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Review Article

Endoscopic Methods Used in Russia with Questionable Indications

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Abstract

This review is focused on bronchoscopy used in Russia with questionable indications in research and practice. Thanks to free online resources, recent textbooks are largely based on the international literature. However, some recommendations have been different from those used internationally. The application of bronchoscopy in asthma, bronchitis, pneumonia and tuberculosis is discussed here in some detail. Besides, a number of techniques applied with questionable indications are briefly delineated, including the overuse of cystoscopy in relation to the overdiagnosis of malignant and premalignant bladder lesions, endobronchial surfactant instillations in adults, laser therapy via bronchoscope in atrophic bronchitis and other conditions. Factors contributing to the persistence of suboptimal practices include partial isolation from the international scientific community, shortages of medical education, unavailability of many internationally used handbooks. The concept of informed consent has only been mentioned in recent studies. In order for human subjects to provide informed consent to participate in research, they must be fully aware of the risks involved and have the option to withdraw at any moment without facing consequences. Children need more protection. As much as possible, techniques utilizing anatomic models and audiovisual technologies must be used for training of specialists in endoscopy.

Keywords: endoscopy; bronchoscopy; bronchial asthma; tuberculosis; russia

Introduction

The previous reports on invasive methods used in Russia with questionable clinical indications [1-3] are updated and continued in this review. This article focuses on bronchoscopy (Bs), which has been used e.g. in patients with bronchial asthma despite the prevailing opinion that it provides little benefit in cases with usual clinical course. Furthermore, a brief description of Bs application in bronchitis and tuberculosis (Tb) is provided. Although uncommon, Bs-related risks and consequences are known [4-9]. Some patients have been exposed to needless risks when treatments are carried out without adequate indications. Thanks to free online resources, some recent Russian-language textbooks are based on the international literature. However, some of the guidelines in other manuals differed from those internationally used. Clinical recommendations are generally avoided here. This gave to the author a possibility to limit citation of international literature: the number of references supporting the narration is quite large already.

Methods

This is a narrative review based predominantly on the Russian-language literature in comparison with international sources. The research question was the adequacy of clinical indications of certain endoscopic procedures used in the recent past and, in part, until today. The search of literature was performed on the PubMed, on the Internet, in libraries and the electronic database eLibrary.ru. The following keywords have been used among others: bronchoscopy, endoscopy, Russia. The data from the literature have been reviewed and synthesized on the basis of the author's observations since the 1970s.

Results

International literature specifies only limited role for Bs in diagnosing and treating bronchial asthma, while asthmatics are at increased risk of complications from this procedure. Indications for Bs in asthma include persistent wheezing that fails to improve with bronchodilators and other therapies. The usual purpose of Bs is to explore alternative causes of the symptoms. Bs is sometimes applied when other diagnostic options have been exhausted [4,5]. In a well-known handbook on asthma, clinical indications for Bs are not mentioned at all [6]. In certain cases, bronchial lavage may be indicated in severe asthma [7-9]. In the Russian professional literature, the purpose of Bs in asthmatic patients was defined as determining connections between the illness and infection, location and characterization of inflammatory lesions [10,11]. The idea that non-specific inflammation is the main cause of asthma has persisted for ling time; while the goal of Bs was said to be its characterization [12,13]. Among other symptoms of asthma, copious bronchial secretions and mucopurulent sputum in a child ostensibly necessitate Bs with biopsy of bronchial mucosa [14,15]. The seminal monograph indicated that Bs is advisable "almost for all subacute and chronic respiratory diseases" in children [11]. Conditions that have been posited as indications for Bs included bronchitis, pulmonary or bronchial inflammation, asthma, dyspnea, diagnosed or suspected Tb, continuous coughing and expectoration [15-22]. Coughing lasting more than 4-6 weeks or a changed

