Review of the Available Evidence on oral Sumatriptan in Adults and Children for the Treatment of Acute Migraine Attacks and Proposal for Inclusion for the WHO Model List of Essential Medicines (EML)

GRADE Evidence Profiles

WHO Collaborating Centre in Evidence-Based Research Synthesis and Guideline Development
Medicines and Medical Devices Area | Health Care and Welfare Directorate | Community Care Service
Emilia-Romagna Region
Bologna (Italy)

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Contents

Author(s): LM
Date:
Question: Sumatriptan (oral) vs. Placebo for acute migraine attack in children and adolescents [a]
Setting: adolescents
Bibliography: Richer L et Al. Drugs for the acute treatment of migraine in children and adolescents. Cochrane Database of Systematic Reviews 2016, Issue 4. Art. No.: CD005220.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Sumatriptan (oral)**	**Placebo**	**Relative (95% CI)**	**Absolute (95% CI)**		
Percentage of pain-free participants at two hours (assessed with: Pain freedom as the absence of pain at two hours before the use of additional or rescue medication)[b]												
1	randomised trials [1,b]	not serious	not serious	not serious	serious [c]	none	5/23 (21.7%)	2/23 (8.7%)	**RR 2.50** (0.54 to 11.60)	**13 more per 100** (from 4 fewer to 92 more)	⨁⨁⨁◯ MODERATE	
Percentage of pain-free participants at two hours (assessed with: Pain freedom as the absence of pain at two hours before the use of additional or rescue medication)												
1	randomised trials [2,d]	not serious	not serious	not serious	serious [c]	none	9/62 (14.5%)	3/30 (10.0%)	**RR 1.45** (0.42 to 4.98)	**5 more per 100** (from 6 fewer to 40 more)	⨁⨁⨁◯ MODERATE	
Percentage of pain-free participants at two hours (assessed with: Pain freedom as the absence of pain at two hours before the use of additional or rescue medication)												
1	randomised trials [3,e]	not serious	not serious	not serious	serious [c]	none	11/66 (16.7%)	5/36 (13.9%)	**RR 1.20** (0.45 to 3.18)	**3 more per 100** (from 8 fewer to 30 more)	⨁⨁⨁◯ MODERATE	
Percentage of pain-free participants at two hours (assessed with: Pain freedom as the absence of pain at two hours before the use of additional or rescue medication)												
1	randomised trials [4,f]	not serious	not serious	not serious	serious [c]	none	43/208 (20.7%)	10/35 (28.6%)	**RR 0.72** (0.40 to 1.30)	**8 fewer per 100** (from 9 more to 17 fewer)	⨁⨁⨁◯ MODERATE	
Percentage of pain-free participants at two hours (assessed with: Pain freedom as the absence of pain at two hours before the use of additional or rescue medication)												
1	randomised trials [5,g]	not serious	not serious	not serious	serious [1,c]	none	16/74 (21.6%)	20/70 (28.6%)	**RR 0.76** (0.43 to 1.34)	**7 fewer per 100** (from 10 more to 16 fewer)	⨁⨁⨁◯ MODERATE	
Percentage of pain-free participants at two hours (assessed with: Pain freedom as the absence of pain at two hours before the use of additional or rescue medication)												
1	randomised trials [6,h]	not serious	not serious	not serious	serious [c]	none	58/222 (26.1%)	14/76 (18.4%)	**RR 1.42** (0.84 to 2.39)	**8 more per 100** (from 3 fewer to 26 more)	⨁⨁⨁◯ MODERATE	
Percentage of participants with any adverse event(s) (assessed with: any unwanted effect that occurred during treatment)												

