INTERACTIONS

Influence on laboratory tests

The influence of different ionic and nonionic CM on clinicochemical parameters determined in serum and urine was examined systematically in the laboratory.

For this purpose, reference sera (normal and pathological values) were mixed with up to 20 vol % CM solution and urine with up to 50 % CM solution. Higher concentrations are unlikely to occur in humans even a very short time after a CM injection.

In this investigation, Ultravist, Urografin (diatrizoate) and iohexol did not affect serum levels of GOT GPT, ϒ-GT, AP, LDH, HBDH, CK, CKMB, ChE, GDH, amylase (with maltotetraose, Biomed) and lipase (Automatic Clinical Analyzer, Du Pont). Meglumine sodium ioxaglate caused suppression of GPT.

Similarly, the urinary enzymes ϒ-GT, LDH, AAP, ß-NAG and amylase were not or only slightly influenced by the above CM. The specific gravity of urine was found to increase after administration of iodinated renal CM.

Protein determination by the biuret assay was not affected by Ultravist, while marked effects were observed for some other CM investigated. No effects on protein levels in urine were observed using the Ponceau S method.

U. Speck, *X-Ray Contrast Media*, https://doi.org/10.1007/978-3-662-56465-3_9

Levels of the substrates BUN, creatinine, uric acid, bilirubin (direct and indirect), glucose, cholesterol and triglycerides were not appreciably affected by Ultravist. In contrast, other CM led to, at times marked, changes in individual parameters. Electrolytes (particularly iron and copper) were affected by all CM tested and very much so by some. Whenever an effect cannot be ruled out with certainty, samples for serum or urinary analysis should be obtained either before CM administration or at the earliest 24 hours afterwards. In patients with severe renal failure and hence delayed CM elimination, it may be necessary to wait even longer.

All tests concerning the thyroid gland can be disturbed for much longer than 24 hours by the iodide administered with the CM. The ability of the thyroid tissue to take up radioisotopes for the diagnosis of thyroid disease is reduced by iodinated CM for 2-6 weeks. Urographic CM affect laboratory test results least, while orally administered cholegraphic agents and iodinated oily CM have a longer-lasting effect.

Interaction with medications

To date, only a few interactions of CM for urography, angiography and CT with medications have been described in association with clinical use. Such interactions are extremely improble since these CM bind hardly at all to plasma proteins, cause no inhibition of enzymes, are not themselves subject to metabolism, and are not absorbed enterally. In cancer patients treated with interleukin-2, more side-effects have been observed after administration of ionic and nonionic contrast media. These side-effects include fever, nausea, vomiting, skin reactions, and diarrhea [66]. On the other hand, butylscopolamine appears to have no influence on contrast medium tolerance [67].

Due to the risk of lactate acidosis it was originally recommended that treatment with biguanides (Glucophage, Metformin) should be withdrawn two days before administration of intravascular X-ray contrast media to avoid accumulation of the exclusively renally excreted Metformin should the contrast medium induce renal failure [68]. This risk would also be eliminated if biguanide therapy were withdrawn from after contrast medium administration until an effect on kidney function can be ruled out [69].

A variety of pharmaceutical substances were tested for their influence on acute tolerance of CM in animal experiments. Even here, interactions possibly of clinical relevance were rarely observed [70, 71]. In cardioangiography, there is a theoretical concern that the cardiodepressive effect of ionic CM caused by calcium binding will be intensified by calcium blockers (verapamil) [72].

One case of thrombotic occlusion of the leg arteries which could not be alleviated with continuous urokinase infusion has been reported in the literature [73]. Patients with cardiac insufficiency and renal dysfunction undergoing angiography should not be given furosemide (diuretic) − even with large quantities of liquid. Patients who received 110 mg furosemide along with 3 liters of fluid exhibited a creatinine rise from 145 ± 13 to 182 ± 16 µmol/l, whereas controls without furosemide showed no rise [74].

There is also evidence that neuroleptic agents (chlorpromazine) potentiate the normally only slight epileptogenic effect even of nonionic CM in myelography [75].

Cholegraphic agents bind to plasma proteins and are eliminated with the bile via an active transport mechanism which is limited in its capacity. They are able to displace drugs and endogenous substances that have the same properties. In this way, the concentrations of free drug in plasma can be increased by the simultaneous administration of biliary CM and their excretion delayed to some extent. The absorption of oral cholegraphic agents relies on their passage from the stomach into the bowel. Drugs which affect the gastric passage of these agents, therefore, alter the rate of their absorption.

