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Review

Effect of Tibolone on Bone Mineral Density in Postmenopausal Women: Systematic Review and Meta-Analysis

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Table S1. Search strategy.

Database	Search strategy	Items found	Date
MEDLINE	("tibolone" [Supplementary Concept]) AND ("Bone Density"[Mesh] OR "Osteoporosis, Postmenopausal"[Mesh])	135	July 17,2020
Cochrane library	tibolone AND (bone density OR osteoporosis)	126	July 17,2020
ScienceDirect:	Tibolone, bone density	37	July 17,2020
Scopus	Tibolone AND "bone density"	194	July 17, 2020
Epistemonikos	tibolone AND (bone density OR osteoporosis)	38	July 17,2020
Lilacs	Tibolona	49	July 17,2020
SciELO	(tibolone) AND (bone)	4	July 17,2020
IMBIOMED	Tibolona	7	July 17,2020
Medigrafic:	Tibolona	6	July 17,2020

Table S2. Characteristics of the excluded studies (n = 24).

Reference	Reasons for exclusion
Geusens *et al.*, 1991[41]	Patients with fractures
Prelevic *et al.*, 1996[42]	Observational study
Lippuner K *et al.*, 1996[43]	Duplicated results
Park *et al.*, 2001[44]	Full text unreachable
Paviainen *et al.*, 1999[45]	Patients with fractures
Pavlov *et al.*, 1999[46]	Patients with fractures
Rymer *et al.*, 2001[47]	Duplicated results
Rymer *et al.*, 2002[48]	Duplicated results
Papaioannou, 2002[49]	Commentary
Arabi *et al.*, 2003[50]	Duplicated population
Roux *et al.*, 2003[51]	Duplicated population
Zayas Jaime *et al.*, 2004[52]	Comparator: premenopausal women
Boyanov *et al.*, 2005[53]	Do not measure bone mineral density
Carvalho Lopes *et al.*, 2005[54]	Full text unreachable
Zhou *et al.*, 2005[55]	Full text unreachable
Bianco *et al.*, 2006[56]	Cohort study
Nie *et al.*, 2006[57]	Full text unreachable
Delmas *et al.*, 2008[58]	Raloxifene as comparator
Caruso *et al.*, 2011[59]	Observational study
Krejovic *et al.*, 2011[60]	Tibolone dose is not indicated
Krejovic *et al.*, 2012[61]	Do not measure bone mineral density
Gupta *et al.*, 2013[62]	Bilateral oophorectomy
Kalder M *et al.*, 2016[63]	Bilateral oophorectomy
Sánchez-Rodríguez, 2017[64]	ISRCTN Registry

Table S3. Evidence of adverse events.

Tibolone vs. Non-Active Controls			
Outcomes	**Tibolone doses (mg)**	**Studies**	**Risk ratio (95%CI), participants.**
Headache	2.5	1[24]	1.71 (0.19 to 15.40), 55
	1.25	1[24]	1.67 (0.19 to 14.98), 56
Weight increase	2.5	1[21]	0.49 (0.04 to 5.31), 302
	1.25	1[21]	1.45 (0.25 to 8.56), 303
Breast pain	2.5	1[24]	8.75 (0.53 to 145.58), 55
	1.25	1[24]	7.38 (0.44 to 124.55), 56

Vaginal discharge	2.5	1[24]	1.71 (0.38 to 7.71), 55
	1.25	1[24]	3.61 (0.90 to 14.42), 56
Edema	2.5	1[24]	0.12 (0.01 to 2.32), 55
	1.25	1[24]	0.56 (0.08 to 3.65), 56
Itching of vulvae	2.5	1[24]	Not estimable
	1.25	1[24]	6.24 (0.36 to 107.40), 56
Acne	2.5	1[24]	0.57 (0.04 to 8.65), 55
	1.25	1[24]	0.56 (0.04 to 8.41), 56
Moniliasis	2.5	1[21]	8.76 (1.12 to 68.33), 302
	1.25	1[21]	3.87 (0.44 to 34.23), 303
Hirsutism	2.5	1[24]	2.92 (0.15 to 57.90), 55
	1.25	1[24]	1.70 (0.07 to 39.95), 56
Paraesthesia	2.5	1[24]	1.75 (0.07 to 41.04), 55
	1.25	1[24]	1.70 (0.07 to 39.95), 56
Melancholia	2.5	1[24]	0.19 (0.01 to 4.56), 55
	1.25	1[24]	0.56 (0.04 to 8.41), 56
Fatigue	2.5	1[24]	2.92 (0.15 to 57.90), 55
	1.25	1[24]	2.84 (0.14 to 56.36), 56
Allergy	2.5	1[21]	0.78 (0.21 to 2.85), 302
	1.25	1[21]	0.09 (0.00 to 1.58), 303
Hot flashes	2.5	1[21]	0.29 (0.11 to 0.76), 302
	1.25	1[21]	0.63 (0.30 to 1.29), 303
Anxiety	2.5	1[21]	1.30 (0.30 to 5.70), 302
	1.25	1[21]	4.52 (1.32 to 15.39), 303
Nervousness	2.5	1[21]	0.42 (0.11 to 1.58), 302
	1.25	1[21]	0.83 (0.29 to 2.41), 303
Herpes simplex infection	2.5	1[21]	2.43 (0.48 to 12.35), 302
	1.25	1[21]	0.19 (0.01 to 4.00), 303
Rhinitis	2.5	1[21]	0.90 (0.44 to 1.86), 302
	1.25	1[21]	0.35 (0.13 to 0.94), 303
Tibolone vs. estrogens			
Weight increase	2.5	1[22]	0.82 (0.49 to 1.37), 149
	1.25	1[22]	0.89 (0.54 to 1.46), 150
Breast pain	2.5	1[22]	0.12 (0.03 to 0.48), 149
	1.25	1[22]	0.11 (0.03 to 0.48), 150
Depression	2.5	1[22]	0.49 (0.16 to 1.57), 149
	1.25	1[22]	0.61 (0.21 to 1.78), 150
Acne	2.5	1[22]	0.65 (0.11 to 3.77), 148

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