STUDY OF INTRAOPERATIVE INDOCYANINE GREEN ANGIOGRAPHY EFFECTIVENESS FOR IDENTIFICATION OF PARATHYROID GLANDS DURING TOTAL THYROIDECTOMY

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The most common complications during thyroidectomy are hypocalcemia and recurrent nerve palsy. According to recent studies, postoperative hypocalcemia rates around 15% to 30% for transient hypocalcemia, and 1% to 7% for definitive [1,2]. Hypocalcemia develops due to accidental damage to the parathyroid glands (PG) or their devascularization [2]. Such factors like small size and variable location of the PG significantly complicate their visualization and can lead to their injury, even with careful dissection by an experienced surgeon [2-4]. Although most authors believe that one intact gland is sufficient to maintain normal levels of serum calcium and hormones in the blood, preserving as many parathyroid glands as possible minimizes the incidence of postoperative hypoparathyroidism [1-3] Autotransplantation of devascularized parathyroid glands is a good method of restoring their function. But a visual assessment of their blood supply is subjective and may differ from the present situation.

Recently, one of the most popular methods for the detection PG and assess their vascularization has become near-infrared (NIR) fluorescence imaging with indocyanine green (ICG) angiography [3-9]. The PG are more vascularized than the surrounding tissues and, due to this, they exhibit strong fluorescence on indocyanine green angiography [3].

This study was conducted to determine whether intraoperative ICG angiography with NIR fluorescent imaging should be used routinely in total thyroidectomy.

Aim was study NIR fluorescent imaging with intraoperative parathyroid gland ICG angiography to help identify and preserve parathyroid glands during total thyroidectomy in order to avoid postoperative hypocalcemia.

Material and methods. For period from 1 April 2017 to 10 September 2019, 58 patients were underwent total thyroidectomy in Odessa regional hospital.

By randomization all patients were divided into two groups: in the first group (control group), 28 patients underwent standard total thyroidectomy, in the second group (ICG group) 30 patients underwent NIR-assisted total thyroidectomy with ICG angiography.

The indications for surgery were following: 1) thyroid cancer; 2) multinodular goiter 3) Graves disease.

Parathyroid autofluorescence was detected using a near infrared/indocyanine green endoscopic system (Karl Storz, Tuttlingen, Germany). The system comprises a high-end full high-definition camera system (H3-Z 3-Chip Full HD camera, Karl Storz;) connected to a 10-mm 0-degree indocyanine green laparoscope (Hopkins™ II, Karl Storz).

ICG angiography were applied during the surgical procedure for all participants of the first group. General anesthesia with endotracheal intubation was administered to all patients. A 4 to 5 cm length Kocher transverse collar incision, was made 1 cm below the cricoid cartilage. The strap muscles were divided in the midline along the entire length until the thyroid gland was exposed. The sternohyoid muscles were separated from the underlying sternothyroid muscle by dissection until the internal jugular vein and nerves are identified.

The inferior thyroid vessels were dissected and divided as close to the surface of the thyroid gland as possible to minimize devascularization of the parathyroids or injury to the recurrent laryngeal nerves.

ICG preparation was injected intravenously by the anesthesiologist with a standard dose of 15 mg. The parathyroid glands took up the dye within 2 minutes and remained fluorescent up to 15 minutes. After injection ICG, the video was recording by the assistant of surgeon in real time.

In the ICG angiography, the parathyroid fluorescence intensity (FI) depends on the amount of ICG took up by the parathyroid. The mechanism for the parathyroid to take up the dye should be related to the abundant blood supply of endocrine organs. Thereby, FI of the parathyroid reflects vascularization of the parathyroid. In ICG angiography applications, the different grades of grey can be applied as the standard of different levels of the parathyroid function. The parathyroid glands were scored from score 0 to score 2 according to the FI after ICG angiography. Score 0, score 1 and score 2 represents weak FI, moderate FI and strong FI respectively. For the parathyroid glands which were visually evaluated as well vascularized, but were valued as devascularized in ICG angiography, the surgeons will conduct the parathyroid autotransplantation.