1	randomised trials [1]	not serious	not serious	not serious	serious [c]	none	8/23 (34.8%)	2/23 (8.7%)	**RR 4.00** (0.94 to 16.84) [i]	**26 more per 100** (from 1 fewer to 100 more)	⨁⨁⨁◯ MODERATE	
Percentage of participants with any adverse event(s) (assessed with: any unwanted effect that occurred during treatment)												
1	randomised trials [2]	not serious	not serious	not serious	serious [c]	none	19/62 (30.6%)	6/30 (20.0%)	**RR 1.53** (0.70 to 3.40) [i]	**11 more per 100** (from 6 fewer to 48 more)	⨁⨁⨁◯ MODERATE	
Percentage of participants with any adverse event(s) (assessed with: any unwanted effect that occurred during treatment)												
1	randomised trials [3]	not serious	not serious	not serious	serious [c]	none	11/66 (16.7%)	5/36 (13.9%)	**RR 1.20** (0.45 to 3.20) [i]	**3 more per 100** (from 8 fewer to 31 more)	⨁⨁⨁◯ MODERATE	
Percentage of participants with any adverse event(s) (assessed with: any unwanted effect that occurred during treatment)												
1	randomised trials [5]	not serious	not serious	not serious	serious [c]	none	12/74 (16.2%)	10/70 (14.3%)	**RR 1.13** (0.52 to 2.45) [i]	**2 more per 100** (from 7 fewer to 21 more)	⨁⨁⨁◯ MODERATE	
Percentage of participants with any adverse event(s) (assessed with: any unwanted effect that occurred during treatment)												
1	randomised trials [4]	not serious	not serious	not serious	serious [c]	none	129/445 (29.0%)	16/85 (18.8%)	**RR 1.50** (0.97 to 2.40) [i]	**9 more per 100** (from 1 fewer to 26 more)	⨁⨁⨁◯ MODERATE	
Percentage of participants with any adverse event(s) (assessed with: any unwanted effect that occurred during treatment)												
1	randomised trials [6]	not serious	not serious	not serious	serious [c]	none	239/289 (82.7%)	102/252 (40.5%)	**RR 2.04** (1.70 to 2.40) [i]	**42 more per 100** (from 28 more to 57 more)	⨁⨁⨁◯ MODERATE	

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. The dosages used in the included studies range from 25, 50 to 100 mg. In some studies it depends on body surface area or body weight
b. Number of randomized partecipants: 31; population for analysis:23 in each group, cross over study
c. small sample size, few events, and wide confidence intervals.
d. Rothner 1999b. Randomized (N = 119); withdrawn (N = 27); intention-to-treat and primary efficacy analysis (N = 92)
e. Rothner 1999c. Randomized (N = 139); withdrawn (N = 37); intention-to-treat and primary efficacy analysis (N = 102)
f. Rothner 1999a. Randomized (N = 347); withdrawn (N = 117); intention-to-treat and primary efficacy analysis (N = 273)
g. Fujita 2014. Randomized (N = 178); withdrawn (N = 34); intention-to-treat and primary efficacy analysis (N = 144)
h. Winner 1997. Randomized (N = 355); withdrawn (N = 194); intention-to-treat and primary efficacy analysis (N = 298), Cross over study
i. Relative Risk for outcome "Any adverse event " not available, data calulated.

References

1. 1997b, Hamalainen. .
2. 1999b, Rothner. .
3. 1999c, Rothner. .
4. 1999a, Rothner. .
5. 2014, Fujita. .
6. 1997, Winner. .

Author(s):
Date:
Question: Sumatriptan 50 mg compared to placebo in the acute treatment of migraine
Setting: outpatients
Bibliography: Derry CJ, Derry S, Moore RA. Sumatriptan (oral route of administration) for acute migraine attacks in adults. Cochrane Database of Systematic Reviews 2012, Issue 2. Art. No.: CD008615. DOI: 10.1002/14651858.CD008615.pub2.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**sumatriptan 50 mg**	**placebo**	**Relative (95% CI)**	**Absolute (95% CI)**		
percentage of participants with moderate to severe pain that where pain free at 2 h (assessed with: patient diary)												
13	randomised trials	not serious [a]	not serious	not serious	not serious	none	1080/3922 (27.5%)	282/2525 (11.2%)	**RR 2.7** (2.4 to 3.1)	**19 more per 100** (from 16 more to 23 more)	⨁⨁⨁⨁ HIGH	
percentage of participants with mild pain that where pain free at 2 h (assessed with: patient diary)												
7	randomised trials	not serious [b]	not serious	not serious	not serious	none	357/783 (45.6%)	168/731 (23.0%)	**RR 2.03** (1.74 to 2.37)	**24 more per 100** (from 17 more to 31 more)	⨁⨁⨁⨁ HIGH	
Adverse event (any) rate within 24 h postdose in patients with moderate to severe baseline pain intensity												
10	randomised trials	not serious	not serious	not serious	not serious	none	667/2114 (31.6%)	389/1614 (24.1%)	**RR 1.3** (1.2 to 1.4)	**7 more per 100** (from 5 more to 10 more)	⨁⨁⨁⨁ HIGH	
Adverse event (any) rate within 24 h postdose in patients with mild baseline pain intensity												
5	randomised trials	not serious	not serious	not serious	not serious	none	104/642 (16.2%)	43/600 (7.2%)	**RR 2.26** (1.62 to 3.16)	**9 more per 100** (from 4 more to 15 more)	⨁⨁⨁⨁ HIGH	

