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Evaluation of Clinical Efficacy and Safety in Treatment of Patients with Moderate and Severe Forms of Psoriasis with Combined Low Dose Methotrexate and Narrow Band UVB Therapy

Ilona Hartmane, Ingmārs Mikažāns, Iveta Ivdra, Andra Dērveniece

Ilona.Hartmane@rsu.lv
Riga 1st hospital, Dermatology and Sexually Transmitted Diseases Clinic;
Rīga Stradiņš University, Department of Infectology and Dermatology, Latvia

Abstract

Psoriasis is a chronic relapsing, genetically and immunologically associated disease. Question rises about treatment methods of psoriasis in cases when systemic therapy methods are applied, particularly, in moderate and severe cases of the disease. In routine dermatological praxis in Latvia, the novel biological medicines are not freely available for psoriasis patients; therefore, it is important to gather information and experience about such treatment methods that provide good clinical efficacy, increase safety of their administration, as, for example, application of complex methods.

The aim of the current investigation was to collect and analyse data about treatment of patients presenting with moderate and severe onset of psoriasis with a complex method, using immunosuppressing medicine methotrexate (MTX) in low doses in combination with narrow band UVB phototherapy (Nb-UVB). Retrospective analysis of patients' medical documentation in the period between 2013 and 2016 was performed on those patients' data, who had complete documentation on immunological investigation of blood tests at the onset and completing the therapy course. The studied patients were divided into two groups to be compared according to two main morphofunctional criteria. Patients of group 1 (n = 34) received methotrexate 10 mg s/c in regimen once a week for the period of four to six weeks and 311 nm UVB phototherapy with the initial dose 0.1–0.3 J/cm^2, according the skin type and protocol of administration – three times a week; increasing the dosage in every next therapy session by 0.1–0.2 J/cm^2, undergoing 10–24 procedures in the treatment course (mean 17 ± 4.2) with the total irradiation dosage 19.9 ± 3.6 J/cm^2. Patients of group 2 (n = 28) were treated using methotrexate as monotherapy 2.5 mg twice a day *per os* for five days (total dose in the treatment course 25 mg); intervals 3–4 days; 4–6 treatment courses in total.

The obtained results show that in complex therapy in 28 (82.3 %) group 1 patients and in 12 (42.8 %) group 2 patients (MTX monotherapy) significant clinical improvement has been achieved to 80 % of the study group. In six (17.7 %) group 1 patients and nine (32.1 %) group 2 patients satisfactory improvement was achieved (PASI decrease for 79–75 %). In seven (25 %) group 2 patients a less rapid improvement was obtained (PASI 74–50 %) As the result of complex therapy, decrease of PASI at the end of the second week of the treatment in patients of group 1 was for 38 %, but in group 2 (MTX monotherapy) – for 21 %.

Complex method of moderate and severe psoriasis therapy, using MTX in low dosage and 311 nm UVB phototherapy, is clinically effective and pathogenically valid. Upon application of the complex method, rapid clinical improvement and disappearance of psoriatic lesions were detected, as well as no side effects were observed. The complex method of therapy is safe and improves the quality of patients' lives.

Keywords: psoriasis, phototherapy, methotrexate UVB phototherapy.

Introduction

Psoriasis is a chronic relapsing, genetically and immunologically associated disease with extensive epidermal proliferation, presenting with incomplete differentiation of epidermocytes, alterations in blood vessels and infiltrates of inflammatory immunocompetent cells in epidermis and dermal papillary layer (Hartmane, 2004; Griffiths & Barker, 2007). Psoriasis has several variants of clinical expressions; it can affect joints. In case of psoriasis, differentiation of naive lymphocytes to T-helper type 1 (Th1) and T-helper type 17 (Th17) cells occur under the influence of interleukins (IL)-12 and 23, produced by activated dendritic cells. As a result, migration of Th1 and Th17 lymphocytes into skin is initiated, whereas Th1 lymphocytes induce synthesis of tumour necrosis factor – alfa (TNF-α) and gamma- interferon (γ-IFN), and Th17 lymphocytes – IL-17A–IL-17F, IL-1β, IL-6, IL-22, etc. In keratinocytes, synthesis of interleukins, haemokynes and antimicrobial peptides is activated as the result of elevated concentration of anti-inflammatory cytokines. Proliferation of keratinocytes and neoangiogenesis are accelerated, as well. Due to these processes, psoriatic skin lesions appear – papules, which are erythematous, infiltrated and presenting with desquamation and convergence, causing clinical appearance of skin lesions of different sizes, covered with silvery scales (Griffiths & Barker, 2007; European S3 guidelines, 2009; Hartmane et., 2016; Nacionālais veselības dienests, 2016).

A more pressing question arises about treatment methods of psoriasis in cases when systemic therapy methods are applied, particularly, in moderate and severe cases of the disease. In routine dermatological praxis in Latvia, the novel biological medicines are not freely available for psoriasis patients; therefore, it is important to gather information and experience about such treatment methods, which provide good clinical efficacy, increase safety of their administration, as, for example, application of complex methods (European S3 guidelines, 2009; Hartmane et al., 2016; Lebwohl et al., 2004). Nowadays, more topical is a wider administration of combined methods using systemic medications and phototherapy that simultaneously increase clinical efficacy and minimise duration period of UV irradiation in patients, decreasing risks of development of side effects (Mrowietz et al., 2014).

According to the literature data, morbidity of psoriasis in the world varies between 2 % and 4.9 % (Mrowietz et al., 2014; Hartmane et al., 2016). According to statistical data of Riga 1st hospital, in 2013 psoriasis was treated and clinically observed in 1368 patients, in 2014 – 1402 patients, in 2015 – 1497 patients and in 2016 – 1561 patients.

Aim

The aim of the current investigation was to collect and analyse data about treatment of patients presenting with moderate and severe onset of psoriasis with combined method, using immunosuppressing medicine methotrexate (MTX) in low doses in combination with narrow band UVB phototherapy (Nb-UVB), as well as provide recommendations according to the obtained results about practical application of this method in dermatological praxis.

Material and Methods

Retrospective analysis of patients' medical documentation in the period between 2013 and 2016 was performed on those patients' data who had complete documentation on immunological investigation of blood tests at the onset and completing the therapy course. Thereby, data on 62 patients with moderate form of psoriasis were gathered. There were 32 female and 30 male patients aged 22–64, whose duration of the disease varied between 8 and 23 years. Psoriasis area and severity index (PASI) varied from 30.2 ± 7.3.

Severity of the disease, according to PASI, was determined as follows:

1) mild to moderate form – area of psoriatic lesions < 10 % or PASI < 10 %;
2) moderate to severe form – area of psoriatic lesions > 10 % or PASI > 10 %;
3) moderately severe to severe form – area of psoriatic lesions > 10 % or PASI 10–20 %;
4) severe form – area of psoriatic lesions > 20 % or PASI > 20 % (Nacionālais veselības dienests, 2016).

Psoriatic patients included in the analysis were treated with combined method, applying narrow band UVB 311 nm phototherapy and methotrexate. In psoriasis, phototherapy has immunosuppressive influence on functions of antigen-presenting cells and production of cytokines. It induces apoptosis also in pathogenically significant cells. In phototherapy, the dosage is determined according to the phototype of patient's skin. Inception dosage is 0.1–0.3 J/cm^2 2–5 times per week, in treatment course of 25 procedures (Goktas et al., 2006; Menter et al., 2010). According to the literature data, methotrexate is one of the most effective medicines in cases of vastly spread skin and joint forms of psoriasis (European S3 guidelines, 2009; Mrowietz et al., 2014). In psoriasis, low dosages methotrexate is used as anti-inflammatory and immunomodulatory treatment. It stimulates release of adenosine in psoriatic lesion, decreases release of leukotrienes, tumour necrotic factor α (TNF- α) and other cytokines, as well as provide the switching of synthesis of cytokines from Th1 (IL-2, γ-interferons) to Th2 (IL-10). Advantage of the use of methotrexate is determined by different options of its administration: *per os*, intramuscular and subcutaneously. In case of psoriasis, this medication is used in mean dosage 15 mg per week (Asawanonda & Nateetongrungsak, 2006; Mrowietz et al., 2014). Among systemic drugs used in psoriasis therapy, by means of efficacy, only biological preparations are more effective than methotrexate. Although, there are cases when methotrexate is used both as start-up therapy before the biological medicaments, and in combination with them (Schmitt et al., 2008).

Analysed patients were divided in two groups to be compared according to two main morphofunctional criteria. Patients of group 1 (n = 34) received methotrexate 10 mg s/c in regimen once a week for 4 to 6 weeks and 311 nm UVB phototherapy with the initial dose 0.1–0.3 J/cm^2, according to skin type and protocol of administration – three times a week; increasing the dosage in every next therapy session by 0.1–0.2 J/cm^2, undergoing 10–24 procedures in the treatment course (mean 17 ± 4.2) with the total irradiation dosage 19.9 ± 3.6 J/cm^2. Patients of group 2 (n = 28) were treated, using methotrexate as monotherapy 2.5 mg two times a day *per os* for the period of five days (total dose in the treatment course 25 mg); intervals 3–4 days, 4–6 treatment courses in total. Morphologic and functional criteria, according to which the selection of psoriasis patients was performed included PASI and in laboratory tests approved alterations of complimentary to psoriasis immunologic parameters – lymphocytes CD3$^+$, CD4$^+$, CD8$^+$, CD3 HLA-DR. PASI was applied to evaluate the objective clinical improvement during therapy. Immunological parameters, in turn, allow analysing the efficacy of the administered methods of treatment on the pathogenetical events in psoriasis disease.

Due to the data being analysed retrospectively, patients were divided into groups according to the randomness principle. In both groups, the number of patients was equal according to age and gender. The relevance of normal distribution of both groups of selected patients was confirmed by non-parametrical test of Kolmogorov-Smirnov for analysis of one selection, as well as by graphical curves P-P and Q-Q of percentiles and quartiles. For the comparison of data the T test for confrontation of two independent selections was applied.

According to medical documentation, all patients had to undergo digital dermatoscopy investigation, to exclude possibility of malignant skin lesions, as well as blood tests and biochemical investigation of blood to evaluate the functions of liver and kidneys.

Results and Discussion

The efficacy of the complex therapy with MTX and 311 nm UVB phototherapy was evaluated as follows:

1) obvious improvement – PASI decrease by 80 %;
2) moderate improvement – PASI decrease by 79–75 %;
3) improvement – PASI decrease by 74–50 %;
4) no effect – PASI decrease less than 50 %;
5) worsening – remaining of negative dynamics or regression of the pathological process.

As the result of complex therapy, decrease of PASI at the end of the 2nd week of treatment in patients of group 1 was by 38 %, but in group 2 (MTX monotherapy) – by 21 %. Hereafter, less but more stable decrease of PASI was detected (see Figure 1). At the end of the therapeutic course (4–6 weeks) PASI in group 1 reached 5.3 ± 0.2 ($p < 0.01$) and in group 2 – 8.4 ± 0.7. Decrease of PASI in group 1 was determined on average by 80 %, but in group 2 – by 68 %.

The obtained results show that in complex therapy in 28 (82.3 %) group 1 patients and in 12 (42.8 %) group 2 patients (MTX monotherapy), a significant clinical improvement has been achieved by 80 %. In 6 (17.7 %) group 1 patients and 9 (32.1 %) group 2 patients, a satisfactory improvement was achieved (PASI decrease by 79–75 %). In 7 (25 %) group 2 patients, a less rapid improvement was obtained (PASI 74–50 %) (see Figure 2).

It must be admitted that in those patients who were treated with MTX, the therapeutic efficacy was lower than in those patients who received the complex therapy. In group 1 patients treated with the complex method, side effects or complications were not observed, approving the high safety of the method. In group 2, temporary side effects such as nausea, headache, elevated ALAT in plasma and moderate thrombocytopenia were documented in six patients.

