 women years) 1.43–1.61
- Anordrin [in combination with Mifepristone as Emergency Contraception]: 86.1–90.6% reported in studies

Side effects and tolerability

- Main side effects reported [Estetrol, Centchroman]: amenorrhoea, metrorrhagia
- Centchroman compared to Cu-IUD: better satisfaction and continuation rates at 6 months
- Estetrol compared to CHC: comparable efficacy, and lower/comparable side effect profile

Thromboembolism risk

- Estetrol showed lower risk than CHC in clinical trials
- Little reported about Centchroman and thromboembolism risk in clinical trials, but observational studies show little effect at 1 year
- Need to be validated in long-term studies

Language and terminology

Identified inconsistency in how SERMs are defined in the literature.

- Centchroman: “non-hormonal, non-steroidal, anti-estrogen” “synthetic”
- **Is Estetrol a SERM?** – Heterogenous action on estrogen receptors, molecular interactions differ to SERMs. Referred to in early literature as SERM but not in recent marketing – now referred to as “naturally occurring estrogen”
- Language around “Hormonal” and “Non-Steroidal” may influence how SERMs are positioned and perceived

Cancer

SERMs have an established role in cancer therapeutics; how this translates to contraceptive benefit is less clear

- Anti-cancer properties (including breast, ovarian, pancreatic) reported in many laboratory studies with Centchroman
- Clinical Trial with Centchroman in treatment resistant breast cancer showed response rate 40.5% with median duration of response 6 months
- One case study reported endometrial and cervical hyperplasia on extended use
- Estetrol shown to have anti-breast cancer effects in laboratory studies

Potential other benefits

- Lower C450 action of Estetrol and minimal drug interactions reported with Centchroman
- Anti-osteoporosis effect of Centchroman in clinical trials
- Role of Centchroman in controlling dysfunctional menstrual bleeding, improving mastalgia and fibroadenoma symptoms

Gap mapping

- Very small number of clinical trials [30] with most of these on Estetrol
- Largest clinical trial with Centchroman included 2087 women – referenced in National Guidance but unable to find published results
- No Centchroman trials outside India, and no head-to-head comparisons with hormonal contraception
- Little human trial evidence available with Anordrin–
- Little real-world or long term data on SERM use



CONCLUSIONS

- No consensus on what defines a SERM or hormonal contraception – difficult to homogenise a group with much heterogeneity
- Interrim findings show SERMs have shown potential as regular-use and emergency contraceptive options but current conclusions are from low quality, heterogenous data