Serum calcium and parathyroid hormone (PTH) levels were compared between the two groups of patients in 1, 3 -10 days after surgery and then 1, 3, 6 months later.

Results and discussion. Patient demographics were similar between both groups. No differences existed in comorbidities, including cardiac, pulmonary, vascular, or renal disease (Table 1). In the first group, on based of a visual assessment of the PG, autotransplantation the PG were conduct in only 4 cases (in 3 cases - one gland, in one case - 2 glands). In the second group, autotransplantation was performed in 11 patients (in 8 cases - one gland, in 2 cases - two, in one case - 3).

Hypocalcaemia (calcium level below 200 mmol/l) was observed in either group. The transient postoperative hypocalcemia was observed in 5 patients of the control group (17,86 %) and in the 2 patients of ICG group (6,67 %) on 5-10 postoperative days. There was no statistical difference in calcium or PTH levels between the groups on POD 30 (Table 2). But in the first group 1 patient at 3 months after surgery had hypoparathyroidism. Two patients in the control group experienced typical symptoms of hypocalcaemia but had PTH levels in the normal range on POD 30, without calcium supplementation. One had a calcium level of 2·05 mmol/l, PTH level of 3·7 pmol/l and mild finger paraesthesia, which rapidly improved after oral calcium supplementation (dose 1 g). The other patient also experienced finger paraesthesia, with calcium and PTH values of 2·29 mmol/l and 5·2 pmol/l respectively. The symptoms improved a few minutes after oral calcium supplementation (1 g). For patients in the control group, standard oral supplementation kept calcium levels within normal limits; higher doses or additional active vitamin D were never needed.

Table 1. Demographic and Clinical Features of Patients

Demographic and Clinical Features of Patients		
	Control group (n=28)	**ICG group (n=30)**
Age (years)a	43.24 (12.15)	44.38 (11.22)
Gender ratio (M:F)	10:18	12:16
ASA score	1.88 (0.33)	1.87 (0.42)
Indication for surgery		
Multinodular goiter	23	19
Thyroid cancer	7	4
Graves disease	2	3
Duration of hospital stay (days)a	2.93 (1.47)	2.71 (1.32)

ASA = American Society of Anesthesiologists; F = female; M = male. Numerical values in parentheses are percentages or specifically indicated. aValues are mean (SD)

Table 2. Postoperative results

	Control group (n = 28)	**ICG group (n = 30)**	**Difference** b	***P* value**d
Calcium (mmol/L)a				
POD 1	2.218 (0.011)	2.22 (0.013)	−0.0032 (−0.0132, 0.0071)	.562
POD 30	2.214 (0.026) c	2.332 (0.024)	−0.0046 (−0.0175, 0.0082)	.463
PTH (pmol/L)a				
POD 1	3.224 (1.281)	3.198 (1.267)	−0.01613 (−0.03972, 0.01213)	.529
POD 30	4.331 (1.291) c	4.317 (1.282)	−0.01714 (−0.04975, 0.01547)	.246

POD = postoperative day. aValues are mean (SD). bValues in parentheses are 95% confidence intervals.

cCalcium and parathyroid hormone (PTH) levels were significantly higher on POD 30 than POD 1 in the ICG and control groups (mean difference in calcium 0.0967 [95% CI 0.0924 to 0.1008] mmol/L, P<.001; mean difference in PTH 1.088 [0.984 to 1.192] pmol/L, P<.001). dPaired t test.

Thyroid and parathyroid surgery has become very safe during the last century [1-3]. However, hypoparathyroidism remains a current concern, with significant, 1-30% rates of post-thyroidectomy hypoparathyroidism [1,2]. There is currently no gold standard on how to detect and preserve parathyroid glands and their vascularization during thyroidectomy [5,6]. Both the blood supply and the localization of parathyroid glands are crucial factors for the preservation during surgery but anatomical variability in this area is high demanding great experience and flexibility in the surgeon. Some parathyroids receive their blood supply directly from the thyroid gland (8,2 %), which makes it very difficult to preserve [2].