Analysis of this investigation demonstrates that before the start of therapy, the immunoregulatory alterations in psoriasis patients are characterised with elevated concentration of T-helper (Th) lymphocytes in blood serum, which determine the inflammatory reaction and the decreased level of cytotoxic T lymphocytes ($CD3^+$) in the background of the decreased total number of T lymphocytes. In patients who received the complex therapy, normalisation of the immunoregulatory parameters of cell immunity were defined after the treatment course, such as lowering of the Th level and increasing of concentration of cytotoxic T lymphocytes in blood. Content of the activated CD3/HLA-DR cells after therapy showed no significant alterations and remained within the normal range (see Figure 3).

Figure 1. Data of therapeutic efficacy of complex treatment method in comparison with 311 nm UVB and MTX monotherapy

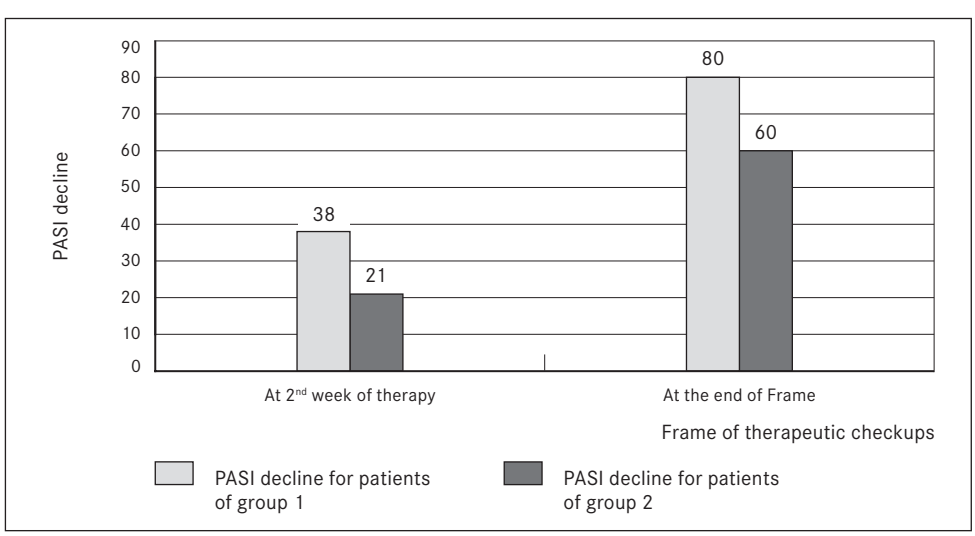


Figure 2. Changes of PASI in psoriasis patients after complex therapy (group 1) and MTX monotherapy (group 2) course

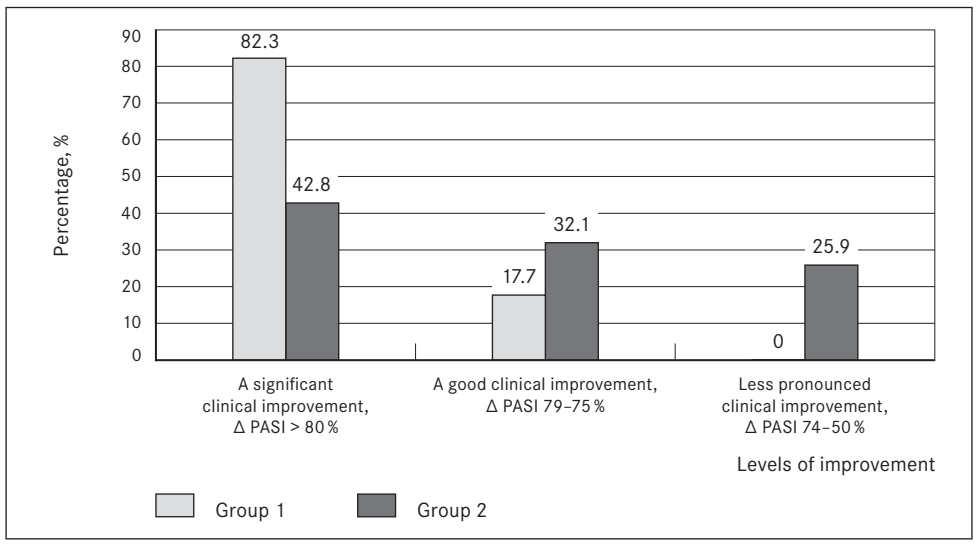
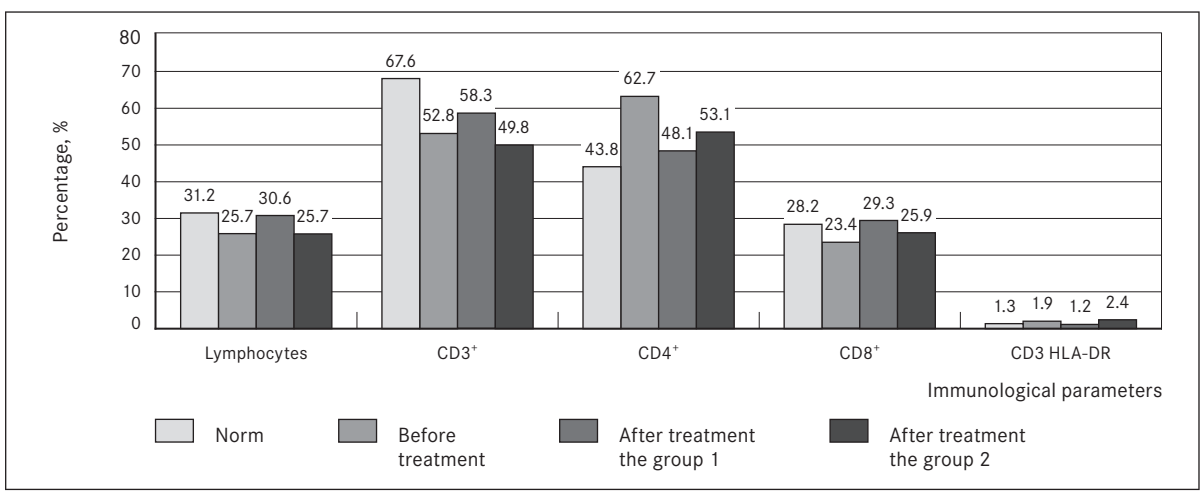


Figure 3. Immunological parameters in psoriasis patients before and after therapy



Conclusions

1. Complex method of moderate and severe psoriasis therapy, using MTX in low dosage and 311 nm UVB phototherapy, is clinically effective and pathogenically valid.
2. Applying the complex method, rapid clinical improvement and disappearance of psoriatic lesions were detected, as well as no side effects were observed.
3. Complex method of therapy is safe and improves the quality of patients' lives.

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Influence of Noise in Ambulance Vehicles on Emergency Service Personnel in North Germany and Latvia

Inka Janna Janssen, Jānis Dundurs

Inka-janssen@web.de
Rīga Stradiņš University, Department of Occupational and Environmental Medicine, Latvia

Abstract

Continuous noise exposure has an enormous damaging impact on hearing and general health status of the population. Although preventable, noise induced hearing loss (NIHL) is one of the most widespread irreversible occupational diseases worldwide, and thus is declared as a serious occupational hazard (World Health Organisation, 1997).

Several studies give evidence that noise creates physical and psychological stress, commonly presented as reduced attentiveness, sleep disturbances, cardiovascular dysfunction and mental health alteration (Jansen, 1967; OSHA, 2011).

Protection of health and from hazards at work should be in everybody's interest. Therefore, the research aims for the evaluation of the impact of occupational noise on hearing, general security of health, quality of life and productivity of those working in stressful environments, which is shown in this study at the example of emergency service working personnel.

Keywords: noise induced hearing loss, ambulance service personnel, North Germany, Latvia.

Introduction

Daily, noise has a ubiquitous potential hazardous effect on our body. The World Health Organisation (WHO) stated that worldwide 16 % of hearing loss in adults is attributed to occupational noise. NIHL is a sensorineural hearing loss, explained by permanent threshold shift of hearing sensitivity. NIHL not only affects the auditory system but also has psychosocial effects and is proved to have interference with general health by sleep disturbances or cardiovascular symptoms.

Aim

The aim of the study was to detect and define sound pressure levels that ambulance service workers are exposed to during their shifts in ambulance vehicle in North Germany and Latvia, especially with the focus on differences during signal and non-signal uses and different speed levels, and by this determine whether the noise has a hazardous character. Furthermore, the assessment of prevalence of auditory symptoms of the investigated personnel and possible correlations explaining NIHL are targeted, and finally the suggestion of protective measures to avoid further harm is proposed.

Methods

The collection of the study data is composed of two parts.

Firstly, the noise level in the ambulance vehicle was identified by measuring with the help of a Sound Level Meter (Model: Lutron SL-4013), which was placed at the level of the head of personnel in the front cabin of the ambulance vehicle. This equipment was programmed to collect data in fast mode, using the weighting curve "A". Also protective foam in the microphone, in order to minimise other noise effects, was used. The ambulance cars were analysed in terms of technical specifications, physical dimensions for proper comparison of ambulance service in Germany and Latvia. For each country, four similar cars were chosen: Mercedes-Benz, Sprinter 315, CDI model, 4-door, manual, manufacturing year 2010/2014 (Riga, Latvia) and a similar model from year 2012 (Aurich, Germany) This model is a standard Sprinter with high ceilings. The front cabin design layout is constituted likewise.

The sirens are located bilaterally on the roof and front spoiler of the ambulance car.

The type of sirens and frequency for Latvia and Germany differ especially in frequency of sound melody. Germany uses sirens of type "Martin-Horn 2298 GM" DIN 14610 EC with a 4 membrane-bell and volume of 125 dB (A) at a one-metre distance.

Differences are found in frequency of sound melody. Due to road traffic regulations in Germany "§ 55 Abs. 3 S. 1 StVZO", the following sound melody is mandatory for emergency vehicles "a'a'/d'd". There is no standardised sound melody throughout a signal trip in Latvia, instead the driver can choose manually between different frequencies.

Measurements were recorded by the medical personnel during 20 emergency trips with a duration range from 10 to 15 minutes. These measurements were performed on different days, periods and shifts. During the constant speed of 50 km/h, 70 km/h and 100 km/h, the noise level was recorded carefully under equal conditions of weather, street condition, density of surrounded houses and closed windows and no radio.

The second part includes a questionnaire constituted of 14 questions sent electronically by the use of www.visidati.lv and distribution of printed format. In total n = 207 workers responded (Germany n = 102; Latvia, n = 105). The obtained data were analysed statistically by the use of SPSS 2013. For evaluation of relations between the groups, 2×2 Table Crosstabs and Pearson's Chi-Square contingency test were used. Mann-Whitney test was used to detect frequencies among the survey population.

Results

In Germany the minimum noise level is measured at 50 km/h without signal use with 63.57 dB (A), and the maximum is measured at 100 km/h with signal use with 84.83 dB (A).

In comparison, in Latvia the minimum is measured at 50 km/h without signal use with 67.33 dB (A), and the maximum is measured at 100 km/h with signal use with 90.7 dB (A).

For both countries, it is noticeable that the noise level during signal use is enormously elevated compared to trips without signal use. Comparing Latvian with German emergency cars, non-signal trips are measured with a higher average noise level with a mean difference of 5.24 dB (A), and during signal use the noise level in Latvian emergency cars is also higher by an average difference of 2.47 dB (A). This means, Latvian emergency personnel is exposed to an overall higher noise level during emergency trips than German emergency personnel (see Table 1).

Comparing the two populations, Latvian emergency personnel is dominated by females whereas in Germany the majority is formed by men. Further, it is obvious that the Latvian emergency personnel in generally composed of a rather young team, age range of 18 to 30 years. In return, German personnel shows a wider range of age distribution, observed to be between 18 and 40 years; the vast majority of Latvian workers have been on average employed for five years, while the investigated German ambulance service personnel has been working on average over a 5-year period.

According to the amount of shifts per week and the density of emergency occurrence, both countries have four shifts of 12 hours during a seven day working week, and parallels are seen in the average amount of trips which are set at approximately six non-signal and five signal trips for both countries.