coughing pattern in a smoker have been considered as strong indications for Bs [22]. The latter procedure was used and recommended for children and adults having asthma with both severe or mild course including remissions [15,23-31], as well as in bronchitis with symptoms of allergy and/or bronchospasm [23,29]. Bs was viewed as initial diagnostic tool for different types of asthma, being repeatedly used for monitoring [15,28]. Certain experts performed up to 15 Bs per treatment course for bronchospasm in a child [32]. Importantly, Bs in asthma led to complications more frequently than in other respiratory conditions. Nonetheless, the same experts reported in one paper ~400 Bs in 200 asthma patients, resulting in no changes of diagnoses [33]. Lev Ioffe and Fyodor Uglov were primarily responsible for the extension of indications for Bs [13,34-38]. Ioffe posited in official guidelines that "Bs must be undertaken in all pulmonary diseases" [34]. Uglov reporrted ~7,500 Bs performed at his institution both on minors and the elderly, mainly for inflammatory conditions such as bronchitis, pneumonia, and asthma (524 cases of the latter), stressing importance of dynamic monitoring of airway inflammation [13,36]. His conclusion was that Bs is essential for diagnostics of almost all respiratory conditions, recommendable also at early stages. Decisions regarding further treatment were to be made in light of the Bs results [36]. Resections of lung segments or lobes deemed abnormal by operators were carried out after a series of therapeutic endoscopies; more references and images are in the book [3]. This was considered a radical asthma treatment [13]. Uglov et al. pointed out effectiveness of therapeutic Bs as a treatment of moderate or severe bronchitis by performing up to six Bs for each therapy course [37]. In particular, symptoms of atrophic bronchitis, or mucosal atrophy, were deemed to be adequate indication for Bs [15]. In accordance with instructions by leading specialists, Bs has been performed in both children and adults with non-specific respiratory ailments, also at provincial hospitals and policlinics [37]. At that, challenges with local anesthesia have been noticed, necessitating general anesthesia for up to 25% of patients [39,40]. Significant discomfort might have been behind those "challenges" without any benefit for patients. Undoubtedly, Bs has been performed according to indications in many cases. However, the procedure was generally known to be used excessively both in practice and for research. Repeated Bs in children under local anesthesia led to psychological distress, caused damage to teeth, larynx, and bronchi [41]. It was evident for inside observers that widespread implementation of endoscopy occurred after a directive of healthcare authorities. Their meddling in research and practice has been known to take place. The authorities favored approaches suitable for large cohorts of patients. Moreover, a reason for the excessive use of invasive methods was the training of medical personnel [1,3]. As a result of the authoritative management style, suboptimal methods persisted for decades.

Laser treatment via Bs has been applied both in children and in adults for asthma, chronic pneumonia and bronchitis [42-46], including cases with mucosal atrophy after exposure to ionizing radiation [42,47-49]. Analogously to other forms of electromagnetic radiation, laser generates heat, which at higher energies may cause local damage especially in conditions of tissue atrophy. From the viewpoint of general pathology, atrophy would advance as a result of repeated injury. According to the international literature, main reasons for laser bronchoscopy include tumors and hemoptysis [50]. Moreover, bronchoscopic administration of nitric oxide (NO) has been employed in Tb, non-specific inflammatory disorders and bronchial asthma [15,51-53]. This technique has been described in the most authoritative "National manual" [22]. In the international literature, we have not found any accounts of NO use through bronchoscope, only via inhalation [54], which must be sufficient for a gas reaching alveoli without hindrance. The same is generally true for ozone therapy, where asthma, bronchitis, pneumonia and Tb are listed among indications [55,56]. Biopsies of bronchial mucosa were taken in connection with ozone therapy of asthmatics [57]. In the monograph titled "Therapeutic bronchoscopy in the complex therapy of respiratory organs" [15] several pages are dedicated to the ozone therapy without mentioning the method used. The method is described in an earlier book by the same expert: bronchoscopic instillations of ozonized saline [58]. It seems that, on the contrary to the past, some invasive procedures without clinical indications are disguised these days. There is abundant literature on ozone therapy in Russia. Note that ozone therapy lacks robust evidence of efficacy and poses safety risks. Regulatory agencies, such as the U.S. Food and Drug Administration (FDA), warn against its use due to toxic properties and lack of proven benefits at tolerable exposure levels [59]. Flexible and rigid bronchoscopes have been employed in chronic bronchitis and asthma in adults and children [14,60,61]. In cases of acute pneumonia in children, Bs was purportedly aimed at assessing the nature of bronchial mucosal inflammation. In chronic pneumonia, Bs was considered necessary with the same rationale as well as to rule out Tb and congenital abnormalities [10]. Recent papers have advocated Bs for pediatric pneumonia and other inflammatory disorders with duration ≥4 weeks [21,62,63]. Another doubtful indication has been a round pulmonary shadow [18,21,22,62,64-66]. Even with improvements in Bs technique, its diagnostic performance for pulmonary nodules is still lower than that of trans-thoracic aspiration [67]. As discussed above, another questionable suggestion is the sweeping endorsement of Bs for all patients suspected of having "chronic non-specific" or obstructive lung disease [68,69]. Below are listed further examples of excessive endoscopy application, both for research and for practical purposes. Bs was used as a screening method for chronic non-specific respiratory conditions such as bronchitis and asthma, found in approximately 4% of children residing in the areas of Moscow province with industrial air pollution [70]. Furthermore, Bs was utilized as a screening modality for dust-exposed workers including both healthy ones and those having mild respiratory derangements, being performed repeatedly to assess dynamics [71,72]; in atrophic and other kinds of bronchitis, in acute and chronic pneumonia [15,73-76], for instance, among army conscripts with suspected pneumonia (reported 1478 procedures in 977 individuals ~19 years old) [77]. A series of studies with the excessive use of cystoscopy and "mapping" biopsies with overdiagnosis of microinvasion, in situ and precancerous urinary bladder conditions [78-81] has been addressed previously [82] with reproduced histological images [83]. The topic of cystectomy is avoided in the papers discussing carcinoma in situ, microinvasion and severe dysplasia [78-81]. Anyway, cystoscopies and "mapping" bladder biopsies were carried out without adequate indications. The overuse of renal biopsies resulting in overtreatment has been highlighted previously [3,82]. A recent study utilized and endorsed Bs with biopsies in renal insufficiency (end-stage kidney disease) [84] without any conceivable benefit for the patients. Endoscopic examinations of the alimentary tract have been conducted in the same condition without clear indications [38]. Lavage fluid collected via Bs from individuals with lung cancer and those with Tb (including solitary tuberculomas) was examined by infrared spectral analysis for research with no comprehensible implications for theory and practice [85]. Bronchial biopsies were obtained from patients with histologically confirmed lung cancer; while the quality of histological specimens was poor [49], implying discomfort without affecting treatment and outcomes (some images are reproduced and commented in [1,3]). Certain histopathological descriptions have raised doubts, like the atrophy of bronchial mucosa in asthma patients including children. For example, atrophy of varying degrees was described in ~80% of pediatric patients [60]. This sounds unusual for a pathologist. Excessive surgical radicalism in Tb and other respiratory conditions has been

