
How article was found:
-- Searched PubMed by individually searching for “angiotensin receptor blocker”, “ACE inhibitor”, and “angioedema”. I then used the advanced search to combine these individual searches, yielding about 30 articles. There was a recent meta-analysis from April this year which referenced the article I ultimately ended up choosing. I
-- I had previously searched TRIP for articles using keyword search “ARB angioedema” and came across one of the retrospective studies in the meta-analysis I chose.

Type of study: meta-analysis

Describe research question:
P: In patients with history of angioedema with use of ACE inhibitor
I: switched to ARB,
C: none
O: what is the risk of developing angioedema.

Relevance of question: Incidence of angioedema with ACE inhibitors occurs in up to 1% of patients. Case reports have reported wide range of angioedema after switching to an ARB. Since these medications are often necessary for management of heart failure, diabetes, and hypertension, there needs to be a better defined risk of angioedema with switching to an ARB.

Methods:
-- Literature search of MEDLINE, EMBASE, BIOSIS, Current Contents.
  -No limits
  -Jan 1990 to May 2007
  -Key words: angiotensin-converting enzyme inhibitors, ACE inhibitors, angiotensin II type 1 receptor blockers, angiotensin receptor blockers, angioneurotic edema, angioedema, candesartan, eprosartan, irbesartan, losartan, olmesartan, telmisartan, valsartan.
-- Inclusion: study population had angioedema after ACEI and subsequently given ARB. Followed for at least 1 month. Included RCTs, prospective and retrospective cohorts
-- Excluded: case reports and case series
-- Data extraction: Standardized checklist (study design, pt demographics, length of follow up, number patients developed angioedema after ACEI, number patients switched to ARB, number patients with angioedema on ARB, comorbidities, other hypertensive meds, complement testing done). Done by 2 authors independently. Differences resolved by third author.
-- Calculated percent of patients with definite and possible angioedema with CIs
-- Evaluated for heterogeneity using I2 statistic.

Critical appraisal:
-- Positive: Searched multiple engines. Key word choices appropriate. Exclusion of case reports/series. Standardized data extraction. Long follow up overall (20 months average). No statistical heterogeneity between trials.
-- Negative: Small number of studies found, thus required use of retrospective studies introducing possible bias. The primary outcome of the RCT included was aimed at CV outcomes, not occurrence of angioedema. One of the retrospective studies only did not have
follow up info on 28 of the 64 patients. Separated confirmed and possible angioedema due to ARB – unclear how one could distinguish this. Small number of patients leading to wide CIs (imprecise results).

Results:
-- 254 citations screened – 3 were included – 2 retrospective and 1 RCT
-- 164 pts had angioedema on ACEI, 71 received ARB, 8 of these developed angioedema
  - 3 confirmed, 5 possible
-- For possible cases, risk 9.4%, CI 1.6 – 17%
-- For confirmed cases, risk 3.5%, CI 0 – 9.2%
-- No statistical heterogeneity
-- If you look at the RCT only, no patients developed angioedema with placebo. Thus, if you calculate a NNH (7.7% of patients on ARB had angioedema) = 13.

Can they be applied?: Yes. Risk of angioedema is certainly lower with ARB if they had it with an ACEI. Should still discuss the up to 10% risk of angioedema when switching to an ARB with your patients before starting.

ALSO: Researchers repeated search to include articles from June 2007 to Dec 2008 and added 1 trial to analysis (TRANSCEND trial, evaluating telmisartan in CV disease).
  - Result: 75 patients had angioedema on ACEI; none had angioedema on ARB, 1 patient had angioedema on placebo.
  - When combined with previous data: risk of angioedema due to ARB use was 2.5%, CI 0 – 6.6%.
  - Raises question of whether or not this is drug specific.