Evaluating the amount of hours the workers are exposed to noise during trips, the German ambulance service personnel is approximately 63 minutes longer exposed to noises from signal and 43 minutes longer exposed to non-signal noises during a 12-hour shift. Comparing both countries for their total emergency trip related noise exposure during a 12-hour shift, German personnel is in total exposed to noise 68 % of their work time, and Latvian personnel – 53 % in total (see Figure 1).

Looking closer at the NIHL symptoms given in the questionnaire, the respondents were allowed to choose more than one symptom, and indeed, most respondents indicated more than one symptom. Where, in comparison, Germans assigned 1–2 fitting symptoms and Latvians choose 2–3.

For both countries a common pattern of complaints and also highest incidences are found in the following two symptoms: difficulties of understanding during background noises (Germany 30.2 %, n = 42 and Latvia 26.6 %, n = 46) and *tinnitus* (Germany 38.8 %, n = 52 and Latvia 23.8 %, n = 41).

Other similarities but with lower frequency are given for hyperacusis (Germany 6 %, n = 6 and Latvia 5.8 %, n = 10), pain or pressure in the ear (Germany 13.4 %, n = 13.4 and Latvia 13.4 %, n = 23) and difficulties understanding speech, particularly women and children (Germany 7.9 %, n = 11 and Latvia 10.4 %, n = 18).

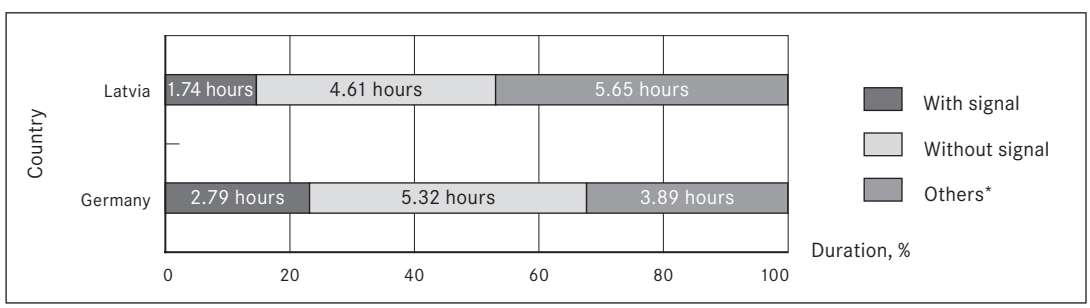
Comparing the main differences, Latvian emergency workers show a much higher incidence of symptoms such as *vertigo* (23.8 %, n = 41), changes in sound perception (7.5 %, n = 13), difficulties in determination of sound direction (5.8 %, n = 10) and difficulties using the phone due to poor understanding of the partner (13.3 %, n = 23).

German emergency personnel shows higher prevalence only for difficulties understanding electronic audio devices such as TV, radio thus need to increase the volume (20.9 %, n = 28) (see Figure 2).

Table 1. Results of noise level measured in dB (A) shown in total average and average of three different speed levels, Germany and Latvia in comparison

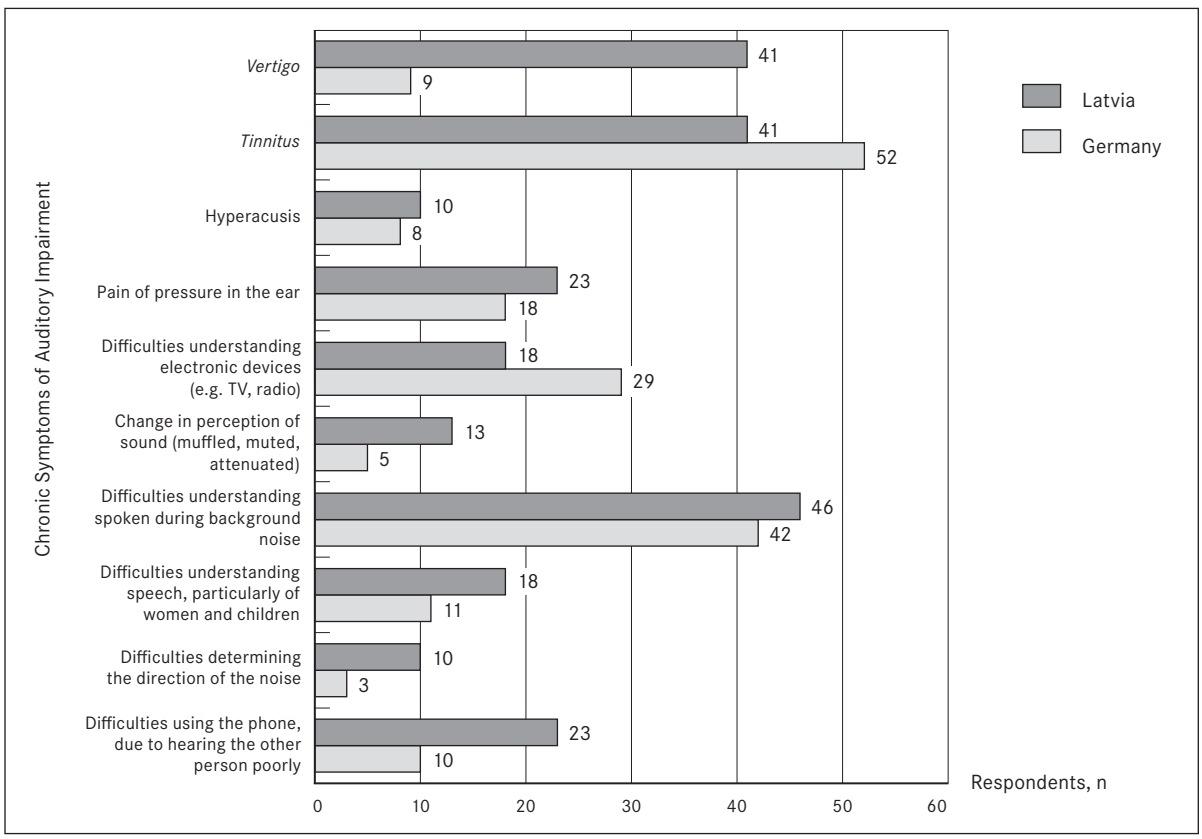
Speed levels	Germany		Latvia	
	Without signal	With signal	Without signal	With signal
Average	66.6	84.8	71.9	86.6
50 km/h	63.6	84.4	67.2	83.3
70 km/h	65.2	84.8	72.4	85.9
100 km/h	71.4	84.8	76.1	90.7

Figure 1. Time of exposure of the survey population to signal and non-signal trips during a 12-hour shift



* Others include the time during the 12-hour shift outside emergency car.

Figure 2. Prevalence of chronic auditory symptoms for each country of the survey population in absolute number, Germany and Latvia in comparison



Discussion

When persons with normal hearing are exposed to high noise levels over a prolonged period of time and by this reaching or exceeding the limit of permissible noise level exposure equivalent of 85 dB (A) over an 8-hour period, a shift of hearing threshold may appear. A threshold shift is an average deterioration of hearing 10 dB (A) or more in the frequency ranges of 2.000, 3.000 and 4.000 Hz in both ears, defined by Occupational Safety and Health Administration (OSHA, 2011).

This deterioration of hearing can be of a temporary nature, or, in opposite, at continuous exposition can result in a permanent threshold shift and hearing loss. The degree of hearing loss depends on the level of the sound pressure level, the duration of exposure, the frequency of noise and individual predispositions.

Applying this to the investigated population of the German and Latvian ambulance service, the Latvian personnel is exposed up to 5.24 dB (A) (non-signal) and 2.47 dB (A) (with signal) louder noise. Both countries demonstrate an exposure to hazardous noise level of approximately 85 dB (A) to 90 dB (A) during signal trips, which reaches and partly exceeds the exposure limits of 85 dB (A).

Sound measurements of this study show that during non-signal trips, the noise pressure level varies depending on the speed by 2–6 dB (A). The faster the speed level, the greater the noise level. During signal trips, Latvians experience and increase in noise level by 2–4 dB (A) depending on the speed level, but for Germans the noise level stays almost constant at different speed levels.

However, during a 12-hour shift, the Latvian survey population is exposed for approximately two hours to signal trips with an average noise level of approximately 87 dB (A), and the German survey population – approximately three hours to signal trips with an average noise level of 85 dB (A).

Referring to OSHA regulations, both countries are not exceeding the limit of permissible noise level exposure equivalent. Thus, the exposure to noise during emergency trips with signal are considered to be safe for the auditory system. Nonetheless, especially the Latvian emergency personnel indicates a great dominance for auditory changes, clearly shown in the study data. This indicates a failure of guidelines and imply a continuation of the study or re-evaluation of the guidelines.

Conclusion

Latvian emergency personnel clearly dominates with higher total number in eight out of ten auditory symptoms.

Statistical investigations for relations according to the study show that there is no significant relation between countries, age, gender or length of employment towards symptoms ($p > 0.05$) and thus cannot be attributed to the general population.

However, in a long-term view it is of importance to develop further preventive health measures for ambulance personnel in both countries, since the high noise levels during signal trips have harmful potential to the auditory system, health and subsequently, quality of life.

1. NIHL is one of the oldest and most common occupational induced health issues worldwide.
2. Common pattern and highest prevalence for auditory symptoms for both, Latvian and German ambulance services are:
   - difficulties of understanding during background noises;
   - *tinnitus*;
   - *vertigo*;
   - difficulties understanding electronic audio devices such as TV, radio, thus need to increase the volume.
3. Latvian ambulance service personnel has a higher risk of development of NIHL due to high frequency of sound melody of the sirens and exposure to higher sound level during signal trips, caused by poor street conditions.
4. For both countries, the noise level is remarkably elevated during signal trips compared to non-signal trips.
5. Speed level influences the noise level during trips without signal by 2–6 dB (A). The higher the speed, the higher the noise level during non-signal trips.
6. During emergency trips with signal use, the noise level reaches and partly exceeds safety limits of 80–85 dB (A).
7. Education of ambulance workers and management about preventive measures, importance of NIHL development and risk as well as regular audiometry check-ups are needed.

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Safety and Efficacy of Narcotrend Controlled Sedation with Dexmedetomidine *vs.* Propofol during Elective Colonoscopy

Evija Micķeviča, Mareks Margaliks [1], ***Biruta Mamaja*** [2, 3]

evija.mickevica@rsu.lv
Rīga Stradiņš University, Faculty of Medicine, Latvia
[1] *University of Latvia, Residenture Development Programme, Latvia*
[2] *Rīga Stradiņš University, Department of Anaesthesiology and Reanimatology, Latvia*
[3] *Riga East Clinical University Hospital "Gaiļezers", Latvia*

Abstract

The aim of the study was to evaluate safety and efficacy of sedation with dexmedetomidine *vs.* propofol during elective colonoscopy.

72 patients ASA I–III undergoing colonoscopy, included in a prospective study, were randomised into two groups of 36: dexmedetomidine (group D) (1 μg/kg/10 min, followed by 0.2–0.6 μg/kg/h) or propofol (group P) (TCI 2–6 μg/ml).

Depth of sedation was assessed by Narcotrend monitoring and sedation scales. Rescue analgesics (fentanyl i/v 0.1 mg) were used by procedure needs.

Safety was determined by hemodynamic (heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP)) and respiratory parameters, and patients discharge time from hospital. Efficacy was determined by sedation score and satisfaction of patients and endoscopists.

Demographic characteristics of patients were similar in both groups.

In group D, after 10 minutes mean HR decreased from 75.0 ± 11.9 to 60.1 ± 8.7 ×/min (−19.0 %) ($p < 0.001$), atropine was required in seven (19.4 %) patients, mean SBP – from 142.4 ± 22.9 to 121.1 ± 20.1 mm Hg (−15.0 %) ($p < 0.001$), mean DBP – from 70.6 ± 11.9 to 63.9 ± 11.6 mm Hg (−9.5 %) ($p < 0.001$), six (16.7 %) patients had hypotension treated with i/v fluid.