New optical-based techniques, without radiation, have been developed to help detect parathyroid glands (in particular autofluorescence) and confirm their vascularization (in particular ICG angiography) [10,11]. The angiography imaging system is essential for a wide range of surgeries [8,10,11]. An initial objective of the study was to identify that ICG angiography has emerged as powerful platforms for predicting the function of the parathyroid immediately after thyroidectomy and at the same time, the fluorescence imaging system is fast becoming a key instrument in the thyroid and the parathyroid surgeries [12]. The combination of NIR-AF with ICG can highlight not only the anatomy, but also the vascularization and, consequently, functioning of the glands. In fact, injecting ICG at the end of the procedure allows verifying the vitality of PGs and can be considered a valid predictor of postoperative calcium level as highlighted by different authors. In particular, Vidal Fortuny et al. highlighted that at least one well vascularized PG at the end of the surgical procedure is predictive of a normal postoperative PTH levels [3].

Data from several studies suggest that ICG administration may have some complications [13]. Recent work by researchers has established that some rare reactions like anaphylactic or urticarial reactions may occur. During the past 34 years, only 17 adverse reactions has been reported and no more information has become available on the ICG dye allergic reactions [14] What we know about ICG dye allergic reactions is largely based upon the fact that the ICG substance contains 5% of sodium iodine for solubility and the patients allergic to ICG were all iodine allergic and renal insufficient. But these reactions were reported to be 0.00167% and mostly occur in patients with history of allergy to iodides [14]. Accompanied with the anaesthesia team who are ready to treat allergic reactions, the ICG angiography possesses safety of a rather high degree.

With regard to autotransplantation of the parathyroid glands, on the one hand, what is considered ischemic PG requires replantation. But, on the other hand, replantation does not guarantee that it is accustomed to the new location and will function normally. Therefore, the best use of the system to ensure safe blood flow to the parathyroid gland is when dissecting the surrounding tissue. Therefore, ICG visualization not only of the identification of PG, but also for a more

reliable determination of the viability of the glands. This study has shown that intraoperative angiography with ICG is simple and reproducible. Although the laparoscopic imaging camera system is currently expensive, it produces high-quality images and can also be used in other surgical procedures, making the equipment more cost-effective.

Conclusion. Near-infrared fluorescent imaging with intraoperative parathyroid gland indocyanine green angiography is a safe and an easily repeatable method. This technique provides improved detecting and assessment of the perfusion of the PG. The need for autotransplantation of the PG can be determined more objectively using ICG imaging than simple visualization.

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SUMMARY

STUDY OF INTRAOPERATIVE INDOCYANINE GREEN ANGIOGRAPHY EFFECTIVENESS FOR IDENTIFICATION OF PARATHYROID GLANDS DURING TOTAL THYROIDECTOMY

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Postoperative hypocalcemia is a common complication of thyroidectomy. This problem is most often associated with accidental devascularisation or excision of the parathyroid glands (PG).

Aim was study near-infrared fluorescent imaging with intraoperative parathyroid gland indocyanine green angiography to help identify and preserve parathyroid glands during total thyroidectomy in order to avoid postoperative hypocalcemia.

For period from 2017 to 2019 years, 58 patients in Odessa regional hospital were underwent total thyroidectomy. Indications for surgery were multinodular goiter (n=42), thyroid cancer (n=11) and Graves' disease (n=5). By randomization all patients were divided into two groups: in the first group, 28 patients underwent standard total thyroidectomy, in the second group 30 patients underwent near-infrared-assisted total thyroidectomy with indocyanine green (ICG) angiography. Parathyroid autofluorescence was detected using a near infrared/indocyanine green endoscopic system (Karl Storz, Germany). Serum calcium and parathyroid hormone levels were compared between the two groups of patients in 1, 7 -15 days after surgery and then 3, 6 months later.