The same effect is likely to occur in the presence of substances or foodstuffs which have an influence on the absorption of pharmaceutical substances from the bowel (e.g., carbon, gel-forming substances, fats, and coffee).

Interaction of contrast media with additives and during interventional procedures

In the course of some diagnostic or interventional radiological procedures, X-ray contrast media are treated in a special manner, mixed with therapeutic agents, or come into contact with high local concentrations of equally undiluted drugs in the body. This may result in precipitation of the contrast medium, the therapeutic agent, or both, inactivation of the drugs, or occurrence of other undesirable and sometimes hardly predictable effects (table 13).

Active agent	Diatrizoic Acid	Ioxaglate	Iopromide
Heating of the CM up to 100° C e.g. for the purpose of embolization	possible	possible	possible
Compound with ethanol	?	?	possible
Mixing before injection			
Papaverine	+	+	-
Phentolamine mesylate	+	+	-
Tolazolin	-	-	-
Diphenhydramine	+	+	-
Prostaglandin E1	-	-	-
Pheniramin	-	-	-
Cimetidine	+	+	-
Na-heparin	-	-	-
Protamine	+	+	-
Vasopressin	-	-	-
Epinephrine	-	-	-
Hydrocortisone Na-succinate	-	-	-
Methylprednisolone Na-succinate[a)]	-	-	-
Lidocaine	-	-	-
Diazepam	+	-	-
Nitroglycerin	-	-	-
Benzylpenicillin	-	-	-
Ampicillin	-	-	-
Erythromycin[a)]	-	-	-
Gentamicin	-	+	-
Chloramphenicol	-	-	-
Urokinase	-	-	-

+ = Solution stays clear , - = Solution precipitates

* = 50 % loss off efficiacy when adding iopromide corresponding 170 mg Iodine/ml

Table. 13. Data on interactions found in literature [76, 77]

Effects on blood coagulation

Nonionic contrast media come closer to the ideal of completely pharmacologically inert substances than ionic contrast media. Ionic contrast media inhibit enzymes involved with blood coagulation as well as other processes more strongly than nonionic X-ray contrast media.

Ionic X-ray contrast media are
- more anticoagulative [78]

Nonionic X-ray contrast media are
- less anticoagulative [78]

Sample	Coagulation time in sec.
Plasma without additives	11 (10.5–10.9)
Plasma + physiol. NaCl	12 (11.9–12.0)
+ Angiografin	68 (68.0–69.5)
+ Ultravist-300	17 (16.4–16.8)

Table 14. Thromboplastin time of human plasma without and with the addition of 25 volume percent test solution; n = 4, mean and 95 % confidence limits

The anticoagulative effect of contrast is viewed by some radiologists as additional protection against thrombus formation during imperfect performance of catheter angiography.

Laboratory examinations have shown significant differences in the anticoagulative effect of ionic (e.g., Angiografin) and nonionic contrast media (Ultravist) (table 14). The addition of small quantities of heparin to nonionic X-ray contrast media ensures effective inhibition of blood coagulation, similar to that characteristic of ionic contrast media (fig. 20). It was shown that 5 IU heparin/ml Ultravist is sufficient to completely suppress the formation of thrombi under standard experimental conditions. Even with a volume of 300 ml heparinized contrast medium, no systemic anticoagulative effects should be expected. The good tolerance of the nonionic contrast medium remains unchanged.

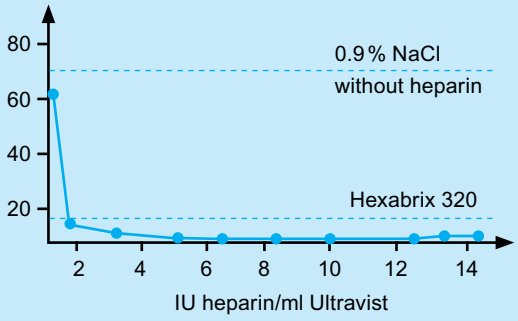

Fig. 20. Size of blood clots after 90 min. Incubation of 2 ml human blood in 10 ml plastic syringes with 5 ml test solution; not mixed, maximum contact surface