In group P, after 10 minutes mean HR decreased from 80.2 ± 13.6 to 68.7 ± 12.1 ×/min (−14.3 %) ($p < 0.001$), atropine was required in one (2.8 %) patient, mean SBP – from 142.2 ± 30.4 to 110.7 ± 23.7 mm Hg (−22.1 %) ($p < 0.001$), mean DBP – from 70.6 ± 12.9 to 60.1 ± 12.4 mm Hg (−14.9 %) ($p < 0.001$), three (8.3 %) patients had hypotension treated with i/v fluid.

All patients in both groups had spontaneous breathing during all procedure. In group D, six (16.7 %) patients required O supply *vs.* 25 (69.4 %) in group P. Jaw thrust was required only in 10 cases in group P.

Although there was difference between the groups' mean NI after induction (group D: 82.2 ± 10.4, group P: 71.8 ± 19.3, $p < 0.001$), patients in both groups fell asleep, but after insertion of colonoscope in group D, NI was higher (group D: 97.0 ± 1.9, group P: 69.4 ± 17.6, $p < 0.001$), to advance the procedure rescue analgesics were required to all patients in group D and only one patient in group P.

More frequently patients in group P than patients in group D were satisfied or highly satisfied with the received sedation (94.5 % *vs.* 44.4 %, p < 0.001).

Dexmedetomidine use at a loading dose of 1.0 µg/kg/10 min caused dissatisfaction in endoscopists.

Sedation with dexmedetomidine more frequently cause bradycardia required for atropine (20 % *vs.* 3 %) and longer discharge time, but sedation with propofol more frequently cause adequate spontaneous breathing depression.

Sedation with dexmedetomidine cause less satisfaction of both patients and endoscopists.

Keywords: colonoscopy, dexmedetomidine, propofol.

Introduction

Nowadays colonoscopy is the standard procedure for diagnosis, screening, treatment and follow up for many colorectal diseases. Although some patients can tolerate colonoscopy without any sedation and analgesics requirements, it is a distressful procedure for most patients (Techanivate et al., 2012). Conscious sedation is a common strategy for improving patient comfort during this procedure that is typically not well tolerated (Nishizawa et al., 2017). Patients should be kept at a level where they can respond to verbal commands and should respond purposefully when stimulated. Spontaneous ventilation is adequate, cardiovascular function is usually maintained (Amornyotin et al., 2014).

Sedation for colonoscopy using intravenous propofol has become standard in many countries (Riphaus et al., 2017) because of its rapid onset and offset of action. The most important disadvantage of propofol is the risk of rapidly induced deep sedation, with possibility to respiratory and cardiovascular depression (Eberl et al., 2016).

Dexmedetomidine is quite a new short-acting selective α2-agonist which recently has entered the medicine of Latvia with sedative, anxiolytic and analgesic properties and appears to have no clinically important adverse effects on respiration (Eberl et al., 2013). However, although dexmedetomidine seems to be an alternative option for sedation during colonoscopy procedures the sympatholysis it induces can cause hypotension and bradycardia (Riphaus et al., 2017).

Aim

The aim of the study was to evaluate safety and efficacy of sedation with dexmedetomidine *vs.* sedation with propofol during elective colonoscopy procedure.

Material and Methods

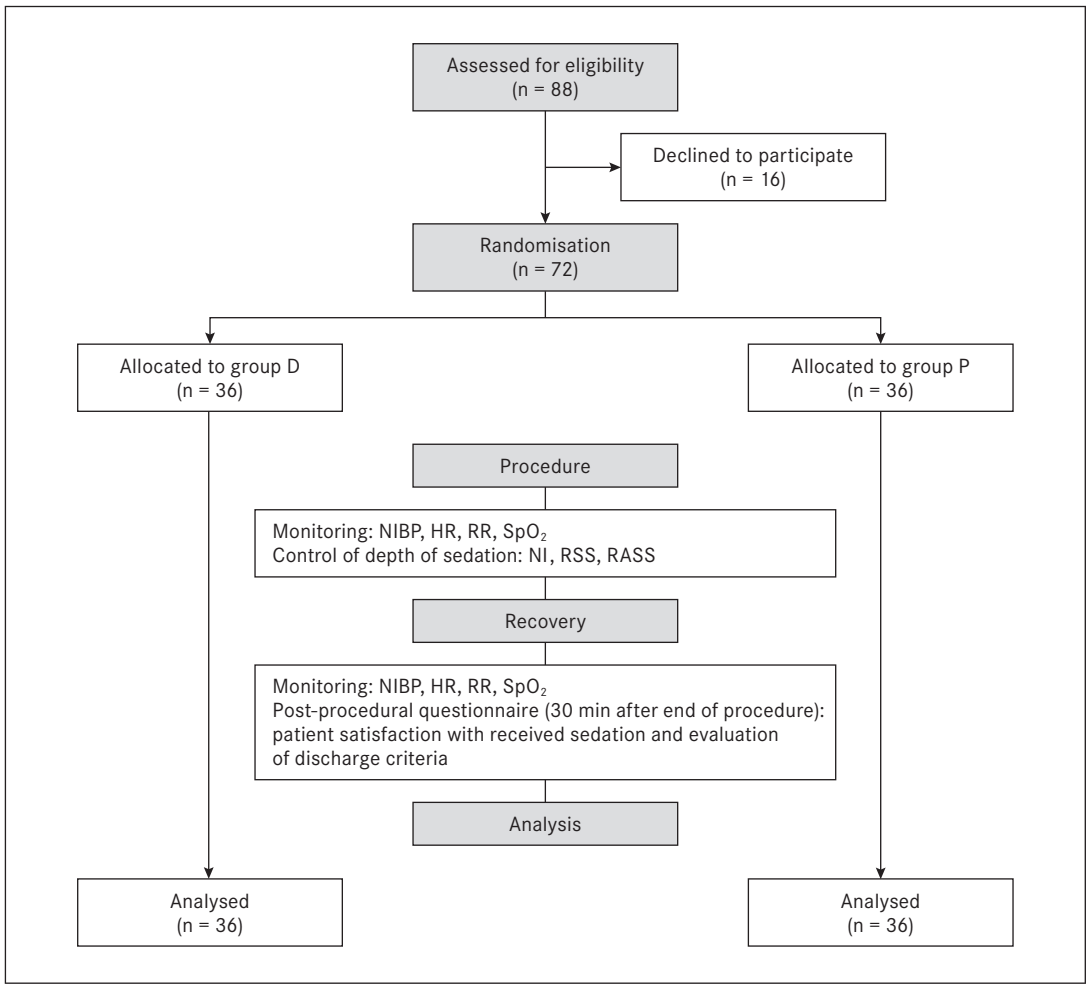
This prospective, randomised, single-blind study was conducted with a population of patients undergoing ambulatory elective colonoscopy in Riga East Clinical University Hospital "Gaiļezers", Latvia. The study was approved by the Ethical Committee of Rīga Stradiņš University (Riga, Latvia), and written, informed consent was obtained from all of the participants.

Eligible patients for participation in this clinical study were those scheduled for elective colonoscopy, aged above 18 years and American Society of Anaesthesiologists physical status (ASA) I–III, who have given the written informed consent.

The exclusion criteria were as follows: non-invasive systolic blood pressure < 90 mm Hg, heart rate < 60 beats per minute and / or related brady-dysrhythmias (advanced heart block), impaired liver function, impaired renal function, know allergic or adverse reaction to dexmedetomidine or propofol (soy bean, egg), pregnancy, psychiatric or emotional disorder, chronic use of or addiction to opiates, sedatives or antidepressants.

A total of 72 adult patients were randomly allocated into two groups of 36 to receive either dexmedetomidine or propofol sedation in a 1 : 1 ratio. The study flow chart is shown in Figure 1.

Figure 1. Study flow chart



D – dexmedetomidine; HR – heart rate; n – number of patients; NI – Narcotrend index; NIBP – non-invasive blood pressure; P – propofol; RASS – Richmond Agitation Sedation Score; RR – respiratory rate; RSS – Ramsey Sedation Score; SpO_2 – peripheral oxygen saturation.

Sedative Intervention

Patients were blinded to the sedation regimen they were supposed to get. Sedation within both groups was performed by an anaesthesiologist and anaesthesia nurse who were not blinded to the used form of sedation. Endoscopist and endoscopic nurse were also not blinded.

No premedication was provided in all cases.

In dexmedetomidine (D) group, patients received a loading dose of intravenous dexmedetomidine (Dexdor: Orion Corporation, Finland) 1 μg/kg over 10 minutes. After this loading bolus, the procedure was started and dexmedetomidine continued throughout the procedure till ileocecal valve was reached within the range of 0.2–0.6 μg/kg/h titrated to a targeted level of sedation.

In propofol (P) group, patients received sedation with propofol (Propofol 1 % MCT Fresenius, Germany) using a propofol Target Controlled Infusion (TCI) system Schnider Effect Site pharmacokinetic model, starting with a targeted effect site concentration of 2 μg/ml titrated to a targeted level of sedation continued till ileocecal valve was reached. Rescue analgesics (0.1 mg intravenous fentanyl) were given in response to pain.

All patients had continuous EEG recording in an attempt to assess depth of sedation using Narcotrend monitoring. Patients were assessed for the level of sedation before sedatives were given (baseline), after induction dose before the colonoscopy started, when colonoscopy started (insertion of colonoscope), after first 5 and 10 minutes of colonoscopy, after the end of colonoscopy (withdrawal of colonoscope) and during recovery in a procedure room. Narcotrend is an electroencephalogram (EEG) monitor designed to measure the depth of sedation. Narcotrend algorithm is based on pattern recognition of the raw EEG and classifies the EEG traces into different stages from A (awake) to F (increasing burst suppression down to electrical silence) referring to a range of Narcotrend index from 100 (awake) to 0 (electrical silence) (see Table 1) (Kreuer et al., 2004; Kreuer & Wilhelm, 2006).

Level of sedation was measured also by Ramsey Sedation Scale (RSS) (see Table 2) and Richmond Agitation Sedation Scale (RASS) (see Table 3) (Sessler, Grap & Ramsey, 2008) five minutes after insertion of colonoscope.

Table 1. Narcotrend stages and the respective Narcotrend index ranges

Clinical condition	Narcotrend stage	Narcotrend index
Awake	A	95–100
Sedated	B	80–94
Light anaesthesia	C	65–79
General anaesthesia	D	37–64
General anaesthesia with deep hypnosis	E	13–36
General anaesthesia with increasing burst suppression	F	0–12

Table 2. Ramsey Sedation Scale

Score	Definition
1	Anxious and agitated or restless or both
2	Cooperative, oriented and tranquil
3	Responds to commands only
4	Brisk response to a light glabellar tap or loud auditory stimulus
5	Sluggish response to a light glabellar tap or loud auditory stimulus
6	No response to a light glabellar tap or loud auditory stimulus

Table 3. Richmond Agitation Sedation Scale

Score	Term	Description
+4	Combative	Overtly combative or violent, immediate danger to staff
+3	Very agitated	Pulls on or removes tube(s) or catheter(s) or exhibits aggressive behaviour towards staff
+2	Agitated	Frequent non-purposeful movement or patient-ventilator dyssynchrony
+1	Restless	Anxious or apprehensive but movements non-aggressive or vigorous
0	Alert and calm	
–1	Drowsy	Not fully alert, but has sustained (> 10 seconds) awakening, with eye contact to voice
–2	Light sedation	Briefly (< 10 seconds) awakens with eye contact to voice
–3	Moderate sedation	Any movement (but no eye contact) to voice
–4	Deep sedation	No response to voice, but any movement to physical stimulation
–5	Unarousable	No response to voice or physical stimulation

Colonoscopy Procedure and Monitoring

Colonoscopies were performed by three experienced endoscopists using a video colonoscope.

The following parameters were measured continuously and recorded every five minutes: heart rate (HR), non-invasive systolic (SBP) and diastolic (DBP) blood pressure, respiratory rate (RR), peripheral oxygen saturation (SpO_2).