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. quality of included trials has been evaluated with Oxford quality score. Trials having a score of 2 out of 5 (2/13 RCT included in the analysis) were considered to be at greater risk of bias and therefore analysed separately. There was no significant difference between the two groups of studies (score =2 e score = 3 to 5 of 5).
b. Of the six studies originally analysed comparing sumatriptan 50 mg with placebo in participants with mild baseline pain intensity, two had a quality score of 2 of 5. There was no significant difference between the two groups of studies

Author(s):
Date:
Question: Sumatriptan 50 mg compared to ASA 1.000 mg in the acute treatment of migraine
Setting: outpatients
Bibliography: Derry CJ, Derry S, Moore RA. Sumatriptan (oral route of administration) for acute migraine attacks in adults. Cochrane Database of Systematic Reviews 2012, Issue 2. Art. No.: CD008615. DOI: 10.1002/14651858.CD008615.pub2.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**sumatriptan 50 mg**	**ASA 1.000 mg**	**Relative (95% CI)**	**Absolute (95% CI)**		
proportion of participants that where pain free at 2 h (assessed with: patient diary)												
2 [1,a]	randomised trials	not serious	not serious	not serious	not serious	none	116/359 (32.3%)	97/367 (26.4%)	**RR 1.22** (0.97 to 1.53)	**6 more per 100** (from 1 fewer to 14 more)	⊕⊕⊕⊕ HIGH	
adverse event (any) rate within 24 h												
2 [1,b]	randomised trials	not serious	not serious	serious[C]	not serious	none	64/361 (17.7%)	55/369 (14.9%)	**RR 1.18** (0.85 to 1.64)	**3 more per 100** (from 2 fewer to 10 more)	⊕⊕⊕◯ MODERATE	

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. 2 studies, 726 participants
b. 2 studies, 730 participants
c. Indirectness due to a short follow-up (24 hours). Rare and potentially severe adverse events associated with use of ASA at analgesic dose, generally occurring in the medium-long term, may be undetected during such a short follow up.

References

1. Derry CJ, Derry S,Moore RA. DOI:. Sumatriptan (oral route of administration) for acute migraine attacks in adults.. Cochrane Database of Systematic Reviews 2012, Issue 2. Art. No.: CD008615.; update 2015.

Author(s):
Date:
Question: Oral sumatriptan 50 mg compared to eletriptan 40-80 mg in the acute treatment of migraine
Setting: outpatients
Bibliography: Derry CJ, Derry S, Moore RA. Sumatriptan (oral route of administration) for acute migraine attacks in adults. Cochrane Database of Systematic Reviews 2012, Issue 2. Art. No.: CD008615. DOI: 10.1002/14651858.CD008615.pub2.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**oral sumatriptan 50 mg**	**eletriptan 40-80 mg**	**Relative (95% CI)**	**Absolute (95% CI)**		
percentage of participants that where pain free at 2 h vs eletriptan 40 mg (assessed with: patient diary)												
2 [1]	randomised trials	not serious	not serious	not serious	not serious	none	64/362 (17.7%)	86/359 (24.0%)	**RR 0.74** (0.55 to 0.98)	**6 fewer per 100** (from 0 fewer to 11 fewer)	⨁⨁⨁⨁ HIGH	
percentage of participants that where pain free at 2 hrs vs eletriptan 80 mg (assessed with: patient diary)												
2 [1]	randomised trials	not serious	not serious	not serious	not serious	none	64/362 (17.7%)	104/344 (30.2%)	**RR 0.58** (0.44 to 0.76)	**13 fewer per 100** (from 7 fewer to 17 fewer)	⨁⨁⨁⨁ HIGH	

CI: Confidence interval; **RR:** Risk ratio

References

1. Derry CJ, Derry S,Moore RA. DOI:. Sumatriptan (oral route of administration) for acute migraine attacks in adults.. Cochrane Database of Systematic Reviews 2012, Issue 2. Art. No.: CD008615.; update 2015.