discussed previously [1,3]. The average number of therapeutic Bs per Tb patient increased from 2 in 1995 to 5.6 in 2015 [53]. As before, emphasis is placed on the important role of Bs in the diagnosis, monitoring and management of Tb [18]. In many institutions and research cohorts, Bs was employed for all types of Tb, including localized forms (tuberculomas) also in children [86-94]. Bs has been used as a part of the diagnostic process for suspected Tb with the sputum negative for Mycobacteria, including suspected primary Tb in infants [10]. Bs served as a screening tool for Tb in patients with subfertility, both with positive and negative tuberculin tests [95]. Other studies employed the procedure as a second-step screening technique for Tb in children [96]. Of note, there are less invasive diagnostic methods for the above-named purposes e.g. gastric aspiration and induced sputum [97-99]. The Russian Ministry of Health instructed to perform up to 32 therapeutic Bs per each treatment course in patients with destructive Tb [100], whereas the principle of informed consent has not always been clearly understood and adhered to. Patients with alcohol use disorders, diagnosed or suspected to have comorbidity of Tb (including smear-negative cases), have been treated with Bs; while the treatment was sometimes compulsory or based on misinformation of patients [3]. In particular, endoscopic and surgical biopsies have been taken from supposed alcoholics for research; reviewed previously [101,102]. The procedural tended to be lower in supposed alcoholics; in particular, some of them were infected with viral hepatitis. Of note, viruses can be transmitted by endoscopy [103]. Not surprisingly, the incidence of hepatitis B was found to be five times higher in Tb patients than in the general population of Russia [104]. The enhanced frequency of viral hepatitis or of its markers in Tb patients including children has been reported [105]. Endoscopic assessment of treatment results has been applied in pulmonary Tb also with non-specific bronchial inflammation [15,64,66,106]. The international literature suggests that in smear-negative Tb, bronchoscopy's role should be confined to patients who do not respond to therapy and/or those with a strong suspicion of alternative diagnosis [67]. The I.M. Sechenov Medical Academy (presently deemed University) is a prominent establishment known for authoring textbooks and monographs on endoscopy, the latter used extensively for diagnostic, therapeutic and scientific purposes. As previously mentioned, Bs was applied in pneumonia, bronchitis, and asthma [107,108], whereas complications have been observed [109]. In particular, endoscopy with biopsy was broadly used for research in pediatric immunopathology [110-114]. As noted earlier, bronchial biopsy samples have been utilized for investigation, with morphometric and other quantitative parameters changing according to the authors' concept [49,115,116]. For instance, molecular and histochemical markers of inflammation were influenced in a similar way both by medical and surgical therapies of bronchial asthma despite different mechanisms of action [117]. The surgical asthma treatment with questionable indications are discussed in [1]. The concept of informed consent has not always been adequately understood and followed, corresponding statements appearing only in recent publications. For example, in a research where Bs was carried out on children with moderate to severe asthma, informed consent was acquired from parents or caregivers [118], who could have been misinformed about indications. There has been a stereotype: post-graduate students and doctoral candidates came to Moscow and other centers from different parts of the Russian Federation and adjacent countries, paying for preparation of specimens, literature review, etc. Some patients entering the studies were misinformed about clinical indications. Certain researchers planning emigration completed their dissertations under time pressure. For example, endoscopies with intestinal biopsies were performed in infants to complete the research under guidance of Moisei Kuberger, e.g. telling to the mother that it is necessary to rule out malabsorbtion [119]. Certain individuals (Aleksandr Kantsedik) recruited patients including children for suchlike research. Besides, Kuberger applied and recommended endoscopic laser therapy of non-bleeding duodenal ulcers in children [120,121], which is generally at variance with the international practice. Patented bronchoscopic techniques included notable examples. Monitoring chronic catarrhal bronchitis through serial bronchial washings collected via Bs every other day [122]; diagnostics of bronchitis in children and adults, including laser treatment for "atrophic bronchitis deformans" [123-125]; management of pulmonary Tb with endobronchial instillations of surfactant solutions derived from bovine lungs or human amniotic fluid every other day for 3-8 weeks [126]. Note that exogenous surfactant may have physical sense within aerated alveoli; while in bronchi it is a foreign substance that must be expectorated by the patient [127].