Total procedure time, all drugs, drug amounts and time of administration, time from the end of the procedure until discharge time, any respiratory and cardiovascular event or other complications and side effects (nausea, vomiting, dizziness) and all actions visibly taken to prevent or treat these problems, such as supply of oxygen, apply of jaw thrust, bag-mask ventilation or use of any airway device, were also recorded.

If the event of bradycardia (HR < 50 bpm) occurred, 0.5 mg of atropine was administrated. In case of hypotension (SBP < 90 mm Hg), normal saline solution was administrated intravenously. If SpO_2 decreased to 94 % or less, oxygen was delivered by facemask. If oxygen supply did not help to increase SpO_2, a jaw thrust manoeuver was applied.

Outcome Assessment

The primary outcome was safety of sedation, determined by hemodynamic and respiratory parameters, need for oxygen supply and a jaw thrust manoeuver application, need for bag-mask ventilation and / or use of any airway device and patients discharge time from hospital.

A secondary outcome was efficacy of sedation, classified by sedation score and satisfaction levels of patients and endoscopists.

In recovery room 30 minutes after the end of procedure, patients were asked to rate their satisfaction or dissatisfaction with the received sedation ranging from 1 (very dissatisfied) to 5 (highly satisfied), and discharge criteria was assessed.

Discharge criteria require that a patient is awake and alert with stable vital signs, is able to ambulate without assistance and is free of side effects of the drugs employed during the procedure.

Satisfaction of endoscopists with both sedation forms was assessed in the end of clinical study period.

Statistical Methods

Data statistical analysis was performed using Microsoft Excel 2016 and SPSS 22.0 (Statistical Package for Social Sciences). All data were checked for normal distribution using Kolmogorov-Smirnov and Shapiro-Wilk tests. For normally distributed data Student's T test, Chi-Square test was used. Non-normally distributed data were compared using Mann-Whitney test. A p value of less than 0.05 was considered significant.

Results

In total, 72 patients were included into the study; 36 patients received propofol (group P) and another 36 received dexmedetomidine (group D). All patients successfully completed colonoscopy procedure.

There was no significant difference between the groups regarding demographic characteristics, ASA and mean duration of colonoscopy (see Table 4).

Mean HR 10 minutes after the start of infusion in group D decreased from 75.0 ± 11.9 bpm to 60.1 ± 8.7 bpm (−19.9 %; $p < 0.0001$) (see Table 5).

Mean HR 10 minutes after the start of infusion in group P decreased from 80.2 ± 13.6 bpm to 68.9 ± 12.1 bpm (−14.1 %; $p < 0.0001$) (see Table 5).

In group D, mean HR almost approached bradycardia level (60 bmp) 10, 15, 20 minutes after the start of infusion, not observed in group P (Figure 2).

Mean systolic blood pressure 10 minutes after the start of infusion in group D decreased from 142.4 ± 23.0 mm Hg to 121.1 ± 20.1 mm Hg (−15.0 %; $p < 0.0001$), mean diastolic blood pressure decreased from 70.6 ± 11.9 mm Hg to 63.9 ± 11.6 mm Hg (−9.5 %; $p < 0.0001$) (see Table 6).

Table 4. Patients' characteristics and procedure data

Parameters	Group D	Group P	p value
Female, n (%)	19 (52.8)	25 (69.4)	0.648
Male, n (%)	17 (47.2)	11 (30.6)	0.618
Mean age, years	57.6 ± 16.5	63.0 ± 15.0	0.140
Mean body mass, kg	78.4 ± 13.3	78.5 ± 13.0	0.978
Mean body mass index, kg/m^2	26.3 ± 2.8	28.0 ± 4.8	0.099
ASA I, n (%)	18 (50.0)	12 (33.3)	0.324
ASA II, n (%)	15 (41.7)	18 (50.0)	
ASA III, n (%)	3 (8.30)	6 (16.7)	
Mean duration of colonoscopy, min	15.6 ± 5.2	15.6 ± 5.6	0.778

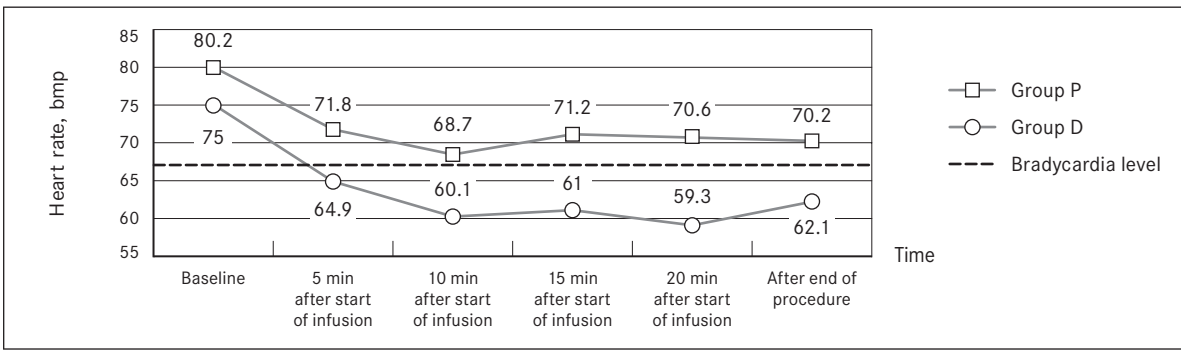
ASA – American Society of Anaesthesiologists' physical status; D – dexmedetomidine; P – propofol.

Table 5. Mean heart rate during sedation in both groups (beats per minute, SM ± SD)

Time	Group D	Group P	p value
Baseline	75.0 ± 11.9	80.2 ± 13.6	0.070
5 min after start of infusion	64.8 ± 9.7	71.8 ± 10.7	0.003
10 min after start of infusion	60.1 ± 8.7	68.7 ± 12.1	0.002
15 min after start of infusion	61.0 ± 10.3	71.2 ± 11.2	< 0.001
20 min after start of infusion	59.3 ± 7.9	70.6 ± 12.1	0.001
After the end of the procedure	62.1 ± 8.2	70.2 ± 10.4	< 0.001

D – dexmedetomidine; P – propofol; SM – statistic mean; SD – standard deviation.

Figure 2. Changes in mean heart rate during sedation in both groups



Mean systolic blood pressure 10 minutes after the start of infusion in group P decreased from 142.2 ± 30.4 mm Hg to 110.7 ± 23.7 mm Hg (−22.2 %; p < 0.0001) mean diastolic blood pressure decreased from 70.6 ± 12.9 mm Hg to 60.1 ± 12.4 mm Hg (−14.9 %; p < 0.0001) (see Table 6).

Both dexmedetomidine and propofol induced decreases in systolic and diastolic blood pressure after the start of infusion. In group P, significantly larger systolic blood pressure decrease was observed at the 5th (p = 0.002) and 10th (p = 0.022) minute and after the end of the procedure (p = 0.010), and diastolic blood pressure decreased at the 5th (p < 0.0001) minute and after the end of the procedure (p = 0.002) as compared with group D (see Table 6).

Negligible respiratory rate variations were observed in both study groups.

All patients in both groups had spontaneous breathing during the entire procedure, no patient required bag-mask ventilation or use of any airway device (see Table 7).

Table 6. Mean systolic and diastolic blood pressure (SM ± SD) during sedation in both groups (mm Hg)

Time	Group D		Group P		p value SBP	p value DBP
	SBP	DBP	SBP	DBP		
Baseline	142.4 ± 23.0	70.6 ± 11.9	142.2 ± 30.4	70.6 ± 12.9	0.972	0.992
5 min after start of infusion	129.8 ± 20.3	66.8 ± 10.8	111.4 ± 22.0	57.0 ± 13.3	0.002	< 0.001
10 min after start of infusion	121.1 ± 20.1	63.9 ± 11.6	110.7 ± 23.7	60.1 ± 12.4	0.022	0.200
15 min after start of infusion	116.3 ± 19.9	61.7 ± 11.9	109.8 ± 25.0	61.0 ± 15.5	0.067	0.838
20 min after start of infusion	113.9 ± 22.1	62.2 ± 12.6	112.0 ± 28.7	61.3 ± 14.9	0.502	0.855
After the end of the procedure	116.6 ± 18.3	65.0 ± 9.4	105.2 ± 15.9	57.3 ± 10.9	0.010	0.002

D – dexmedetomidine; DBP – diastolic blood pressure; P – propofol; SBP – systolic blood pressure; SM – statistic mean; SD – standard deviation.

Table 7. Respiratory and cardiovascular events and actions taken to treat these problems

Respiratory and cardiovascular events and actions	Number of patients, n (%)		p value
	Group D	Group P	
Need for bag-mask ventilation and / or use of any airway device	0	0	–
Need for oxygen supply	6 (16.7)	25 (69.4)	< 0.001
Need for a jaw thrust manoeuver apply	0	10 (27.8)	< 0.001
Bradycardia required for atropine	7 (19.4)	1 (2.8)	0.028
Hypotension required for fluid infusion	6 (16.7)	3 (8.3)	0.239

D – dexmedetomidine; P – propofol.

To maintain $SpO_2 \geq 94\,\%$, in group D six (16.7 %) patients and in group P 25 (69.4 %) patients required oxygen supply. A jaw thrust manoeuver had to be applied in 10 of the cases (27.8 %) in group P. This was not required in group D. Patients receiving sedation with dexmedetomidine required oxygen supply ($p < 0.0001$) and achievement of correct airway ($p < 0.0001$) less frequently than patients receiving sedation with propofol (see Table 7).

There were seven (19.4 %) patients in group D and one (2.8 %) patient in group P who developed bradycardia and were given atropine. Three patients in group D received the second dose of atropine because bradycardia repeated the second time after the first dose of atropine was given. In group D, bradycardia in range from 44 bpm to 47 bpm developed in interval between the 4th and the 17th minute of infusion. One patient receiving dexmedetomidine had the third episode of bradycardia (HR 43 bpm) three hours after the end of the procedure, atropine was given the third time, and after one hour the patient was discharged from hospital with HR 61 bpm. Patients receiving sedation with dexmedetomidine had more frequent cases of bradycardia required for atropine ($p = 0.028$) than patients receiving sedation with propofol (see Table 7).

There were six (16.7 %) patients in group D and three (8.3 %) patients in group P who developed hypotension and normal saline solution was administrated intravenously. In all patients SBP was increased to normal SBP range after fluid infusion. The incidence of hypotension were insignificantly different between the study groups ($p = 0.239$) (see Table 7).

Dizziness (two patients) and nausea (one patient) were observed after the procedure only in group D.

Most patients (77.8 %) in group D and almost all patients (94.4 %) in group P were discharged from hospital 30 minutes after the end of procedure (Figure 3). Mean time to home readiness was insignificantly longer in group D (49.5 min and 32.5 min in groups D and P, respectively ($p = 0.336$).

Discharge was delayed in group D patients because of the following factors: prolonged drowsiness (six cases), dizziness (two cases), nausea (one case) and bradycardia (one case).

Mean NI in group D after induction of sedation decreased from 98.8 ± 0.6 to 82.2 ± 10.4 (–16.7 %; $p < 0.0001$), in group P – from 98.4 ± 1.0 to 71.8 ± 19.3 (–27.0 %; $p < 0.0001$) (see Table 8). Although there was a significant difference between the groups' mean NI after induction ($p < 0.0001$), patients in both groups after induction fell asleep. Insertion of colonoscope woke up patients in group D. Mean NI was significantly higher and depth of sedation was significantly lower during all colonoscopy procedure in patients receiving sedation with dexmedetomidine. When patients in group D remain unstimulated – after withdrawal of colonoscope, they returned to sedated state (NI 87.3 ± 5.5).

Supplemental fentanyl was required in all 36 (100.0 %) patients receiving dexmedetomidine and only in one (2.8 %) patient receiving propofol to achieve a satisfactory level of sedation to proceed with the procedure ($p < 0.0001$).