Author(s):
Date:
Question: Sumatriptan 50 mg compared to rizatriptan in the acute treatment of migraine
Setting: outpatients
Bibliography: Derry CJ, Derry S, Moore RA. Sumatriptan (oral route of administration) for acute migraine attacks in adults. Cochrane Database of Systematic Reviews 2012, Issue 2. Art. No.: CD008615. DOI: 10.1002/14651858.CD008615.pub2.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**sumatriptan 50 mg**	**rizatriptan**	**Relative (95% CI)**	**Absolute (95% CI)**		
percentage of participants that where pain free at 2 hrs vs rizatriptan 5 mg (assessed with: patient diary)												
2	randomised trials	not serious	not serious	not serious	not serious	none	394/1116 (35.3%)	363/1093 (33.2%)	**RR 1.10** (0.95 to 1.20)	**3 more per 100** (from 2 fewer to 7 more)	⨁⨁⨁⨁ HIGH	
percentage of participants that where pain free at 2 hrs vs rizatriptan 10 mg (assessed with: pain freedom at 2 hours, without the use of rescue medication)												
2	randomised trials	not serious	not serious	not serious	not serious	none	394/1116 (35.3%)	440/1114 (39.5%)	**RR 0.89** (0.80 to 1.00)	**4 fewer per 100** (from 0 fewer to 8 fewer)	⨁⨁⨁⨁ HIGH	
percentage of adverse events (any) within 24 h vs rizatriptan 5 mg (patients with moderate or severe migraine)												
2	randomised trials	not serious	not serious	not serious	not serious	none	276/578 (47.8%)	238/582 (40.9%)	**RR 1.17** (1.03 to 1.33)	**7 more per 100** (from 1 more to 13 more)	⨁⨁⨁⨁ HIGH	
percentage of adverse events (any) within 24 h vs rizatriptan 10 mg (patients with moderate or severe migraine)												
2	randomised trials	not serious	not serious	not serious	not serious	none	276/578 (47.8%)	276/599 (46.1%)	**RR 1.04** (0.92 to 1.17)	**2 more per 100** (from 4 fewer to 8 more)	⨁⨁⨁⨁ HIGH	

CI: Confidence interval; **RR:** Risk ratio

Author(s): LM
Date:
Question: Oral sumatriptan 100 mg rispetto a placebo per acute migraine attacks
Setting: Adult patients with acute attacks of migraine of moderate/severe or mild intensity
Bibliography: Derry JC et al. Sumatriptan (oral route of administration) for acutemigraine attacks in adults (Review). Cochrane Cochrane Database of Systematic Reviews 2012.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**oral sumatriptan 100 mg**	**placebo**	**Relative (95% CI)**	**Absolute (95% CI)**		
The proportion of participants pain-free at two hours in patients with moderate or severe baseline pain intensity												
16 [1,a]	randomised trials	not serious	not serious	not serious	not serious	none	1291/4017 (32.1%)	272/2554 (10.6%)	**RR 3.2** (2.8 to 3.6)	**23 more per 100** (from 19 more to 28 more)	⨁⨁⨁⨁ HIGH	
The proportion of participants pain-free at two hours in patients with mild baseline pain intensity												
5 [b]	randomised trials	not serious	not serious	not serious	not serious	none	358/618 (57.9%)	151/622 (24.3%)	**RR 2.41** (2.06 to 2.81)	**34 more per 100** (from 26 more to 44 more)	⨁⨁⨁⨁ HIGH	
Any adverse event within 24 h in patients with moderate or severe baseline pain intensity												
12 [c]	randomised trials	not serious	not serious	not serious	not serious	none	931/2171 (42.9%)	255/1086 (23.5%)	**RR 1.69** (1.50 to 1.91)	**16 more per 100** (from 12 more to 21 more)	⨁⨁⨁⨁ HIGH	
Any adverse event within 24 h in patients with mild baseline pain intensity												
4 [d]	randomised trials	not serious	not serious	not serious	not serious	none	89/471 (18.9%)	32/470 (6.8%)	**RR 2.75** (1.87 to 4.05)	**12 more per 100** (from 6 more to 21 more)	⨁⨁⨁⨁ HIGH	

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. 16 studies, 6571 partecipants with acute migraine attack of moderate-severe intensity
b. 5 studies, 1240 partecipants with acute migrain attack of mild intensity
c. 12 studies, 3257 partecipants with acutr migraine attack of moderate-severe intensity
d. 4 studies, 941 partecipants with moderate-severe migraine attack of mild intensity

References

1. al, Derry,GC,et. Sumatriptan (oral route of administration) for acutemigraine attacks in adults (Review). 2012.