In the first group, on based of a visual assessment of the PG, autotransplantation the PG were conduct in only 4 cases (in 3 cases - one gland, in one case - 2 glands). In the second group, autotransplantation was performed in 11 patients (in 8 cases - one gland, in 2 cases - two, in one case - 3). The transient postoperative hypocalcemia was observed in 5 patients of the first group (17,86%) and in the 2 patients of second group (6,67%) on 5-10 postoperative days. In the first group 1 patient at 3 months after surgery had permanent hypocalcemia.

Near-infrared fluorescent imaging with intraoperative parathyroid gland indocyanine green angiography is a safe and an easily repeatable method. This technique provides improved detecting and assessment of the perfusion of the PG. The need for autotransplantation of the PG can be determined more objectively using ICG imaging than simple visualization.

Keywords: Total thyroidectomy, parathyroid glands, ICG angiography.

РЕЗЮМЕ

ЭФФЕКТИВНОСТЬ ИНТРАОПЕРАЦИОННОЙ АНГИОГРАФИИ С ИНДОЦИАНИНОМ ЗЕЛЕНЫМ ДЛЯ ОБНАРУЖЕНИЯ ПАРАЩИТОВИДНЫХ ЖЕЛЕЗ ВО ВРЕМЯ ТОТАЛЬНОЙ ТИРЕОИД-ЭКТОМИИ

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Послеоперационная гипокальциемия - частое осложнение тиреоидэктомии. Эта проблема чаще связана со случайной деваскуляризацией или удалением паращитовидных желез (ПЖ).

Целью исследования явилось определение флуоресцентной визуализации в ближнем инфракрасном диапазоне с помощью интраоперационной ангиографии паращитовидных желез с индоцианиновым зеленым для идентификации и сохранения паращитовидных желез при тотальной тиреоидэктомии и исключения послеоперационной гипокальциемии.

За период с 2017 по 2019 гг. 58 пациентам Одесской областной больницы выполнена тотальная тиреоидэктомия. Показаниями к операции были многоузловой зоб (n=42), рак щитовидной железы (n=11) и болезнь Грейвса (n=5). Путем рандомизации все пациенты разделены на две группы: в первой группе 28 пациентам выполнена стандартная тотальная тиреоидэктомия, во второй группе 30 пациентам выполнена тотальная тиреоидэктомия с применением флуоресцентной визуализации в ближнем инфракрасном диапазоне и введением индоцианинового зеленого. Аутофлуоресценцию паращитовидных желез определяли с помощью эндоскопической системы ближнего инфракрасного диапазона/индоцианинового зеленого (Karl Storz, Германия). Уровни сывороточного кальция и паратироидного гормона сравнивали между двумя группами пациентов спустя 1, 7-15 дней после операции, а затем спустя 3 и 6 месяцев.

В первой группе на основании визуальной оценки ПЖ аутотрансплантация проведена в 4 случаях (в 3 случаях - одна железа, в одном случае - 2 железы). Во второй группе аутотрансплантация выполнена 11 пациентам (в 8 случаях - одна железа, в 2 случаях - две, в одном случае - 3). Временная послеоперационная гипокальциемия наблюдалась у 5 (17,86%) пациентов первой группы и у 2 (6,67%) пациентов второй группы спустя 5-10 дней после операции. В первой группе у 1 пациента спустя 3 месяца после операции развилась перманентная гипокальциемия.

Флуоресцентная визуализация в ближнем инфракрасном диапазоне с помощью интраоперационной ангиографии паращитовидных желез с введением индоцианина зеленого является безопасным и легко воспроизводимым методом. Данный метод обеспечивает улучшенное обнаружение и оценку перфузии ПЖ. Необходимость аутотрансплантации ПЖ может быть определена более объективно с помощью визуализации индоцианином зеленым, чем простой визуализацией.