When the depth of sedation between the groups was compared using the RSS (see Table 9) and RASS (see Table 10), the scores of group D, at the 5th minute after colonoscopy was started, were significantly higher than those of group P.

Although NI monitoring during all colonoscopy procedure in group D showed that patients were awake (NI 94.6–97.0), most patients were cooperative, oriented and tranquil, evaluated by RSS, or alert and calm, evaluated by RASS.

Figure 3. Discharge time from hospital after the end of the procedure

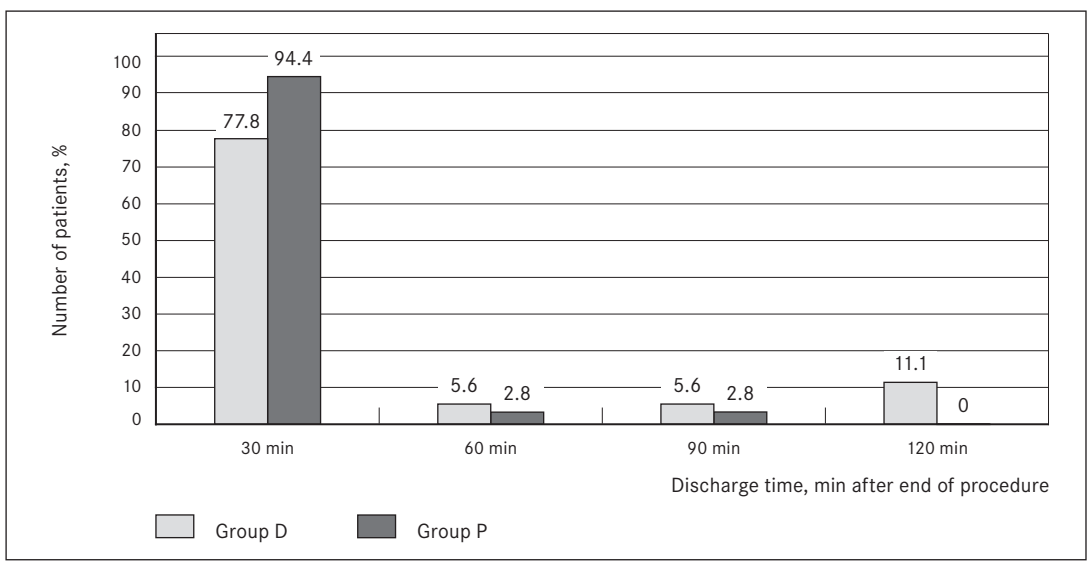


Table 8. Mean Narcotrend index (SM ± SD) during sedation in both groups

Time	Group D	Group P	p value
Baseline	98.8 ± 0.6	98.4 ± 1.0	0.169
After induction (before insertion of colonoscope)	82.2 ± 10.4	71.8 ± 19.3	< 0.001
Insertion of colonoscope	97.0 ± 1.9	69.4 ± 17.6	< 0.001
5 minutes after insertion	95.3 ± 2.9	58.8 ± 19.9	< 0.001
10 minutes after insertion	94.6 ± 3.3	65.7 ± 19.7	< 0.001
Withdrawal of colonoscope	87.3 ± 5.5	81.6 ± 14.6	< 0.001
During recovery in procedure room	96.53 ± 1.58	97.76 ± 1.06	0.001

D – dexmedetomidine; P – propofol; SM – statistic mean; SD – standard deviation.

Table 9. Measuring depth of sedation using Ramsey Sedation Score in both groups

Score	Number of patients , n (%)		p value
	Group D	Group P	
1	5 (13.9)	0	0.037
2	23 (63.9)	0	< 0.001
3	5 (13.9)	2 (5.6)	0.238
4	3 (8.3)	14 (38.9)	0.009
5	0	20 (55.6)	< 0.001
6	0	0	–

D – dexmedetomidine; P – propofol.

Table 10. Measuring depth of sedation using Richmond Agitation Sedation Scale in both groups

Score	Number of patients, n (%)		p value
	Group D	Group P	
+4	0	0	–
+3	0	0	–
+3	0	0	–
+1	5 (13.9)	0	0.037
0	22 (61.1)	0	< 0.001
−1	2 (5.6)	0	0.337
−2	5 (13.9)	3 (8.3)	0.338
−3	2 (5.6)	12 (33.3)	0.024
−4	0	21 (58.3)	< 0.001
−5	0	0	–

D – dexmedetomidine; P – propofol.

From analysis of post-procedure questionnaires, satisfaction scores of sedation and remembrance of the procedure among patients was significantly different between the groups. Only 44.4 % of all the patients in group D were satisfied or highly satisfied with the received form of sedation, and 94.5 % of all the patients in group P ($p < 0.001$). 33 (91.7 %) patients in group D and five (13.9 %) patients in group P recalled mild to moderate pain or discomfort during the colonoscopy procedure ($p < 0.001$).

Dexmedetomidine use at a loading dose of 1.0 μg/kg over 10 minutes, which resulted in a delay of the beginning of colonoscopy procedure, caused dissatisfaction of all three endoscopists, who performed all procedures.

Discussion

Sedation has always been a critical component of performing colonoscopy procedures which is an uncomfortable and stressful procedure for most patients. The aim of sedation for these procedures is to increase a patient's comfort, improve endoscopic performance and increase patient and endoscopist satisfaction (Amornyotin et al., 2014). Over the past 15 years, propofol has become the drug of choice for sedation due to its favourable pharmaceutical properties and outstanding safety profile (Lewis & Cohen, 2013); however, propofol is associated with respiratory depression and airway obstruction (Amornyotin et al., 2014). There are many publications of propofol use for sedation during colonoscopies, even the effect of sex aspects were investigated when propofol is used as sedation for gastrointestinal endoscopy (Riphaus et al., 2017). The α2-receptor agonist dexmedetomidine has sedative and anxiolytic properties. At therapeutic doses, it is not associated with respiratory depression (Arain & Ebert, 2002). Because of these properties, it has been hypothesised that dexmedetomidine might prove useful outside the operating room for sedation for colonoscopies.

In literature, the described clinical study results of dexmedetomidine use for sedation during colonoscopy are still controversial.

Dere K. et al. (2010) comparing the effects of dexmedetomidine *vs.* midazolam during colonoscopy proved that dexmedetomidine provides more efficient hemodynamic stability, higher Ramsay sedation scale scores, higher satisfaction scores and lower numerical pain rating scale scores in colonoscopies. According to their results, dexmedetomidine can be used safely as a sedoanalgesic agent in colonoscopies.

Sula H. et al. (2012) compared sedation during colonoscopy with the standard regimen of propofol *vs*. dexmedetomidine. They concluded that both regimens are suitable for safe sedation during colonoscopy procedure. The authors found that the use of propofol caused more desaturation, whereas dexmedetomidine caused more hypotension. The latter result is similar to the clinical study performed within the study described in this article. We also found that patients receiving sedation with dexmedetomidine required less frequent oxygen supply and jaw thrust manoeuver application, but the incidence of hypotension was higher compared to patients receiving sedation with propofol. The research data indicated that 50 % of cases in patients sedated with propofol Narcotrend system showed deeper sedation level than moderate sedation. This can explain why adequate spontaneous breathing depression was observed more frequently in propofol group.

Jalowiecki et al. (2005) used dexmedetomidine, meperidine with midazolam or fentanyl on demand in colonoscopy and observed 4/19 (21.1 %) cases of hypotension (mean arterial pressure 50 % of baseline) in dexmedetomidine group, four (21.1 %) cases of bradycardia required for atropine and nine cases of pain that required additional opioids. From the analysis of the obtained results, in dexmedetomidine group hypotension treated with intravenous fluid infusion was performed in six cases (16.7 %), bradycardia required for atropine was observed in 7/36 (19.4 %) patients.

Risk for developing bradycardia is also highlighted in instruction of drug manufacturer (European Commission). Due to the potential bradycardia, the dose of dexmedetomidine was not increased; thus, adequate level of sedation as observed in propofol group could not be achieved. Patients sedated with dexmedetomidine during colonoscopy procedure were awake according to Narcotrend index, cooperative, oriented and tranquil, according to Ramsey Sedation Scale, or alert and calm, according to Richmond Agitation Sedation Scale. As a result of lower depth of sedation rescue analgesics were required in all patients receiving sedation with dexmedetomidine.

Although there was no significant difference between the groups regarding the incidence of hypotension, it was observed more frequently in dexmedetomidine group.

Developing of hypotension can explained by sympatholysis induced by dexmedetomidine (Eberl et al., 2016) and patients hypovolemia that is caused by bowel preparation to procedure (Lewis & Cohen, 2013), or even the combination of both factors.

In the beginning of year 2017, first meta-analysis was published where Nishizawa T. et al. (2017) compare dexmedetomidine *vs*. propofol for gastrointestinal endoscopy. They conducted meta-analysis of data from six randomised controlled trials that compared dexmedetomidine with propofol and concluded that, in gastrointestinal endoscopy, patient satisfaction level was higher in propofol administration, when compared to dexmedetomidine, but the risk of complications was similar. In the study perfomed within our research, dexmedetomidine sedation was also less satisfactory for patients than sedation with propofol, cardiovascular complications occurred more frequently in patients sedated with dexmedetomidine, but respiratory complications more frequently in patients sedated with propofol. Sedation with dexmedetomidine was less satisfactory for patients than sedation with propofol because the depth of sedation with dexmedetomidine was lower and did not provide an appropriate degree of memory loss or decreased awareness as provided by propofol sedation. Complicated administration regimen of dexmedetomidine resulted in less satisfaction than propofol among endoscopists, as well. Administration regimen and dosage of dexmedetomidine was in line with other studies and is in line with drug manufacturer recommendations and with the recommended maximum dosage approved by the Food and Drug Administration for procedural sedation.

The cost of dexmedetomidine should be taken into account, if practitioners are planning to use it in everyday practise. A two ml ampule of dexmedetomidine is still very expensive; its cost is significantly greater than an ampule of propofol, but when the patent of drug expires, generic drug will appear with a more available price.

Conclusions

1. Comparing safety of sedation:
   - sedation with dexmedetomidine more frequently causes bradycardia required for atropine (20 % *vs*. 3 %) and longer discharge time from hospital than sedation with propofol;
   - sedation with propofol more frequently causes adequate spontaneous breathing depression required for oxygen supply and a jaw thrust manoeuver application than sedation with dexmedetomidine.
2. Comparing efficacy of sedation:
   - higher Narcotrend index and lower sedation scale scores of sedation with dexmedetomidine, and request for rescue analgesics to proceed with the procedure cause less satisfaction in patients;
   - slow induction of dexmedetomidine sedation, which resulted in delay of the onset of colonoscopy procedure, causes dissatisfaction in endoscopists.

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Assessment of Fat Mass Index and Fat-Free Mass Index in Young Athletes

Līga Kalniņa [1], ***Guntars Selga*** [2],
Melita Sauka [3], ***Viesturs Lāriņš*** [4]

liga.kalnina69@inbox.lv
[1] *Pauls Stradins Clinical University Hospital, Latvia*
[2] *Rīga Stradiņš University, Department of Oral Medicine, Latvia*
[3] *University of Latvia, Riga*
[4] *Latvian Academy of Sports Education, Department of Sports Medicine*

Abstract

Fat mass (FM) and percentile body fat (% BF) is commonly used as an assessment tool, especially to evaluate nutrition status of children. As the body mass index is linked with height, it is possible to calculate fat mass index (FMI) and fat-free mass index (FFMI). FMI or FFMI can be used to assess changes in fat-free mass linked to growth; whether there is a change due to shorter height or to a change in body composition.

The data presented were gathered as part of health check-ups by specially-trained medical team of the State Sport Medicine Centre between 2008 and 2012. The study population comprised 6,048 young athletes (4,249 boys and 1,799 girls) aged 10–17 years. During the study period, 13,788 measurements were taken (9,813 on boys and 3,975 on girls). The athletes represented 27 different sports divided into three groups according to weight control practices. Body mass and total body fat was measured using multi frequency 8-polar bioelectrical impedance analyser (X-Scan pluss II, Korea).