Author(s): LM **Date**:
Question: Oral sumatriptan 100 mg compared to acetylsalycilic acid 900 mg+metoclopramide 10 mg for acute migraine attack
Setting: Adult patients with acute attacks of migraine of moderate-severe intensity
Bibliography: Derry GC et al. Sumatriptan (oral route of administration) for acutemigraine attacks in adults (Review). Cochrane Database of Systematic Reviews 2012.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**oral sumatriptan 100 mg**	**acetylsalycilic acid 900 mg+metoclopramide 10 mg**	**Relative (95% CI)**	**Absolute (95% CI)**		
The proportion of participants pain-free at two hours												
2 [a]	randomised trials	not serious	not serious	not serious	not serious	none	71/275 (25.8%)	48/300 (16.0%)	**RR 1.62** (1.17 to 2.25)	**10 more per 100** (from 3 more to 20 more)	⨁⨁⨁⨁ HIGH	
Any adverse event within 24 hours												
2	randomised trials	not serious	not serious	serious[b]	not serious	none	112/300 (37.3%)	78/321 (24.3%)	**RR 1.53** (1.20 to 1.94)	**13 more per 100** (from 5 more to 23 more)	⨁⨁⨁◯ MODERATE	

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. 2 studies with 575 partecipants. Patients with moderate -severe baseline pain intensity
b. Indirectness due to a short follow-up (24 hours). Rare and potentially severe adverse events associated with use of ASA at analgesic dose, generally occurring in the medium-long term, may be undetected during such a short follow up.

Author(s): LM
Date:
Question: Oral sumatriptan 100 mg compared to oral almotriptan 12.5 mg for acute migraine attack
Setting: Adult patients with acute attacks of migraine of moderate intensity
Bibliography: Derry GC et al. Sumatriptan (oral route of administration) for acutemigraine attacks in adults (Review). Cochrane Database of Systematic Reviews 2012,

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**oral sumatriptan 100 mg**	**oral almotriptan 12.5 mg**	**Relative (95% CI)**	**Absolute (95% CI)**		
The proportion of participants pain-free at two hours vs almotriptan 12.5 mg												
2 [a]	randomised trials	not serious	not serious	not serious	not serious	none	129/387 (33.3%)	102/367 (27.8%)	**RR 1.20** (0.97 to 1.49)	**6 more per 100** (from 1 fewer to 14 more)	⨁⨁⨁⨁ HIGH	
Any adverse event within 24 h - not measured												
-	-	-	-	-	-	-	-	-	-	-	-	

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. 2 studies with 754 partecipants. Patients with moderate -severe baseline pain intensity

Author(s): LM
Date:
Question: Oral sumatriptan 100 mg compared to oral eletriptan for acute migraine attack
Setting: Adult patients with acute attacks of migraine of moderate/severe intensity
Bibliography: Derry GC et al. Sumatriptan (oral route of administration) for acutemigraine attacks in adults (Review). Cochrane Database of Systematic Reviews 2012,

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**oral sumatriptan 100 mg**	**oral eletriptan**	**Relative (95% CI)**	**Absolute (95% CI)**		
The proportion of participants pain-free at two hours vs eletriptan 40 mg												
3 [a]	randomised trials	not serious	not serious	not serious	not serious	none	271/1130 (24.0%)	366/1133 (32.3%)	**RR 0.74** (0.65 to 0.85)	**8 fewer per 100** (from 5 fewer to 11 fewer)	⨁⨁⨁⨁ HIGH	
The proportion of participants pain-free at two hours vs eletriptan 80 mg												
2 [b]	randomised trials	not serious	not serious	not serious	not serious	none	55/299 (18.4%)	103/305 (33.8%)	**RR 0.54** (0.41 to 0.72)	**16 fewer per 100** (from 9 fewer to 20 fewer)	⨁⨁⨁⨁ HIGH	
Any adverse event within 24 h (for both dosages 40 and 80 mg) - not measured												
-	-	-	-	-	-	-	-	-	-	-	-	

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. 3 studies with 2263 partecipants. Patients with moderate -severe baseline pain intensity
b. 2 studies with 604 artecipants. Patients with moderate -severe baseline pain intensity

Author(s): LM
Date:
Question: Oral sumatriptan 100 mg compared to oral rizatriptan 10 mg for acute migraine attack
Setting: Adullt patients with acute attacks of migraine of moderate intensity
Bibliography: Derry GC et al. Sumatriptan (oral route of administration) for acutemigraine attacks in adults (Review). Cochrane Database of Systematic Reviews 2012,