Discussion and conclusion

The overuse of endoscopy may occur worldwide. According to an estimate, 30% or more of the procedures are performed in certain clinical settings with questionable indications [128]. In Russia, some invasive procedures are used more frequently these days. As mentioned above, between 1995 and 2015, the average number of therapeutic Bs per Tb patient increased from 2 to 5.6 [53]. Excessive use of surgery has been discussed previously [1,3]. For example, the overuse of gastrectomy (resection) for peptic ulcers is reappearing today, notably, in military-medical institutions [129]. In recent publications, gastrectomy has been designated as the most frequent, main or singular surgical treatment of gastric ulcers [129-132]. As before, appeals to "radicalism" can be heard, advantages of early surgery for uncomplicated ulcers being emphasized [129,132]. The military needs trained surgeons. Of note, military and medical ethics differ from each other. The relatively brief life expectancy in Russia is a strategic advantage since it requires fewer healthcare expenditures and retirement funds. The ethical and legal foundations of medical practice and research are neither sufficiently understood nor adequately followed in Russia. The designation "deontology" is frequently applied to medical ethics in this country. Textbooks and monographs on deontology tend to address the topic superficially, offering truisms and general statements but lacking task-oriented instructions. Factors contributing to the persistence of suboptimal practices include partial isolation from the international scientific community, shortages of medical education, unavailability of many internationally used handbooks [133,134]. Some translations of foreign manuals are of low quality. Thanks to the free Internet resources, foreign literature is largely available in Russia these days, many guidelines being adjusted to international standards. However, some published instructions have remained without due commentaries. Most importantly, the human factor has not sufficiently changed since the Soviet time. Some colleagues encountered harassment and impediments to their careers when they did not collaborate in dubious research and practice. Trimming of statistics has been not unusual [116]. In conditions of paternalism, misinformation of patients, persuasion and compulsory treatments are deemed permissible [135]. Suboptimal practices have been used as per instructions by healthcare authorities and leading experts' publications. For example, millions of women in Russia underwent Halsted and lately of Patey mastectomy with removal of Pectoralis muscles without indications, often without informed consent [1,3]. The overuse of gastrectomy for peptic ulcers has been mentioned above. Justifications of surgical hyper-radicalism could be heard in private conversations among medics, for example: "The hopelessly ill are dangerous" i.e. may commit reckless acts undesirable by the state. For example, glioblastoma patients were routinely operated on, while it was believed by some staff that the treatment was generally useless, just forcing many patients to spend the rest of their lives in bed [136]. Finally, the obstacles to the import of drugs and medical equipment should be mentioned. Domestic products are promoted sometimes despite

questionable quality and possible counterfeiting. Today, the economical upturn enables acquisition of modern equipment; and scientific research is encouraged by the government. Considering the human factor, shortcomings of medical practice, research and education, governmental directives and increase in funding is unlikely to be a solution. Measures for improvement of the healthcare in Russia must include participation of authorized foreign advisers.

Conflict of interests

The authors have no conflict of interest to declare. The authors declared that this study has received no financial support.

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