Mean of FFMI varies from 17.33 kg/m^2 at 10 years of age to 19.52 kg/m^2 at 17 years of age for males in group I; from 16.44 kg/m^2 to 18.51 kg/m^2 in group II; and from 16.77 kg/m^2 to 19.05 kg/m^2 in group III, accordingly. Mean of FFMI for female varies from 15.73 kg/m^2 to 17.17 kg/m^2 in group I; from 14.20 kg/m^2 to 16.07 kg/m^2 in group II; and from 15.30 kg/m^2 to 16.50 kg/m^2 in group III, accordingly.

Mean of FMI in young male athletes varies from 5.84 kg/m^2 at 10 years of age to 4.57 kg/m^2 at 17 years of age for males in group I; from 4.02 kg/m^2 to 3.69 kg/m^2 in group II; and from 4.59 kg/m^2 from to 4.07 kg/m^2 in group III, accordingly. In female young athletes' population, FMI varies from 8.69 kg/m^2 to 7.59 kg/m^2 in group I; from 6.40 kg/m^2 to 6.81 kg/m^2 in group II, and from 7.63 kg/m^2 to 7.37 kg/m^2 in group III, accordingly.

Developed assessment scales of FMI and FFMI for young athletes can be used in daily practice to evaluate height-independent fat and fat-free (lean) mass to prevent negative impact on health linked with nutritional status and physical load.

Keywords: young athletes, fat mass index, fat-free mass index.

Introduction

Every competitive athlete needs maintenance of good health with optimal weight and body composition (Rodriguez et al., 2009). Based on Joint Position Statement, various attributes of physique (body size, shape and composition) are considered to contribute to success in various sports. Of these, body mass ("weight") and body composition are often focal points for athletes since they are most able to be manipulated, and the assessment and manipulation of body composition may assist in progression of an athletic career (AND, DC, ACSM, 2016). Body weight can influence an athlete's speed, endurance, and power, but body composition can affect an athlete's strength, agility, and appearance. To improve body profile, athletes typically use a weight-loss strategy by increasing activity, reducing energy intake, or doing both. This strategy results in an undesirable change in body composition. Risks include changes in the hormonal milieu that are associated with higher risk of skeletal problems, including higher stress fracture risk, and modifications in metabolic rate. Poorly achieved weight loss nearly always reduces muscle mass and increases fat mass, making it more difficult for an athlete to achieve top performance.

Commonly FM and % BF is used as assessment tool, especially to evaluate nutrition status of children. In this case it is difficult to assess if the changes are linked with weight loss or with growth. For this reason body composition parameters have to be evaluated linked with height. Height-independent body composition parameters (FMI, FFMI) allow height-independent interpretation of nutrition status. With an inadequate caloric intake, a body catabolises the metabolic (lean) mass to lower the need for energy so survival is assured (Baumgartner et al., 1998; Kyle et al., 2003; Eissa et al., 2009; Rodriguez et al., 2009; Sundgot-Borgen et al., 2013; Meleleo et al., 2017). Evaluating FFMI regularly allows to maintain desirable body composition of young athletes without losing lean mass, therefore, prevent negative impact on health linked with nutritional status and physical load.

Aim

The aim of this study was to establish age- and sex-stratified reference values for young athletes' fat mass index and fat-free mass index in Latvia.

Material and Methods

The data presented were gathered as part of health check-ups by specially-trained medical team of the State Sport Medicine Centre between 2008 and 2012. The study population comprised 6,048 young athletes (4,249 boys and 1,799 girls) aged 10–17 years from a representative mix of urban and rural areas and sports disciplines throughout Latvia. During the study period, 13,788 measurements were taken (9,813 on boys and 3,975 on girls). The athletes represented 27 different sports divided into three groups according to weight control practices (Sundgot-Borgen et al., 2013): group I, weight-class sports in which short-term weight control practices are used; group II, aesthetic sports in which leanness is preferred; and group III, weight control is not highlighted. Respondents' mean training load was 4.18 (standard deviation (SD) 1.29) sessions per week, each session lasting approximately 1.5 hours.

Height was measured to the nearest 0.1 cm with an ultrasonic height meter (UHM-101, Korea) with children standing bare feet. Body mass and total body fat was measured using multi frequency 8-polar bioelectrical impedance leg-to-hand analyser (X-Scan pluss II, Korea). The subjects were required to adhere to standard BIA testing guidelines, as given in the manufacturer's manual and measured in light clothes.

The study was conducted in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki (6^{th} revision, 2008). The study design was approved by Rīga Stradiņš University Ethics Committee before the data collection was initiated. Participation was based on written applications filed by sport organisations and clubs. Individual athletes and their parents received information about the study before the tests, and their consent was obtained before the data collection. All data stratified by chronological age groups were computed as the mean ± 1SD. Eight chronological age groups were used for analysis, ranging from 10 years (10.0–10.9 years) to 17 years (17.0–17.9 years).

Results

Fat mass index is a height-adjusted assessment of fat mass. The percentile distributions of FMI for young athletes, categorised by gender and age, are shown in Table 1 and 2. Mean of FMI in young male athletes in the current study varies from 5.84 kg/m^2 at 10 years of age to 4.57 kg/m^2 at 17 years of age for males in group I; from 4.02 kg/m^2 to 3.69 kg/m^2 in group II; and from 4.59 kg/m^2 to 4.07 kg/m^2 in group III, accordingly. Median of FMI (50 percentile) decreasing in age groups from 10 years old to 14 years old in group I and III. Median in group II (aesthetic sports) is lower compared to group I and II. According to female young athletes' population, FMI varies from 8.69 kg/m^2 to 7.59 kg/m^2 in group I; from 6.40 kg/m^2 to 6.81 kg/m^2 in group II, and from 7.63 kg/m^2 to 7.37 kg/m^2 in group III, accordingly. Median of FMI (50 percentile) decreases mainly in the first year after being involved in sport.

Table 1. Tabulated fat mass index (kg/m^2) percentile values by exact age in young male athletes

Age (full years)	N	Mean	SD	FMI Percentiles									
				5	10	20	40	50	60	80	85	90	95
Group I – weight-class sports													
10	170	5.84	2.99	1.68	1.92	3.01	4.48	5.52	6.36	8.99	9.60	10.55	11.06
11	212	4.70	2.58	1.20	1.49	2.20	3.71	4.38	5.14	7.03	7.34	7.96	9.61
12	210	4.49	2.69	1.06	1.30	2.00	3.37	4.03	4.49	6.73	7.39	8.54	9.83
13	191	4.58	2.72	1.26	1.70	2.44	3.33	3.95	4.55	6.34	7.32	8.80	10.65
14	201	3.65	2.24	1.10	1.30	1.70	2.70	3.20	3.70	5.26	5.83	6.89	8.20
15	184	4.00	2.04	1.33	1.80	2.39	3.24	3.49	4.02	5.54	5.83	6.82	8.65
16	194	4.28	1.99	1.70	2.05	2.63	3.62	4.00	4.50	5.71	6.03	6.71	8.38
17	151	4.57	1.96	2.06	2.30	2.96	3.71	4.12	4.82	5.96	6.56	7.40	8.94
Group II – aesthetic sports													
10	31	4.02	2.56	0.56	0.92	1.76	2.94	3.97	4.18	5.93	6.31	7.57	9.74
11	33	4.14	2.49	1.48	1.74	2.06	3.03	3.42	4.01	5.85	6.27	7.15	10.04
12	44	3.11	1.73	0.68	1.05	1.64	2.30	2.76	3.01	4.33	4.37	5.77	7.16
13	40	3.24	1.89	0.70	0.93	1.60	2.80	3.15	3.45	4.29	5.00	5.55	6.85
14	33	3.36	1.84	0.90	1.00	1.57	2.77	3.55	3.90	4.52	4.81	5.66	7.14
15	32	3.18	1.34	1.47	1.68	1.86	2.48	2.88	3.56	4.40	4.80	5.25	5.81
16	19	3.32	1.71	0.60	1.00	1.60	3.10	3.30	3.60	4.34	4.43	5.61	6.01
17	18	3.69	1.24	1.90	2.02	2.48	3.28	3.56	4.09	4.90	5.17	5.71	6.12
Group III – non–weight-sensitive sports													
10	848	4.59	2.69	1.20	1.50	2.11	3.40	4.10	4.81	6.87	7.52	8.52	9.88
11	1128	4.32	2.55	1.10	1.50	2.09	3.20	3.76	4.43	6.37	7.21	8.18	9.42
12	1220	4.00	2.29	1.10	1.43	1.97	2.97	3.51	4.16	5.92	6.55	7.23	8.52
13	1461	3.63	2.05	1.10	1.40	1.93	2.78	3.19	3.63	5.07	5.59	6.40	7.95
14	1066	3.52	1.83	1.20	1.50	1.93	2.74	3.20	3.64	4.87	5.38	5.91	7.24
15	1055	3.58	1.75	1.30	1.69	2.10	2.93	3.30	3.74	4.76	5.19	5.67	6.61
16	910	3.77	1.56	1.54	1.95	2.50	3.20	3.62	4.03	4.94	5.32	5.87	6.60
17	568	4.07	1.60	1.81	2.20	2.70	3.50	3.90	4.31	5.24	5.66	6.02	6.96

Fat-free mass index is a height-adjusted assessment of fat-free mass. The percentile distributions of FFMI for young athletes, categorised by gender and age, are shown in Table 3 and 4. FFMI increases (50 percentile) in male population approximately by 1.99 kg/m^2 in group I and 1.89 kg/m^2 in group II and, by 2.83 kg/m^2 in group III. It means, that adolescent males gain more muscle mass in non-weight sensitive sports.

In young female athletes' population, FFMI (50 percentile) increases by 1.69 kg/m^2 in group I and 1.53 kg/m^2 in group II and, by 1,15 kg/m^2 in group III. There is no big difference in gaining fat-free mass between these three sport groups as it is seen in male population.

Table 2. Tabulated fat mass index (kg/m^2) percentile values by exact age in young female athletes

Age (full years)	N	Mean	SD	FMI Percentiles									
				5	10	20	40	50	60	80	85	90	95
Group I – weight-class sports													
10	31	8.60	3.69	1.56	2.88	6.92	7.79	8.62	9.29	10.46	11.86	12.72	17.39
11	36	6.52	2.93	2.27	2.87	3.48	5.36	5.97	6.98	9.09	9.80	11.44	11.85
12	39	6.42	2.82	1.90	2,60	4.00	5.80	6.29	6.59	9.17	9.76	10.34	11.93
13	33	7.42	2.50	3.41	3.66	5.35	6.54	7.20	8.23	9.37	9.93	10.13	13.08
14	35	6.89	2.42	2.72	3.78	4.71	6.25	6.89	7.67	8.64	9.05	10.60	11.38
15	45	7.72	2.15	3.73	5.66	5.99	7.29	7.69	7.97	9.33	9.77	10.67	12.06
16	53	8.03	2.08	4.43	5.58	6.13	7.57	7.90	8.60	9.60	10.49	10.82	12.08
17	28	7.59	2.60	3.31	3.98	5.58	6.70	7.00	8.31	10.10	10.53	11.13	13.04
Group II – aesthetic sports													
10	178	6.40	2.74	1.70	1.90	3.38	6.18	6.81	7.60	8.71	9.01	9.70	10.46
11	174	5.57	2.63	1.50	1.85	2.50	5.17	5.85	6.44	7.85	8.10	8.76	10.12
12	175	5.27	2.32	1.48	2.06	2.92	5.09	5.52	5.96	7.06	7.46	8.20	9.08
13	156	5.41	2.30	1.97	2.20	2.80	5.09	5.74	6.36	7.23	7.72	8.24	9.08
14	122	5.92	2.12	2.43	3.03	4.00	5.51	6.03	6.55	7.87	8.13	8.73	9.55
15	97	6.16	2.08	3.00	3.30	4.20	5.69	6.40	6.82	8.04	8.59	9.16	9.45
16	58	6.19	2.00	2.97	3.20	4.26	5.79	6.38	6.73	7.82	8.05	8.62	8.85
17	47	6.81	2.13	2.92	4.00	4.76	6.68	7.05	7.33	8.49	8.83	9.22	10.34
Group III – non-weight-sensitive sports													
10	251	7.63	3.61	2.10	2.62	4 47	6.59	7.74	8.59	10.34	10.97	12.43	13.98
11	396	6.63	2.95	2.20	2.70	4 00	5.79	6.43	7.11	9.13	9.82	10.49	11.37
12	485	6.37	2.65	2.33	2.80	4 01	5.54	6.19	6.97	8.51	9.09	9.93	10.90
13	542	6.58	2.49	2.60	3.10	4.19	6.00	6.62	7.30	8.76	9.24	9.75	10.48
14	503	7.01	2.42	3.10	3.70	4.80	6.40	7.15	7.70	9.19	9.56	10.03	10.73
15	421	7.18	2.03	3.55	4.26	5.44	6.65	7.40	7.89	8.91	9.30	9.79	10.30
16	326	7.18	2.18	3.52	4.27	5.29	6.66	7.26	7.90	9.08	9.43	9.83	10.68
17	225	7.37	1.96	3.95	4.50	5.72	7.00	7.45	7.87	8.96	9.29	9.83	10.62

