of an iodinated contrast medium, but not of a nonionic one. Am J Cardiol 2000; 86: 106.


Ionic or non-ionic contrast media in stent placement

In their paper on acute and subacute stent occlusion[1] Scheller and colleagues recommend the use of ioxaglate in coronary interventions when stent placement is anticipated. Among 3990 consecutive patients undergoing coronary stent placement at a single institution over a period of 4-5 years, 1808 patients ‘received non-ionic contrast media’ while 2182 patients were ‘given the ionic ioxaglate’. Both acute (1.3% vs 0.3%, P=0.001) and subacute stent occlusion (2.4% vs 0.7%, P=0.001) occurred more frequently in patients receiving non-ionic contrast media. Moreover, the incidence of the combined clinical endpoint at 12 months (CABG, TVR, and overall mortality) was ‘significantly reduced by the use of ioxaglate’ (22.9% vs 16.3%, P=0.001).

These data, derived from a very large cohort of patients, seem to be very impressive and convincing. In his related editorial ‘Ionic or non-ionic contrast media during coronary intervention: does it make a difference?’[2] Legrand states that ‘this is the first study which has demonstrated that an ionic contrast agent may influence late outcome after stenting, reducing death and late revascularization procedure by 29%’. Is this true?

The design of the study merits some consideration and raises some questions:

1) Diagnostic coronary angiography was performed, ‘generally using non-ionic contrast media’. Thus, each and every patient first received a non-ionic contrast medium for the diagnostic angiogram. Moreover, ‘non-ionic’ summarizes five non-ionic monomers with different iodine concentrations and different osmolality and viscosity, and one non-ionic dimer. The latter, ioxidanol, was compared to ioxaglate in the COURT trial[3]. The results of this trial were discussed only in the Legrand’s editorial[2] but not in Scheller’s paper[1]. Instead, it is only mentioned that patients receiving ioxidanol had the highest rate of subacute stent occlusion. It would be interesting to know the stent occlusion rate in the other non-ionic contrast medium subgroups.

2) Subsequently, the patients were allocated to undergo coronary stent placement by either using the same non-ionic contrast medium or by using a different contrast medium, namely the ionic agent ioxaglate. Over the past decade we have learned a lot about the interaction between blood clot formation and contrast media. According to contemporary theories, the non-ionic contrast medium would presumably lead to profound platelet degranulation, reduced inhibition of thrombin generation, and impaired thrombolysis. In Scheller’s patients, all these mechanisms and interactions must have already been activated after the diagnostic coronary angiography, i.e. before the coronary intervention took place. It seems to be difficult to explain the clinical benefits for the patients in whom the ionic contrast medium was subsequently used. One could only speculate whether ioxaglate reversed all negative effects of the various non-ionic contrast media. This would be difficult to understand and even more difficult to believe.

Legrand calls the search for the ideal contrast agent the ‘quest of the Holy Grail’. The Grail has not yet been found. But after Scheller’s study we may know at least what’s in there: it’s neither ionic nor non-ionic — it’s a mixture!

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References


A reply

In his letter to the editor, Dr Schräder poses the rhetorical question of whether the results of our study are ‘true’. To substantiate his doubts, he points out that different non-ionic contrast media (CM) were used in our study and calls for a subgroup analysis. In addition, he refers to the data obtained during the COURT trial[3]. I am very happy to be given this opportunity to discuss the interesting results of the COURT trial since these results were not available when we submitted our paper. The second part of Dr Schräder’s criticism has to do with the sequential use of CM.

Subgroup analysis

It makes no sense, from either a statistical or pharmacological point of view, to conduct a subgroup analysis of the non-ionic monomer CM. These media are very similar with respect to their chemical structure and the additives they contain. Moreover, in vitro studies and clinical data have failed to reveal any differences in terms of acute and late reactions or thrombotic potential[4–6]. In our study as well, patients who received a monomer non-ionic CM exhibited a comparable incidence of subacute stent occlusions of 1.8–2.9% (ns).

Ioxidanol and the COURT trial

In the group of non-ionic CM, the iso-osmolar dimer ioxidanol holds a special position. Non-ionic dimer CM are controversial because they are associated with an elevated incidence of late reactions, reactions which occur when the patient has already left the cathlab room and is often no longer constantly monitored. In a recently published randomized study, the incidence of late skin reactions in patients who had received ioxidanol (12.2%) was much higher than the corresponding rates (4.3% and 4.2%) in patients who had received iopamidol (monomer, non-ionic) and ioxaglate (dimer, ionic), respectively (n=2001)[6]. Schering took its non-ionic dimer off the market years ago as a precautionary measure. The only substance of this kind now on the market is ioxidanol.

The COURT trial was a randomized multicentre trial designed to