Comparison 2: Proteolytic enzymes compared with placebo

Comparison 2a: Oral protease complex compared with placebo

Source: Zakarija-Grkovic I, Stewart F. Treatments for breast engorgement during lactation. Cochrane Database Syst Rev. 2020;(9):CD006946.

Certainty assessment							№ of patients		Effect		Certainty (GRADE)	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Oral protease complex	Placebo	Relative (95% CI)	Absolute (95% CI)		
Breast pain (no improvement)												
1	randomized trials	very serious [a]	not serious	not serious	serious [b]	none	2/35 (5.7%)	8/24 (33.3%)	**RR 0.17** (0.04 to 0.74)	**277 fewer per 1000** (from 320 fewer to 87 fewer)	⊕◯◯◯ VERY LOW	CRITICAL
Breast swelling (no improvement)												
1	randomized trials	very serious [a]	not serious	not serious	serious [b]	none	6/35 (17.1%)	12/24 (50%)	**RR 0.34** (0.15 to 0.79)	**330 fewer per 1000** (from 425 fewer to 105 fewer)	⊕◯◯◯ VERY LOW	CRITICAL
Number of women with adverse effects												
2	randomized trials	very serious [c]	not serious	not serious	very serious [d]	none	Adverse effects were measured and reported in the studies investigating serrapeptase (Kee 1989) and protease (Murata 1965). No women in any of the groups experienced adverse events.				⊕◯◯◯ VERY LOW	CRITICAL

CI: confidence interval; RR: risk ratio.

a. The pooled effect provided by study "C".

b. Small sample size and/or few events.

c. Most of the pooled effect provided by studies "B" or "C" but with a substantial proportion (i.e. > 50%) from studies "C".

d. No meta-analysis done. No events reported.

Comparison 2b: Oral serrapeptase compared with placebo

Source: Zakarija-Grkovic I, Stewart F. Treatments for breast engorgement during lactation. Cochrane Database Syst Rev. 2020;(9):CD006946.

Certainty assessment							№ of patients		Effect		Certainty (GRADE)	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Oral serrapeptase	Placebo	Relative (95% CI)	Absolute (95% CI)		
Breast pain (no improvement)												
1	randomized trials	serious [a]	not serious	not serious	very serious [b,c]	none	5/35 (14.3%)	9/35 (25.7%)	**RR 0.56** (0.21 to 1.49)	**113 fewer per 1000** (from 203 fewer to 126 more)	⊕◯◯◯ VERY LOW	CRITICAL
Breast swelling (no improvement)												
1	randomized trials	serious [a]	not serious	not serious	very serious [b,c]	none	9/35 (25.7%)	12/35 (34.3%)	**RR 0.75** (0.36 to 1.55)	**86 fewer per 1000** (from 219 fewer to 189 more)	⊕◯◯◯ VERY LOW	CRITICAL
Breast engorgement (symptoms not subsided after 3 days of treatment)												
1	randomized trials	serious [a]	not serious	not serious	serious [b]	none	5/35 (14.3%)	14/35 (40.0%)	**RR 0.36** (0.14 to 0.88)	**256 fewer per 1000** (from 344 fewer to 48 fewer)	⊕⊕◯◯ LOW	CRITICAL
Number of women with adverse effects												
2	randomized trials	serious [d]	not serious	not serious	very serious [e]	none	Adverse effects were measured and reported in the studies investigating serrapeptase (Kee 1989) and protease (Murata 1965). No women in any of the groups experienced adverse events.				⊕◯◯◯ VERY LOW	CRITICAL

CI: confidence interval; RR: risk ratio.
a. The pooled effect provided by study "B".
b. Small sample size and/or few events.
c. Wide confidence interval crossing the line of no effect.
d. Most of the pooled effect provided by studies "B" or "C" but with a substantial proportion (i.e. > 50%) from studies "C".
e. No meta-analysis done. No events reported.