Table 3. Tabulated fat-free mass index (kg/m^2) percentile values by exact age in young male athletes

Age (full years)	N	Mean	SD	FFMI Percentiles									
				5	10	20	40	50	60	80	85	90	95
Group I – weight-class sports													
10	170	17.33	1.23	15.29	15.70	16.29	17.06	17.31	17.62	18.32	18.51	18.70	19.53
11	212	17.20	1.29	15.18	15.54	16.06	16.80	17.09	17.45	18.22	18.50	18.90	19.64
12	210	17.48	1.38	15.37	15.79	16.26	17.01	17.40	17.63	18.63	18.90	19.50	19.95
13	191	18.07	1.41	15.61	16.29	16.82	17.80	18.11	18.35	19.16	19.50	19.80	20.48
14	201	18.15	1.34	16.22	16.60	17.07	17.78	18.21	18.31	19.16	19.45	19.80	20.71
15	184	18.81	1.29	16.88	17.32	17.93	18.41	18.68	18.86	19.62	19.98	20.54	21.53
16	194	19.19	1.37	17.25	17.56	18.13	18.80	19.08	19.47	20.21	20.56	20.76	21.60
17	151	19.52	1.34	17.67	18.01	18.45	19.03	19.30	19.70	20.40	20.61	21.49	22.20
Group II – aesthetic sports													
10	31	16.44	1.25	14.67	15.28	15.61	15.98	16.38	16.46	17.13	17.20	17.73	19.41
11	33	16.99	1.25	15.22	16.01	16.20	16.62	16.76	16.90	17.41	18.06	18.26	20.33
12	44	16.79	1.01	14.98	15.50	16.00	16.57	16.74	17.00	17.65	18.00	18.15	18.67
13	40	17.49	1.20	15.72	16.20	16.64	17.08	17.30	17.68	18.15	18.47	18.91	19.78
14	33	17.94	1.36	15.95	16.28	16.79	17.53	17.87	18.10	18.60	19.07	19.60	20.87
15	32	18.11	0.89	16.33	16.94	17.35	17.94	18.12	18.41	18.77	19.02	19.23	19.74
16	19	18.59	0.96	16.40	16.70	17.90	18.43	18.60	19.03	19.47	19.50	19.70	20.10
17	18	18.51	0.94	16.80	17.53	17.74	18.07	18.27	18.52	19.36	19.54	20.15	20.11
Group III – non–weight-sensitive sports													
10	848	16.77	1.11	15.15	15.45	15.80	16.41	16.66	17.00	17.65	17.90	18.17	18.72
11	1128	16.82	1.11	15.21	15.53	15.83	16.44	16.74	17.01	17.68	17.97	18.33	18.78
12	1220	17.11	1.15	15.50	15.78	16.18	16.74	17.00	17.25	18.01	18.35	18.67	19.20
13	1461	17.62	1.21	15.87	16.20	16.61	17.26	17.50	17.78	18.51	18.76	19.10	19.78
14	1066	17.97	1.20	16.14	16.50	17.01	17.60	17.86	18.19	18.91	19.16	19.50	20.00
15	1055	18.42	1.16	16.64	17.10	17.49	18.10	18.36	18.60	19.27	19.50	19.78	20.23
16	910	18.74	1.06	17.18	17.43	17.83	18.44	18.67	18.91	19.60	19.80	20.09	20.54
17	568	19.05	1.03	17.47	17.81	18.19	18.77	19.00	19.27	19.83	20.02	20.33	20.70

Table 4. Tabulated fat-free mass index (kg/m^2) percentile values by exact age in young female athletes

Age (full years)	N	Mean	SD	FFMI Percentiles									
				5	10	20	40	50	60	80	85	90	95
Group I – weight-class sports													
10	31	15.73	1.59	13.31	13.80	14.30	15.07	15.47	15.81	17.49	18.05	18.40	18.74
11	36	15.57	1.29	13.58	13.94	14.24	15.24	15.54	15.71	16.62	16.89	17.01	18.56
12	39	15.87	1.17	13.90	14.62	14.77	15.30	15.79	16.30	16.95	17.00	17.30	18.69
13	33	16.50	1.10	14.99	15.38	15.76	15.95	16.40	16.69	17.44	17.57	17.87	18.74
14	35	16.13	0.88	14.47	14.64	15.56	15.82	16.15	16.53	16.80	16.90	17.10	17.60
15	45	16.79	0.95	14.93	15.43	16.04	16.52	16.78	17.13	17.67	17.82	17.88	18.39
16	53	17.21	1.29	15.39	15.61	16.01	16.72	17.16	17.42	17.94	18.20	19.37	20.08
17	28	17.17	1.27	14.99	15.77	16.31	16.77	17.16	17.28	18.03	18.36	18.76	20.33
Group II – aesthetic sports													
10	178	14.20	0.91	12.88	13.15	13.42	13.89	14.19	14.37	14.79	15.16	15.41	15.85
11	174	14.41	0.96	12.89	13.28	13.66	14.10	14.30	14.54	15.15	15.38	15.61	16.22
12	175	14.80	1.06	13.25	13.48	13.84	14.44	14.69	15.04	15.70	15.90	16.24	16.45
13	156	15.16	1.02	13.47	13.80	14.30	14.97	15.17	15.36	16.00	16.17	16.49	16.80
14	122	15.42	0.97	13.89	14.25	14.67	15.13	15.30	15.45	16.32	16.42	16.69	17.50
15	97	15.58	0.97	14.02	14.44	14.78	15.31	15.51	15.66	16.44	16.59	16.77	17.00
16	58	15.53	0.94	14.10	14.47	14.70	15.34	15.46	15.62	16.22	16.39	16.89	17.42
17	47	16.07	1.15	14.34	14.77	15.18	15.70	15.90	16.15	17.14	17.36	17.62	18.64
Group III – non–weight-sensitive sports													
10	251	15.30	1.33	13.44	13.71	14.10	14.85	15.24	15.51	16.30	16.54	17.07	17.85
11	396	15.43	1.26	13.42	13.93	14.39	15.08	15.31	15.66	16.40	16.71	17.12	17.59
12	485	15.63	1.27	13.64	14.20	14.62	15.22	15.50	15.81	16.66	16.90	17.24	17.75
13	542	15.94	1.10	14.30	14.62	15.00	15.60	15.90	16.13	16.82	17.08	17.30	17.76
14	503	16.22	1.16	14.60	14.83	15.30	15.89	16.13	16.39	17.10	17.33	17.73	18.25
15	421	16.36	1.01	14.88	15.10	15.49	16.03	16.30	16.58	17.20	17.47	17.80	18.20
16	326	16.51	1.12	14.90	15.25	15.61	16.17	16.40	16.69	17.32	17.52	17.82	18.59
17	225	16.50	1.11	14.87	15.15	15.60	16.13	16.39	16.61	17.37	17.50	17.90	18.54

Discussion

Sports dieticians have important opportunities to work with athletes to help promote a healthy body composition, to minimise their reliance on rapid-weight loss techniques and other hazardous practices that may result in performance decrements, loss of fat-free mass, and chronic health risks (AND, DC, ACSM, 2016). This study proposes reference values for FFMI and FMI that are developed by exact age on young athletes aged between 10 and 17 years old using BIA – multi frequency 8-polar bioelectrical impedance leg-to-hand analyser. FMI and FFMI can be used to assess changes in fat mass or fat-free mass linked to growth; whether the changes are due to shorter height or to changes in body composition.

According to research (Loenneke et al., 2012), there was a tendency for the BIA to underestimate FFMI compared to DEXA: 98 % of the estimates were within plus or minus 2 kg/m^2. Therefore, while slightly biased, BIA may provide a reasonable (± 2 kg/m^2) estimate of nutritional status for practitioners who cannot afford more expensive equipment. DEXA is more precise but has issues of cost, accessibility, and its utility is affected by exposure to small radiation dose limit; therefore, BIA is a good alternative, especially when reference values are made for a specific population and device. BIA can give reliable details on body composition differences in competitive and non-competitive adolescents, outlining a progressive decline in ECW and increase in ICW without affecting TBW composition of athletes (Meleleo et al., 2017). A study using eight-mode BIA and DEXA determined no significant difference in body-fat estimation between these methods when applied to children (Yu et al., 2010).

There is little data on FMI and FFMI in athletes' population. In a study (Trexler et al., 2016) in NCAA Division I and II on Collegiate American Football Players it was found that football practitioners may use FFMI to evaluate an individual's capacity for additional FFM accretion, suitability for a specific position, potential for switching positions, and overall recruiting assessment.

According to the current study, young female athletes gain less fat-free mass and loose less fat mass during puberty compared to male athletes. According to this, special attention has to be paid to males' population to assess fat and fat-free mass avoiding unhealthy weight loss and inappropriate nutritional and physical load recommendations since many of them can be classified as overweight using BMI.

In healthy USA non-black adolescents (Eissa et al., 2009), mean of FFMI at the age of 11 and 14 years for boys were 14.2 (SD 1.6) and 16.7 (SD 1.7) kg/m^2 and for girls – 13.4 (SD 1.1) and 15.4 (SD 1.3) kg/m^2, accordingly. From this study, mean of FFMI at the age of 11 and 14 years for non-weight sensitive sports athletes were 16.82 (SD 1.1) and 17.9 (SD 1.2) kg/m^2 for boys and 15.63 (SD 1.3) and 16.22 (SD 1.2) kg/m^2 for girls, accordingly. FFMI in young athletes is higher compared to healthy adolescents from the USA. Analysing FMI mean value from the current study at the age group of 11 and 14 years, it is higher for girls (6.63 (SD 2.9) and 7.01 (SD 2.4) kg/m^2) compared to healthy adolescent girls from the USA (5.0 (SD 2.5) and 4.0 (SD 2.1) kg/m^2) and lower for boys (4.3 (SD 2.5) and 3.52 (SD 1.8) kg/m^2) compared to healthy adolescent boys from the USA (5.0 (SD 2.5) 4.0 (SD 2.1) kg/m^2). Taking into account that the research from the USA uses different BIA device (50 kHz, single frequency) from ours (5 to 500 kHz, multi-frequency), results can be slightly biased; therefore, the data do not differ significantly.

Conclusions

In Latvia we have developed fat mass index and fat-free mass index percentile scales for young athletes for assessment of height-independent body composition parameters. Using developed reference values, health care providers can set norms and maintain optimal body composition for athletes in three different sport groups to prevent a negative impact on health linked changes in the hormonal milieu that are associated with higher risk of skeletal problems, including higher stress fracture risk, and modifications in metabolic rate, avoid relative energy deficiency in sport (RED-s) and optimise physical load.

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Authors