

CONCEPTION OF CREATING X-RAY CONTRAST MEDIUMS OF THE NEW GENERATION

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ABSTRACT

The objective of the present investigation is to create X-ray contrast medium of new generation with both perfect magneto-directing properties and X-ray contrasting. Magnetic features and X-ray contrast properties of diagnostic mediums have been studied in research in vitro. The contents of X-ray of new generation medicine on the base of highly dispersed barium hexaferrite for X-ray-diagnostic of gastrointestinal tract was substantiate. X-ray contrast properties of this medium is in 1.55 times better than traditional barium sulfate suspension with mass fraction of 30% and, thanks to its magnetic properties, it can localize the contrast substance in the required area of gastrointestinal tract.

Keywords: Barium hexaferrite, X-ray diagnostics, Magneto-directing X-ray contrast medium

INTRODUCTION

Gastric cancer (GC) is one of the most widespread oncological diseases. Mortality rate from GC always occupies the second position in the ranking during many years, inferior only to lung cancer. Gastric cancer was the leading cause of cancer death in men and third leading cause of cancer of women [1,2]. Early diagnostics of the disease is a basis for the following effective treatment. Average 5 years probability to survive of the patients after surgical operation on GC is 9.6-11.7%. In comparison, this rate reaches to 80-100% in case of surgical treatment on early stages [3,4].

Solid changes in diagnostics of GC have appeared during recent decades. For instance, wide-embraced endoscopy which is based on fiber optics and is used to get biopsy material from mucous tunic for histological studies is made. However, during this period early diagnostics has not become perfect still according to data analysis [5]. Many authors [4,5] explain this fact with rapid growth of cases of diffuse forms of GC (to 46%) in gastrooncology in recent years. These forms usually locate in the midst of tunics and they cannot be noticed on the surface of mucous tunic. As a result it reduces the opportunities of endoscopy and considerably increases a role of classic radiology [6]. In Japan modified X-ray methods have been chosen as main screening test for GC diagnostics instead of endoscopy. This experience indicates the effectiveness of X-ray examination: 47% cases of GC are detected on early stages [6].

Rapid evolution of technologies has changed status of traditional X-ray diagnostics with a help of modern improved technological facilities. Using of modern equipment, digital technologies, electronic image processing helps to reduce radiation-absorbed dose considerably [4-6].

X-ray diagnostics can be improved to a considerable extend by providing artificial contrasting, such as using definite chemical compounds which make it possible to get images of anatomic structures, that raises value of the obtained information [3-5].

Usually aqueous suspension of barium sulfate with mass fraction 30% is used for X-ray diagnostics of diseases of gastrointestinal tract. Simple aqueous suspension of barium sulfate without any improvement of its physicochemical properties makes insufficient contrasting of gastrointestinal tract. Consequently, it reduces abilities of X-ray examinations and early diagnostics is not assured.

In this cases X-ray contrast medium with magneto-directing properties possess advantages [7,8]. Their using permits to control movements of X-ray contrast mixture with a help of external magnetic field (MF), to move teleologically, to keep in necessary zone of stomach and allows to lower a dose of X-ray contrast medium (XrCM), to detect mechanical features of tissues (method of magnetic palpation). In oncological practice it would promote a better diagnostics; it would make more exact localizations of tumors in organs and

cavities, X-ray diagnostics of which is difficult while using traditional X-ray contrast medium.

Purpose is to substantiate composition and create XrCM of new generation with both perfect magneto-directing properties and better X-ray-contrasting than traditional aqueous suspension of barium sulfate with mass fraction 30% for diagnostics of diseases of hollow organs of gastrointestinal tract.

MATERIALS AND METHODS

High-dispersive powder of barium hexaferrite $\text{BaFe}_{12}\text{O}_{19}$ as magnetic component synthesized by me [9], aqueous solution of sodium amidotrizoate with mass fraction 76% in the form of a medicine "Triombrast" (GSC "Farmak", Ukraine), apple pectin [10,11] have been used for creating samples of magneto-directing X-ray contrast mediums (MXrCM). From 14 to 70 g of aqueous solution of pectin with mass fraction 3% have been mixed in glass, and then from 10 to 35 g of high-dispersive powder of barium hexaferrite have been added. The mixture has been mixed in 60°C conditions during 15 minutes. From 0 to 56 g of medicine "Triombrast" (GSC "Farmak", Ukraine) have been added to the received suspension. Dispersion of sample MXrCM was held with a help of ultrasound dispergator USDN-2T at frequency 44 kHz during 1-3 minutes.