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**oral sumatriptan 100 mg**	**oral rizatriptan 10 mg**	**Relative (95% CI)**	**Absolute (95% CI)**		
The proportion of participants pain-free at two hours vs rizatriptan 10 mg												
2 [a]	randomised trials	not serious	not serious	not serious	not serious	none	143/460 (31.1%)	178/476 (37.4%)	**RR 0.82** (0.69 to 0.98)	**7 fewer per 100** (from 1 fewer to 12 fewer)	⨁⨁⨁⨁ HIGH	
Any adverse event within 24 h												
2 [b]	randomised trials	not serious	not serious	not serious	not serious	none	217/421 (51.5%)	203/435 (46.7%)	**RR 1.10** (0.96 to 1.27)	**5 more per 100** (from 2 fewer to 13 more)	⨁⨁⨁⨁ HIGH	

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. 2 studies with 936 partecipants. Patients with moderate-severe pain intensity
b. 2 studies with 856 partecipants. Patients with moderate-severe pain intensity

Author(s): LM
Date:
Question: Oral sumatriptan 100 mg compared to paracetamol 1000 mg+metoclopramide 10 mg for acute migraine attack
Setting: Adult patients with acute attacks of migraine moderate
Bibliography: Derry GC et al. Sumatriptan (oral route of administration) for acutemigraine attacks in adults (Review). Cochrane Database of Systematic Reviews 2012,

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**oral sumatriptan 100 mg**	**paracetamol 1000 mg+metoclopramide 10 mg**	**Relative (95% CI)**	**Absolute (95% CI)**		
The proportion of participants pain-free at two hours - not measured[a]												
-	-	-	-	-	-	-	-	-	-	-	-	
Any adverse event within 24 h												
2 [b]	randomised trials	not serious	not serious	not serious	not serious	none	304/653 (46.6%)	191/675 (28.3%)	**RR 1.64** (1.42 to 1.89)	**18 more per 100** (from 12 more to 25 more)	⨁⨁⨁⨁ HIGH	

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. for studies that compared oral sumatriptan 100 mg vs paracetamol 1000 mg were available data on outcome: headheache relief at 2 hours, not pain free at 2 h
b. 2 studies with 1328 partecipants. Patients with moderate -severe baseline pain intensity

Author(s): LM-FN

Question: Intranasal sumatriptan 22 mg rispetto a oral sumatriptan 100 mg per acute migraine

Setting: adults outpatients with multiple acute attacks of migraine

Bibliography: Tepper SJ, Cady RK, Silberstein S, Messina J, Mahmoud RA, Djupesland PG, Shin P, Siffert J. AVP-825 breath-powered intranasal delivery system containing 22mg sumatriptan powder vs 100mg oral sumatriptan in the acute treatment of migraines (The COMPASS study): a comparative randomized clinical trial across multiple attacks. Headache. 2015 May;55(5):621-35

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	intranasal sumatriptan 22 mg	oral sumatriptan 100 mg	Relative (95% CI)	Absolute (95% CI)		
Discontinuations due to TEAEs (follow up: 4 months; assessed with: % of patients with TEAEs that led to discontinuation)												
1 [a]	randomised trials	very serious [b]	not serious	not serious	not serious	Publication bias Strongly suspected [c]	4/133 (3.0%)	3/129 (2.3%)	Not estimable		⨁◯◯◯ very low	

CI: Confidence interval

Explanations

a. Randomized Controlled Cross-Over study (treatment period: 12 +12 week), with 275 patients included. The full analysis set includes 262 patients (n. 133 in the intranasal sumatriptan arm and 129 in the oral sumatriptan arm). Efficacy data and part of the safety data are not reported in the table because the authors expressed the results in terms of number of attacks instead of number of patients.

b. Attrition bias (28% and 37%, respectively, excluded from analysis). Missing data replaced with the LOCF. Risk of unblinding due to unbalance in the treatment-related adverse events (abnormal product taste in 26% pts in the intranasal preparation + oral placebo vs 4% in the oral preparation + intranasal placebo. Nasal discomfort in 15% in the intranasal preparation + oral placebo vs 1% in the oral preparation + intranasal placebo. Primary outcome (SPID-30) was formally presented after patients' enrolment was completed"

c. Selective outcome reporting: the denominator in the proportions indicated in Table 4 of the study, regarding discontinuations, should be the number of patients considered as the safety set, as reported in the text of the article (section "Safety and Tolerability", p. 629), and not - as reported in the table - what looks like the number of attacks. Such correction would give different figures, less favorable to the experimental treatment, as reported in the Evidence Profile