რეზიუმე

ტოტალური თირეოიდექტომიის დროს პარათირეოიდული ჯირკვლების იდენტიფიკაციის მიზნით წარმოებული ანგიოგრაფიის ეფექტურობა

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კვლევის მიზანს წარმოადგენდა თირეოიდექტომიის დროს ინტრაოპერაციულად ახლო-ინფრაწითელ დიაპაზონში ფლუორესცენცია (ICG) ანგიოგრაფიის დახმარებით პარათირეოიდული ჯირკვლების იდენტიფიცირება ოპერაციისშემდგომი ჰიპოკალციემიის თავიდან აცილების მიზნით.

2017-2019 წწ. ოდესის საოლქო საავადმყოფოში ჩატარებული იყო 58 ტოტალური თირეოიდექტომია. ოპე-რაციის ჩვენებას წარმოადგენდა: 42 პაციენტთან - მრავალკვანძოვანი ჩიყვი, 11 - ფარისებრი ჯირკვლის კიბო და 5 - გრეივსის დაავადება. პაციენტების რანდომიზირების შემდგომ გამოყოფილი იყო ორი ჯგუფი: I ჯგუფის პაციენტებს (n=28) ჩაუტარდათ სტანდარტული ტოტალური თირეოიდექტომია და II ჯგუფის პაციენტებს (n=30) - ტოტალური თირეოიდექტომია NIR ფლუორესცენციით და ICG ანგიოგრაფიის დახმარებით. პარათირეოიდული ჯირკვლების აუტოფლუორესცენცია ჩატარდა ახლო-ინფრაწითელი იოდიცინ მწვანის ენდოსკოპური სისტემის (Karl Storz, Germany) გამოყენებით. ორივე ჯგუფის პაციენტებში ოპერაციიდან 1, 7-15 დღეს და შემდგომ 3 და 6 თვეში მოხდა კალციუმის და პარათიროიდული ჰორმონის განსაზღვრა სისხლში.

I ჯგუფში პარათირეოიდული ჯირკვლის ვიზუალური დაკვირვების შედეგად პარათირეოიდული ჯირკვლის აუტოტრანსპლანტაცია შესრულდა 4 შემთხვევაში (3 შემთხვევაში - 1 ჯირკვალი და 1 შემთხვევაში - 2 ჯირკვალი). II ჯგუფში პარათირეოიდული ჯირკვლების აუტოტრანსპლანტაცია მოხდა 11 პაციენტთან (8 შემთხვევაში - 1 ჯირკვალი, 2 შემთხვევაში - 2, 1 შემთხვევაში - 3). ოპერაციიდან 5-10 დღის შემდეგ I ჯგუფის პაციენტებთან გარდამავალი ჰიპოკალციემია გამოვლინდა 5 (17,86%) შემთხვევაში, ხოლო II ჯგუფში 2 (6,67%) პაციენტთან. I ჯგუფში ოპერაციიდან 3 თვის შემდეგ 1 პაციენტს აღენიშნა პერმანენტული ჰიპოკალციემია.

ავტორებს გამოტანილი აქვთ დასკვნა, რომ ინტრაოპერაციულად წარმოებული NIR ფლუორესცენცია პარათირეოიდული ჯირკვლების ICG ანგიოგრაფიით არის უსაფრთხო და ადვილად შესასრულებელი პროცედურა. აღნიშნული მეთოდი უზრუნველყოფს პარათირეოიდული ჯირკვლის იდენტიფიცირებას და მისი პერფუზიის ადექვატურ შეფასებას. პარათირეოიდული ჯირკვლების აუტოტრანსპლანტაციის შემთხვევაში ICG ჩვენებით მისი ვიზუალიზაცია განიხილება მეტად ობიექტურად, ვიდრე მარტივი ვიზუალიზაცია.