

Evaluation of co-morbid medical conditions in adults with Down syndrome: Treatment of menopausal symptoms in women with Down syndrome

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BACKGROUND

The age of menopause onset in women with Down syndrome (DS) is known to be earlier than in women without DS (1). Evidence has shown that this earlier onset of menopause may be linked to an increased risk of memory loss and earlier onset of Alzheimer's Disease (AD) in women with DS (2). Despite this, evidence regarding the treatment of menopausal symptoms, particularly with hormone replacement therapy (HRT), has not been reviewed in women with DS.

OBJECTIVES/AIMS

1. Identify original research articles in peer-reviewed medical journals that focus on key questions about the treatment menopausal symptoms in women with DS.
2. Evaluate the quality of the existing evidence, identify deficiencies in current clinical knowledge and suggest directions for future research
3. Begin to formulate practical guidelines to support best medical practices for treatment of menopause in women with DS.

DESIGN/METHODS

Using the National Library of Medicine biomedical literature database PubMed (NCBI 1943-2024), we performed a literature search of the treatment of menopause in women with DS. Critical key questions were formulated *a priori* to inform the search strategy. The MeSH terms ["Down syndrome"] AND [Menopause] were combined in both the title and abstract search fields.

The following key questions were formulated:

- . What are common symptoms of menopause in women with DS?
- . Does pharmacologic treatment of symptoms associated with menopause improve mortality or morbidity?
- . Does age of menopause correlate with onset of dementia in women with DS?

RESULTS/SUMMARY

| Search Term: DS + Menopause No limits applied | NLM/PubMed Limits applied (Human, English, >18yr) |
|--|---|
| Unfiltered Hits = 48 articles | Filtered Hits = 30 articles |
| Reviewed Title/Abstract | Excluded articles = 22 • Not addressing a key Q (14) • Published prior to year 2000 (8) |
| Reviewed Article | Included articles = 8 |

DATA SUMMARY

- Differences in the processing of estrogen are associated with increased risk for Alzheimer's disease
- Earlier age at menopause is associated with increased risk of dementia and mortality
- Women with DS who develop Alzheimer's disease have lower levels of bioavailable estradiol, suggesting a possible protective role for HRT in preserving memory
- No studies evaluating the symptoms or treatment of menopause specifically in women with DS

| PubMedID (PBID) | 11522943 | 14520653 | 14749133 | 16926067 |
|-------------------------|--|--|--|--|
| Included Articles | Patel et al. 2001 | Schupf et al. 2003 | Patel et al. 2004 | Schupf et al. 2006 |
| Publication Year | 2001 | 2003 | 2004 | 2006 |
| Subjects studied (N) | 188 | 163 | 242 | 119 |
| Age range | 21-57 | 40-60 | 40-60 | 42-59 |
| Source of subjects | Community-based | Community-based | Community-based | Community-based |
| Methods | Cross-sectional and longitudinal analyses | Clinical assessment | Cognitive testing | Clinical assessment |
| Study design | Prospective longitudinal cohort | Prospective longitudinal cohort | Prospective longitudinal cohort | Prospective longitudinal cohort |
| Key Question Addressed: | Cognitive declines in postmenopausal women are associated with estrogen deficiency rather than with age. | Free estradiol levels may be lower in women with dementia than in those without dementia and are associated with AD. | Higher endogenous estrogen levels after menopause are associated with better performance on verbal memory. | Low serum levels of bioavailable estradiol are associated with increased risk of AD. |

| PubMedID (PBID) | 20110600 | 22156442 | 22057025 | 32338447 |
|-------------------------|--|---|--|---|
| Included Articles | Coppus et al. 2010 | Zhao et al. 2011 | Chace et al. 2012 | Capone et al. 2020 |
| Publication Year | 2010 | 2011 | 2012 | 2020 |
| Subjects studied (N) | 199 | 279 | 279 | |
| Age range | 45-67 | 31-70 | 31-68 | |
| Source of subjects | Community-based | Community-based | Community-based | |
| Methods | Clinical assessment | Clinical assessment | Clinical assessment | |
| Study design | Prospective longitudinal cohort | Prospective longitudinal cohort | Prospective longitudinal cohort | Review |
| Key Question Addressed: | Earlier age at menopause is significantly associated with increased risk of dementia and mortality risk. | Variants of estrogen receptor (ESR2) are associated with increased risk for AD. | Genetic variations in synthesis of estrogens are associated with increased risk of AD. | No studies reporting treatment data of menopausal symptoms. Impact of HRT (and non hormonal treatments) remains unexplored. |

CONCLUSIONS

Gaps in clinical knowledge: Research needed to address the Key Qs (in your Methods)

What major gaps did you identify in the DS literature

- No studies evaluating the symptoms of menopause specifically in women with DS
- No studies evaluating the treatment of menopause specifically in women with DS
- No studies evaluating the relationship between HRT and the development of AD in women with DS

Additional Gaps and Future Directions

- Are menopausal symptoms different in women with DS?
- What are best treatments for menopausal symptoms in women with DS?
- What role does estrogen play in development of AD?
- Does postmenopausal hormone replacement therapy (HRT) in women with DS affect timing or severity of diagnosis of AD?
- Current standard of practice is to offer same therapeutic options for treatment of menopausal symptoms to women with DS as in women without DS, with special consideration to risk/benefit discussions about the potential side effects
- As women with DS continue to live longer, further study about treatment of menopause in women with DS is warranted

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