Bridge method has been used for studying of magnetic features of samples of MXrCM. Experimental comparative studying of the X-ray contrast properties of diagnostic mediums have been made in research in vitro at the Institute of therapy named by LT Malaya Academy of Medical Science (AMS) of Ukraine. The samples of the new MXrCM, aqueous suspension of barium sulfate with mass fraction 30% and MXrCM offered by Russian scientists – Patent of USSR №1061821, published 23.12.83 (30% of magnetite, 30% of oleic acid, 60% liquid petrolatum) have been mixed in standard test tubes with diameter 15 mm. X-ray images have been made by diagnostic device Iconos R 100 (Siemens, Germany) та CT HiSpeed CT/e Dual (General Electric, USA).

RESULTS AND DISCUSSION

While substantiating of concentration of barium hexaferrite it was taken into consideration that it in a fixed amount must assure magnetic and X-ray contrast properties. It must have necessary level of magnetic features (saturation magnetization is 300 kA/m) in conjunction with better X-ray contrasting in comparison with magnetite Fe_3O_4 . Attenuation index of X-rays for $\text{BaFe}_{12}\text{O}_{19}$ is 1.746 sm^2/g , and for Fe_3O_4 it is 0.869 sm^2/g . Owing to adding barium hexaferrite, XrCM achieves magneto-directing properties, such as ability to follow external MF. As seen from the graphical dependence (Fig. 1), magnetization of the samples of XrCM increases with growth of external MF before reaching definite saturation (direct relation). Value of saturation magnetization of the sample №1 (25%) equals 15 kA/m, for the other samples №2 and №3 (with concentration 30% and 35%) - 19 kA/m and 21 kA/m respectively. The difference of saturation magnetization between

samples №1 and №2 is 21%, while it is just 9.5% between samples №2 and №3. Decrease of the difference of saturation magnetization is conditioned by closer magnetic dipole interaction of particles due to their high concentration. Significant influence of internal MF of magnetic component leads to compensation of native magnetic moments of particles. It has an effect on a value of saturation magnetization and leads to loss of stability of suspension. This fact was mentioned by many authors. [12].

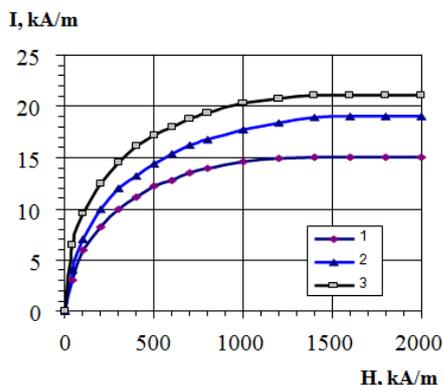


Fig. 1: Graphics of saturation magnetization of samples of MXrCM

1 – concentration of barium hexaferrite 25%, 2 – concentration of barium hexaferrite 30%, 3 – concentration of barium hexaferrite 35%

On the basis of conducted experimental investigations barium hexaferrite is recommended to be part of new MXrCM with mass fraction less than 30%. The increase in quantity of $\text{BaFe}_{12}\text{O}_{19}$ does not effect considerably on magnetic features of MXrCM, but it leads to loss of stability of suspension.

Barium hexaferrite as magnetic component is used for new MXrCM in high-dispersive state. After size reduction of particles, surface energy grows and aggregation increases. If surface-active agents are added in disperse medium of suspension of barium hexaferrite, it is possible to force dispersion of substance, to improve wetting and to guarantee aggregative stability of suspension. Requirements to stabilizers of new MXrCM are exceedingly high: they shouldn't irritate a mucous tunic of stomach, they must be indifferent and mustn't effect on pH of medium. In my opinion, apple pectin satisfies these requirements. It is a high-molecular substance, which is polygalacturonic acid, partly etherified by methanol according to chemical

structure [10,11]. In contradistinction from methylcellulose and sodium carboxymethylcellulose, solutions of pectin are resistant to acid medium of gastric juice. In addition, solutions of pectin have a delectable flavor, bactericidal features to pathogenic agents for gastrointestinal tract (*Shigella*, *Salmonella*, *Vibrio*) and any incidents of hypersensibility to pectin are not mentioned.

