Aims and objectives

Investigation of the safety and diagnostic efficacy of iobitridol (Xenetix®, Guerbet, Roissy, France) in radiological and urological examinations.
Methods and materials

From 2009 to August 2013, as part of a non-interventional study, 77,826 examinations, generally i.v. urography (50.0%) or computed tomography (46.8%), were documented at 149 centres, in which iobitridol or iobitridol in the ScanBag® was routinely used. The patients examined (53.2% males, 46.8% females) were aged between 5 and 101 years (mean 58.6 years, standard deviation 15.6 years).

Patient data (anonymised), risk factors, kidney function, premedication, type of examination, injected contrast medium, image quality and diagnostic values as well as information on safety were documented using a standardised questionnaire. In addition, estimated glomerular filtration rate (eGFR) was calculated using the Cockroft-Gault formula, provided that age, weight and serum creatinine were known.

All analyses were carried out in IBM SPSS Statistics 20 (IBM Corporation, Armonk, New York). The data were descriptively analysed. Relative and absolute frequencies were reported for each variable. Constant variables were classified in advance. For constant variables, additional statistical indicators (mean, standard deviation, number of valid cases, minimum, maximum, 5th percentile, 50th percentile, 95th percentile) were calculated. In case of missing data, in addition to the analysis based on all cases, additional adjusted results were calculated based on the valid cases and listed in the table of results. Unless otherwise specified, the adjusted results were listed in the results section. Relationships in crosstabs were checked using Pearson's chi-square test or Fisher's exact test.
Results

30.5% of the patients were at-risk patients. In these patients, at least one risk factor was documented. The most common risk factors were hypertension (10.7%), allergies (9.7%), diabetes mellitus (6.6%) and thyroid disorder (5.5%). Risk factors were observed more frequently in females than in males (32.5% vs. 28.9%). Allergies (12.0% vs. 7.6%; \( p < 0.001 \)) and thyroid disorders (8.4% vs. 2.9%; \( p < 0.001 \)) were more common in females than males. 309 of the 77,826 patients had experienced previous contrast medium reaction (0.4%).

In 12.3% of the patients, the eGFR was < 90 ml/min (eGFR 60-89 ml/min: 9.1%, eGFR 30-59 ml/min: 3.1%, eGFR < 30 ml/min: 0.1%).

The patients were injected with a mean of 86.6 ml iobitridol (standard deviation 19.2). In computed tomography, a greater volume on average was injected than in i.v. urography (90.3 ml vs. 83.5 ml). Iobitridol was most frequently administered at a concentration of 300 mg iodine/ml (85.6%). Iobitridol at a concentration of 350 mg iodine/ml and 250 mg iodine/ml was administered to 14.2% and 0.2% of the patients, respectively.

A diagnosis was possible in 99.6% of the patients. Diagnostic efficacy was approximately equivalent in computed tomography and i.v. urography (99.9% vs. 99.3%). In patients with an eGFR < 60 ml/min, diagnostic efficacy was slightly lower than the overall average (99.1% in the patient group with an eGFR between 30-59 ml/min and 98.2% in the patient group with an eGFR < 30 ml/min).

Image quality was good or very good in 96.6% of the examinations. The percentage of examinations with good or very good image quality was higher in computed tomography than in i.v. urography (98.1% vs. 95.2%).

Adverse reactions occurred in 408 of 77,826 patients (0.52%) (computed tomography 0.54%, i.v. urography 0.49%). Predominantly mild to moderate adverse reactions were observed at a frequency of uncommon to very rare. There was one uncommon (1 to 10 patients in 1,000) adverse reaction (nausea), 14 rare (1 to 10 patients in 10,000) adverse reactions and 83 very rare (less than 1 patient in 10,000) adverse reactions.

Severe adverse reactions were observed in 22 patients (0.028%) (cardiac disorders (2 patients, 2 indications), eye disorders (3 patients, 3 indications), gastrointestinal disorders (9 patients, 13 indications), general disorders and administration site conditions (5 patients, 6 indications), immune system disorders (5 patients, 5 indications), nervous
system disorders (4 patients, 4 indications), psychiatric disorders (1 patient, 1 indication), respiratory, thoracic and mediastinal disorders (9 patients, 11 indications), skin and subcutaneous tissue disorders (9 patients, 11 indications), vascular disorders (6 patients, 6 indications)). As far as is known, all patients had recovered after the examination.

The adverse reaction rate in patients with an eGFR < 90 ml/min of 0.48% was below the overall average. No increased adverse reaction risk for patients with an eGFR < 90 ml/min was demonstrated.

Adverse reactions occurred more frequently in patients with allergies or previous contrast medium reaction (both p < 0.001). In the patient group with allergies, adverse reactions occurred in 1.29% of females and 0.91% of males. No increased risk of adverse reactions in females was demonstrated (p = 0.119). No increased risk of severe adverse reactions was demonstrated in patients with allergies (p = 0.358) or with previous contrast medium reaction (p = 0.916).

Adverse reactions occurred more frequently in females than males (0.65% vs. 0.42%; p < 0.001).

This correlation was retained when the patients with allergies were excluded from the calculation. The adverse reaction rate was reduced in the patient group without allergies to 0.56% in females and to 0.38% in males.
Fig. 1: Figure 1: The most common risk factors differentiated according to males and females.

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Fig. 2: Figure 2: The most common adverse reactions
Fig. 3: Figure 3: Observed and expected adverse reactions in males and females
Conclusion

Iobitridol is a safe contrast medium for radiologic and urological examinations with a high diagnostic efficacy, even in patients with an eGFR < 60 ml/min. Diagnosis using CT was virtually 100% (99.9%) and 99.3% in i.v. urography. In total, the adverse reaction rate is low and severe adverse reactions are very rare. In patients with allergies the adverse reaction rate is equally high in males and females, whereas in patients without allergies significantly more adverse reactions occur in females than in males. The reason for this fact remains unclear. Maybe there is a still unknown "hidden" factor in females, which is responsible for the higher adverse reaction rate and should be part of future studies.
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