Adding pectin to suspension of new MXrCM makes suspension more stable. 3% aqueous solution of pectin is the most convenient and technological. Due to pectin's ability to complex formation with metal ions, it is assured a fixation of ions Fe^{3+} and Ba^{2+} , that were produced after dissolution of high-dispersive powder of barium hexaferrite in acidic medium. These ions form an insoluble complex and they are excreted from organism. Solution of sodium amidotriozate with mass fraction 76% in the form of a medicine "Triombrast" (GSC "Farmak", Ukraine) plays the role of a liquid carrier of a suspension of MXrCM. This component also potentiates X-ray contrast properties of the offered MXrCM, because it belongs to water-soluble triiodized γ -ray contrast mediums. According to value of DL_{50} (11.75 g/kg), this medicine belongs to a group of "almost nontoxic" substances. Medicine "Triombrast" is used intravenously for angiography and excretory urography. An intracavitary introduction of 76% solution of "Triombrast" after dilution in water (1:2) is possible to be used for X-ray examinations of urinary bladder, renal pelvis and perforated gastric ulcer.

Taking into account the fact that 76% solution of "Triombrast" is used for X-ray examinations of hollow organs of gastrointestinal tract after dilution in water (1:2), it is offered to add it to a composition of a new MXrCM in quantity not more than 50 mass percent.

By this means, this composition of a new MXrCM for X-ray examination of hollow organs of gastrointestinal tract has been substantiated (Table 1)

Table 1: The composition of a new MXrCM

Ingredients	Mass fraction (%)
barium hexaferrite	30.0
76% solution of sodium amidotriozate	50.0
3% aqueous solution of pectin	20.0
Total	100.0

Digital processing of X-ray images of contrast agents (Fig. 2) makes it possible to compare an optical density of X-ray photograph of test tubes with contrast mediums and to define a quantity define a value of radiodensity of the studied substances (in Hounsfield units (HU)). (table 2)



Fig. 2: X-ray images of samples of contrast mediums *in vitro* (from left to right):

empty test tube; sample №1; sample №2; sample №3; sample №4; sample №5

Table 2: X-ray contrast properties of diagnostic forms

S no.	Sample of X-ray contrast medium	Compeering densitometry of optic density (%) Mean±SEM	Contrast quantity (HU) Mean±SEM
1.	magnetite 30 g oleic acid 30 g liquid petrolatum 40 g	16.9 ± 0.5	840 ± 17
2.	barium hexaferrite 30 g 3% aqueous solution of pectin 70 g	26.7 ± 0.8	1323 ± 26
3.	76% "Triombrast" (soluted by water 1:2)	69.6 ± 2.0	3450 ± 69
4.	30% aqueous suspension of barium sulfate	64.5 ± 1.9	3194 ± 96
5.	barium hexaferrite 30 g 76% "Triombrast" 50 g 3% aqueous solution of pectin 20 g	100.0 ± 3.0	4955 ± 99

All the results were expressed as Mean ± S.E.M (n=5). By employing one way ANOVA, all data were found to be statistically significant (p<0.01)

The results of the researches showed that new offered MXrCM has the best X-ray-contrast properties: it is in 5.8 times better than MXrCM offered by Russian scientists and in 1.55 times better than aqueous suspension of barium sulfate with mass fraction 30%, that is a traditional X-ray contrast medium for X-ray diagnostics of diseases of gastrointestinal tract.

CONCLUSION

1. On the basis of conducted researches, a composition of XrCM of new generation with perfect magnetic properties for X-ray examinations of hollow organs of gastrointestinal tract has been substantiated.
2. Experimental comparing researches of X-ray contrast properties of diagnostic mediums in researches in vitro proved that offered XrCM of new generation is the most effective one: it is in 5.8 times better than MXrCM offered by Russian scientists and in 1.55 times better than traditional aqueous suspension of barium sulfate with mass fraction 30%

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